Pharmaceutical Patents Retard Pharmaceutical Invention and Therapeutic Intervention

By

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DECLARATION

No part of this thesis has been submitted in support of an application for any degree or qualification of the University of Kent or any other University or Institute of Learning.

Adam Mannan
March 2012

This thesis is composed of five chapters. All of the chapters are presented and written in the standard format. All references are to be found at the end of the work. All hyperlinks to web based content were verified to be working on 1st July 2009, unless otherwise noted beside the entry.

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THE "SILENT HIGHWAY"-MAN.

"Your MONEY or your LIFE!"

Tenniel, J., The 'Silent Highway' - Man. 'Your money or your life'. (1858) 35 *Punch magazine* 137

PRO RATIO QVAM VIS

For my grand parents, parents and Kasia

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ABBREVIATIONS

ABPI	Association of the British Pharmaceutical Industry
CRADA	Co-operative research and development agreement
EMEA	European Medicines Agency (EU)
EU	European Union
FDA	Food and Drug Administration (USA)
GATT	General Agreement on Tariffs and Trade
GBP	Currency in UK pounds
IPO	Intellectual Property Office (UK), formerly the Patent Office (UK)
ITT	Industrial, trade and technology policies
MSF	*Médecins Sans Frontières*
MCA	Medicines Control Agency (UK)
MDA	Medical Devices Agency (UK)
MHRA	Medicines and Healthcare products Regulatory Agency (UK)
NBE	New biological entity
NCE / NCEs	New chemical entity / New chemical entities
NHS	National Health Service (UK)
NICE	National Institute for Clinical Excellence (UK)
NIH	National Institutes of Health (USA)
OTC / OTCs	Over-the-counter medicine / medicines
PhRMA	Pharmaceutical Research and Manufacturers of America (USA)
PPRS	Pharmaceutical Price Regulation Scheme (UK)
QALY	Quality adjusted life year
SEC	Securities and Exchange Commission (USA)
TRIPS	Agreement on Trade Related Aspects of Intellectual Property Rights
UK	United Kingdom
USA	United States of America
USD	Currency in USA Dollars
USDA	United States Department of Agriculture
WHO	World Health Organisation
WTO	World Trade Organisation

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1999 Health Act

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1977 Patents Act

1968 Medicines Act

1968 Trade Descriptions Act

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2001 Directive 2001/20/EC, on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (Official Journal L121, 1/5/2001: 34-44).

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1985 Directive 85/374/EEC, on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability for defective products (Official Journal L 210, 7/8/1985: 29).

1965 Directive 65/65/EEC, on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products (Official Journal L 22, 9/2/1965: 369)

CANADA

1993 Patented Medicines (Notice of Compliance) Regulations (S.O.R./93-133)

1985 Patent Act

USA

15 U.S.C. § 1 - 7	Sherman (Antitrust) Act
18 U.S.C. § 1962	Racketeering (RICO) Act
19 U.S.C. § 2411	Actions by United States Trade Representative
21 U.S.C. §201(i) & (g)	Federal Food, Drug, and Cosmetic Act – (definitions of 'cosmetic' and 'drug' respectively)
21 U.S.C. §331(z)	Federal Food, Drug and Cosmetic Act – prohibited Acts and Penalties
21 U.S.C. § 355(c)	Drugs and Devices
21 U.S.C §360aa *et sequens*	Drugs for rare diseases or conditions
35 U.S.C. § 200 - 212	Bayh-Dole (University and Small Business Patent Procedures) Act
42 USC § 2181	Inventions relating to atomic weapons

1997 Food and Drug Administration Modernization Act (Section 401)

1974 Trade Act (Section 301)

1938 Federal Food, Drug, and Cosmetic Act (Section 505)

INTERNATIONAL TREATIES AND CONVENTIONS

1994 Trade Related Aspects of Intellectual Property Rights Agreement (TRIPS)

1919 Treaty of Versailles

1883 Paris Convention for the Protection of Industrial Property

ABSTRACT

Pharmaceutical Patents Retard Pharmaceutical Invention and Therapeutic Intervention

Patents on pharmaceuticals have emerged from an industry engendered mythology as the sacred heart of pharmaceutical innovation; without patents on pharmaceuticals there will be no new medicines, no wonder drugs and no life saving medical devices.

Mansfield might be cited as the All-Father of the dependence theory of pharmaceutical innovation on pharmaceutical patents, but his survey indicates nothing more than government reliance on an industry grown dependent on government fiat for its great profitability. In fact an industry that owes its origins and sustainability to government assistance rather than any adeptness at what society perceives as the moral basis for its privileges – that is the innovation of new pharmaceuticals.

This thesis indicates that the pharmaceutical patent fails to stimulate innovation in medicines. Indeed, the empirical indication is that medicine innovation is greatly slowed and inhibited by pharmaceutical patents. These failings of the pharmaceutical patent can be seen within the institutions that distinguish pharmaceutical innovation from other species of innovation and patenting activity.

Moreover, the effect of patents on pharmaceuticals extends much further than simply slowing or denying innovative activity. Pharmaceutical patents are the basis of the extraordinary prices that patented medicines command, which can bar access to existent pharmaceuticals. Innovation and improvement of patented medicines is statistically significantly lower in patented medicines than for generic medicines. Therapies for indications that are not deemed profitable are not investigated. The above normal returns on patented medicines results in those medicines being knowingly designated for people with indications in which they are harmful. Less than one fifth of a big research and manufacturer's revenue is spent on research, development and clinical testing; that is less than half the revenue devoted to marketing.

That elements of the pharmaceutical patent system do not work have been recognised and addressed in a growing body of work. However, very few commentators have admitted that the pharmaceutical patent is the cause of the systemic failings. Thus, most suggested remedies have addressed only particular symptoms, whilst ignoring or aggravating other problems. After an examination of the problems and reform proposals, the solution to the present retardation of pharmaceutical innovation and the artificial barriers to access of pharmaceuticals is recognised as far more complex than merely tweaking the system. It is concluded, that the solution is to restore pharmaceutical knowledge as a public good utilising contemporary technological platforms to increase the proliferation and quality of

pharmaceutical knowledge and to disjoin the manufactured good from the public good, thereby subjecting the manufactured good to competition.

INTRODUCTION

"Perhaps no issue touches as many lives as the cost of medication..."[1]

This thesis is concerned with the availability and accessibility of medicines.[2] It is only concerned with pharmaceuticals[3] and not with other areas of patentable activity. We take as our standpoint that the objective of society is to better life for its members. It is a utilitarian standpoint to the same extent as the justification of the modern patent system applied to pharmaceuticals: Limited resources are available to society and combating disease is an essential value of society; thus society must allocate some of its resources to combat disease. Patents are a legal fiction[4] that, in their modern form, are posited to encourage innovation. We contend that innovation and access to medicines are retarded by the existence of patents over pharmaceuticals. In short, we argue that for the same allocation of resources that occurs in the current patent system, in a system where pharmaceuticals are excluded from patents more pharmaceutical research could be conducted, with greater safety, and a significant reduction in the dramatic difference between the price of new

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[1] Stolberg, S. G., 'A Drug Plan Sounds Great, but Who Gets to Set Prices?' *New York Times*, 9 July 2000

[2] By availability we refer to whether drugs are existent, thereby encompassing the development of new medicines (i4) and by accessibility we refer to the opportunity for as many people as possible to benefit from existent medicines (i5).

[3] Pharmaceuticals are defined in depth at i.1. Pharmaceuticals

[4] Patents for invention are, in Aristotelian terms, accidents of substances and exist only as aspects, properties, or relations of substances by virtue of legal stipulation.

pharmaceuticals and their marginal cost. Since deficiencies in the patent system for the generation of new pharmaceuticals have been evident for some time, there are other concurrent proprietary rights schemes for pharmaceutical inventions, such as data exclusivity,[5] that are also addressed by this thesis.

There is a need for this thesis because, despite rapid technological advances in research and manufacturing capability and a wealth of historical lessons concerning research, particularly pharmaceutical research, we are not achieving our potential in combating disease. Where resources are scarce society ought be looking towards systems that can aspire to an optimum return on allocated resources yet achieve dynamic efficiency in the cause of eradicating disease. That means taking account of both contemporary technologies and historical lessons. As well as preventing resources allocated to research being diverted to rent-seeking activities.

i. **Crisis**

Love and Hubbard succinctly state part of the problem that the patent system imposes as a pharmaceutical innovation incentive.

> "In 2005, prices were $400 to $480 billion higher due to patent monopolies, in return for $51 billion in private sector R&D, and

[5] Section 1.5.5.

probably one-half to two-thirds of the R&D investments were directed towards projects of almost no medical significance."[6]

With the rising costs of health care provision, the dearth of medicines for the treatment of some diseases, and the prohibitive prices of patented medicines, it is of utmost importance that we realise the limitations of the current system of patents on pharmaceuticals and initiate more innovative, safer and more accessible new medicine creation.

"Improvements in health care and life sciences are an important source of gains in health and longevity globally."[7]

However, there are currently insufficient resources available to develop all the medicines required by human beings. This shortage of resources is further exacerbated by the existent incentive systems. There are phenomenal allocations of resources that are not directed towards therapeutic advances in pharmaceuticals or improvement of pharmaceutical safety, [8] but rather to making sales,[9] keeping prices high,

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[6] Love, J., and Hubbard, T., 'The Big Idea: Prizes to Stimulate R&D for New Medicines' (2007) 82 (3) Chicago-Kent Law Review 1519-15461524

[7] U.S. Department of Commerce International Trade Administration. Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation [Washington, December 2004], vii

[8] These misallocations are discussed in Chapter 3: Misallocation and Assembly of Pharmaceutical Knowledge.

[9] Sections 3.3.7 and 3.38

paying competitors to delay market entrance[10] and of course strengthening of property rights over medicines.

Whilst patents on pharmaceuticals are the key component on which the present regime of pharmaceutical innovation and distribution is based, it is in itself only one aspect of a complex system. Thus, for our examination to be both meaningful and useful it must extend beyond the patent right and examine the incidence of the pharmaceutical patent in context. To do this we must also consider: related rights,[11] the organisation of pharmaceutical and medical research, regulatory approval for pharmaceuticals, and pharmaceutical safety as part of the complex system of effect that pharmaceutical patents have on the availability and accessibility of medicines.

Let us introduce the problems in their general form, provide a few examples, and clarify our terms.

Although pharmaceutical innovation is a global issue, this thesis has tried within the scope of resources and where it is reasonable to do so, to be based on the situation in the United Kingdom (UK). Thus, we will begin there.

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[10] Thomas, J., 'Pharmaceutical Patent Litigation Settlements: Implications for Competition and Innovation' (2010) U.S. Congressional Research Service (RL33717) Available at: <http://scholarship.law.georgetown.edu/facpub/574> (Last accessed 18th August 2011)

[11] For example, Data Exclusivity (see, 1.5.5. Post Approval Monitoring, 1.5.6. Evergreening, 1.5.7. Generic Medicines) and Orphan status.

In the UK a system for the regulation of prescription drug prices[12] has been in operation since 1956 and although it has kept down the price of prescription medicines in comparison to many other countries, it has failed to deliver cost effective drugs for the National Health Service (NHS).[13] Each year the NHS spends about £11 billion Great Britain Pounds (GBP) on medicines prescribed in primary care and in hospitals. 72 per cent (about £8 billion GBP) [14] of this expenditure is spent on patented medicines.[15]

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[12] §261 to §268 National Health Service Act 2006. Prior to 1 March 2007, §33 to §38 of the Health Act 1999 provided the statutory basis for the regulation of prescription drug prices.

[13] Office of Fair Trading. The Pharmaceutical Price Regulation Scheme. An OFT Market Study. OFT. London: 2007. Available from:
< http://www.oft.gov.uk/shared_oft/reports/comp_policy/oft885.pdf> (Last Accessed: 1st July 2009)

[14] 2008 estimates by the Department of Health place NH spending on patented medicines at £9bn per annum. See Department of Health, Consultation on a statutory scheme to control the prices of branded NHS medicines. (Launch date: 18 June 2008.) At 13 Available from <http://www.dh.gov.uk/en/Consultations/Liveconsultations/DH_085523>

[15] According to Danzon and Furukawa's estimates from IMS Health MIDAS 2005 data, patented pharmaceuticals in the UK comprise 31.3 per cent of sales volume and 63.3 per cent of medicine costs. Whilst in the USA, patented pharmaceuticals comprise 28.7 per cent of sales volume and 80.6 per cent of medicine costs. Danzon, P., and Furukawa, M., 'International Prices and Availability of Pharmaceuticals in 2005' (2008) 27(1) Health Affairs 211-233, at 227. However on the limitations of IMS Health data see, Gagnon, M-A., Lexchin, J., 'The Cost of Pushing Pills: A New Estimate of Pharmaceutical Promotion Expenditures in the United States,' (2008) 5(1) PLoS Med. Available at: <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0050001> (Last Accessed 7th April 2010).

Patented medicines are typically 20 to 90 per cent greater in price than unpatented bioequivalents (generics),[16] with the result that patients have reduced access to both drugs and other forms of healthcare until alternatives are available, even though the needed pharmaceuticals are existent. This is because a patent over the pharmaceutical invention temporarily converts pharmaceutical knowledge, which is naturally a public good, into a quasi-private good. The difference between public goods and private goods is that public goods are not diminished by one person's use,[17] whereas private goods are. This means that private goods have a cost once obtained, whilst public goods do not. Since knowledge is not depleted by another person learning it, then it is naturally a public good. However, if there is a patent on that knowledge, although the knowledge is not diminished when shared, the patent entitles the owner to charge a rent for exploitation of the knowledge. That is, the patent owner has no right over the fact of knowing the knowledge but they have a right in almost anything[18] constructed or grown that embodies that knowledge.

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[16] EGA FAQ. Available at: <http://www.egagenerics.com/FAQ-generics.htm> (Last Accessed: 1st July 2009); Also see United Nations - Millennium Development Goal 8 Task Force Report 2008, 'Delivering on the Global Partnership for Achieving the Millennium Development Goals.' At: 42. Available at: <http://www.who.int/medicines/mdg/MDG8EnglishWeb.pdf> (Last Accessed: 1st July 2009)

[17] Diminished in the sense of its worth in terms of its purpose, not in money, though changes to monetary might follow diminishment of purpose. For example an apple, partially eating it will diminish its ability to satisfy another's hunger. Or a chair: When you sit in the chair you exclude another from doing so. Knowledge however cannot be diminished by sharing.

[18] 'Almost anything' because in the UK ownership of patent rights in a human being are prohibited §4A(1)(a) Patent Act 1977. In the USA the 13th Amendment still prohibits slavery, but does it encapsulate resistance to all the facets of ownership raised by today's

Pharmaceuticals possibly comprise a more diverse category of patentable subject matter than any other type of invention since they have jurisprudentially and regulatory evolved *sui generis* from chemical patents.[19]

i.1. **Pharmaceuticals**

Pharmaceuticals are a genus of substances that affect the physical or mental functioning of a living organism, particularly chemicals used for the treatment or prevention of an ailment or disease. By reference to the scope of technologies for which patents are available and the requirements précised in the Patent Act[20] it is more or less clear what a patent might be. That is at least in essence. However, defining a pharmaceutical patent is trickier. The definiendum of pharmaceuticals and the products of pharmaceutical companies are quite broad and therefore

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technology and the extent to which patent rights are granted, consider US Patent 6211429 (which is for an animal cloning process) in conjunction with 35 U.S.C. 271(g) (which extends process claims to cover materially unaltered products of the patented process). Thus, what is the status of the child who grows from an embryo cloned using the patented process? They cannot be a slave, but can they donate blood, take part in a clinical trial, or be an organ donor, and if they win a competition do they have to endorse the owner of the patent for the process that birthed them?

[19] The requirements for a pharmaceutical patent or chemical patent application are the same, which would suggest that pharmaceutical patents are not *sui generis*, but are rather a subcategory of chemical patents. This is also a description which works as well. However, there are factors which apply to pharmaceuticals which effect the manner and cost of pharmaceutical patent infringement cases compared to chemical (not pharmaceutical) infringement cases and also to the application of competition law to cases where a pharmaceutical patent is involved. Due to these characteristics and others that will be described I prefer to consider pharmaceutical patents as emerging *sui generis* patents.

[20] Patent Act 1977 (as amended) and patent Regulations.

vague. Spilker[21] identified eighteen business areas related to ethical pharmaceuticals. These are: cosmetics; contract manufacture; pharmaceutical distribution; speciality chemicals; exercise equipment; surgical supplies; medical devices; medical supplies; health foods; generic-drugs; over-the-counter-drugs; diagnostics; pesticides; other drug products; bulk chemicals, dyes and pigments; animal products; agricultural products; bio-technology products. From this list, this thesis is only concerned with generic-drugs; over-the-counter-drugs; other drug products; and biotechnology products.

Further clarification of the definiendum of the interchangeable terms medicine, pharmaceutical and drug are provided by the five elements in Article 1 of Council Directive 65/65/EEC.

Article 1 Directive 65/65/EEC[22]

"For the purposes of this Directive, the following shall have the meanings hereby assigned to them:

1. Proprietary medicinal product: any ready-prepared medicinal product placed on the market under a special name and in a special pack.

2. Medicinal product: any substance or combination of substances presented for treating or preventing disease in human beings or animals. Any substance or combination of substances which may be administered

[21] Spilker, B., Multinational Pharmaceutical Companies: Principles and Practices [Lippincott Williams & Wilkins, 1994, Philadelphia]

[22] (Official Journal L 22, 9/2/1965: 369)

to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings or in animals is likewise considered a medicinal product.

3. Substance: Any matter irrespective of origin which may be:

— human, e.g. human blood and human blood products;

— animal, e.g. micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products, etc.; — vegetable, e.g. micro-organisms, plants, parts of plants, vegetable secretions, extracts, etc.;

— chemical, e.g. elements, naturally occurring chemical materials and chemical products obtained by chemical change or synthesis.

4. Magistral formula: any medicinal product prepared in a pharmacy in accordance with a prescription for an individual patient.

5. Officinal formula: any medicinal product which is prepared in a pharmacy in accordance with the prescriptions of a pharmacopoeia and is intended to be supplied directly to the patients served by the pharmacy in question."

For the patent itself we need to look further than the textual grace of the Patent Act, and briefly consider the synonymic conjurations of a 'patent'. Patents are assumed to encourage inventive genius.[23] Indeed the number of patents registered is often taken as being synonymous with inventiveness.[24] There is no empirical support that demonstrates that the

[23] *Obiter dicta per* Lord Salmon LJ, in Ethyl Corporations Patent [1972] RPC 169 at 193

[24] This is a stance frequently used by government statisticians for showing the vitality of national research. For example consider Sainsbury Review. The Race to the Top: A Review of Government's Science and Innovation Policies. [HMSO, October 2007]; and

patent is a statistically significant form of innovation encouragement. Just as there are no studies to demonstrate that the absence of patents is a statistically significant innovation encouragement with respect to innovation under a patent regime.[25] As this is the case it is incorrect to consider 'patents' as synonymous with invention. In some cases a patent might be regarded as an invention in the sense of the English dictionary meaning of the term, but this when it occurs is anecdotal. It is anecdotal because not all patents are inventions within the usual meaning of the English language, some are registrations of not widely know techniques, or the chemical formula of a substance existent in nature, or a different application of a well known technology.

i.2. **Difficult Inferences**

Studies that do purport to compare innovation inside and outside of a patent system fail methodologically, as they compare different time or geographical localities. At best these comparisons may provide anecdotal indications, but not methodologically valid statistical inferences. Indeed, innovation is the result of a complexity of factors and all the comparable sample populations are homogeneous - either there is a patent system in operation or there is not. In consequence this means that a direct

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Griffith, R. 'How important is business R&D for economic growth and should the government subsidise it?' (2000) Briefing Note No. 12, The Institute for Fiscal Studies. Available at: <http://www.ifs.org.uk/bns/bn12.pdf> (Last Accessed 1st July 2009)

[25] There are however, indications that pharmaceutical industries have historically developed faster where patents were more or less abolished. For example Switzerland until 1978 and India until 2004.

statistical comparison of innovation within systems with patent regimes and without patent regimes is not possible.

Whilst not as convincing as statistical inferences from large populations with very limited variables, anecdotal examinations can provide useful information. However it has to be remembered that anecdotal information applied directly to other regimes is as much vitiated by fallacy[26] as direct statistical comparison of different regimes. This is particularly aggravated in an area of study that is so difficult to quantify and which possesses as many variables and technological cross migrations as innovation. The essential difference between the direct comparison and the constructed comparison is that whilst the former employs deduction to reach a conclusion the later is a creature of inference. By studying trends, cases and data available on innovation that would be unacceptable material to use in direct comparison, we are able to formulate hypothesise that permit a comparison, but in each case it is necessary to bear in mind that the constructed comparison is a suggestive indicia not an inequality evaluation. In areas where a statistical analysis is unavailable then identifying indicia and formulating a conclusion based on an assessment of the overall weight of those indicia is the accepted methodology. Thus, because the number of patents registered is not necessarily an indication of the extent of innovation -in the normal sense of the English language- taking place. Just as the absence of patent registration is not an indication - in the same sense - that innovation was not occurring. If however, we

[26]Frequently through committing an *argumentum ad ignorantiam*

restricted our use of 'innovative' to the meaning within the Patent Act we would use the concept less frequently, but every year we would see statistically that innovation had increased.

i.3. **Empiricism**

In practise this is exemplified by the life of technology sectors. In newer areas of technology, it is a noticeable trend that innovation has little dependence on patents. However, as a technology area ages, it becomes less innovative-in the normal sense of the English language- and a greater dependence on patents to exclude competition becomes evident – the technology progresses less rapidly and yet the patent thickets thicken.[27]

Consider for example antibiotics. We know that antibiotics were employed by Ancient cultures as early as 1500 BCE, although knowledge only allowed moulds to be applied to treat infections, rather than mould metabolites such as we have used since the 1940s.[28] Moulds continued to be used to treat and prevent infections until the 1940s, when a methodology to isolate stable mould metabolites was identified and many antibiotics were characterised including penicillin and streptomycin. If we consider antibiotics as a technology sector starting in 1941, then the number of antibiotic product patents increases almost exponentially from

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[27] This can be seen in the history of computers from 1935 to the present day or the history of medicines from ancient times to the present day.

[28] Edwin Smith Papyrus, which is considered to be an incomplete copy of a much older reference manuscript from the Egyptian Old Kingdom. Translation in, Allen, J., *The Art of Medicine in Ancient Egypt* [Metropolitan Museum of Art, 2005, 1st Ed., New York] 70-72

then until now.[29] During the 1940s and 1950s there is correspondence between the number of new antibiotics isolated and the increase in patents filled. From 1967 to 1984 the number of antibiotic product patents accelerates compared to a reduction in the introduction of new antibiotics. Form 1985 to present day new antibiotic introductions have dwindled.[30] In the last two years January 2010 to January 2012 there has been only one new antibiotic agent, but 85 product patents on antibiotics.[31]

This trend could be viewed in another way: The increase in reliance on patents to retain market presence or dominance correlates to a decrease in innovative output. Thus, more patents reflect less innovation. It is necessary to note that perhaps innovative activity would diminish as the technology area aged in the absence of the patent. Therefore the role of the patent in the diminishment of innovation within a technology area may be negligible. Studies within many technology areas need to be undertaken to identify if as a general proposition increased patenting does retard innovation.

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[29] USPTO data; DrugPatentWatch. Available at: <http://drugpatentwatch.com/>

[30] For example, from 1970 to 1980 there were 55 new antibiotics, from 1980-1990 there were 29 new antibiotics, from 1990 to 2000 there were 22 and from 2000 to 2010 there were only 12. Maryn Mckenna presents a good visual summary of some of this data, see, McKenna, M., 'New antibiotics: Not many and fewer all the time' Wired Science Blog Superbug' (11th February 2011). Available at: http://www.wired.com/wiredscience/2011/02/not-many-antibiotics (Last Accessed 11th February 2011)

[31] The macrocyclic antibiotic Fidaxomicin, which gained USA market approval on the 27th May 2011. FDA News release. Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm257024.htm> (Last Accessed 13th January 2012); USPTO data

However, within the pharmaceutical technology area there are many indicia to suggest that the patent and related rights are significant factors in the retardation of pharmaceutical innovation. These indicia will be examined in this thesis.

Whether patents on pharmaceuticals do stimulate or retard innovation is quite irrelevant in the absence of a policy objective. Thus, it is necessary to emphasise that the indicia in which we are interested are considered with respect to the achievement of specific policy goals. These policy goals are increasing the availability and accessibility of medicines, through improved deployment of resources and use of technologies. It is also necessary to point out at this stage that as part of our perspective medicines ought to be safe and objectives should be addressed in a way that also promotes safety.

i.4. **Availability**

By availability we refer to whether drugs are existent, thereby encompassing the development of new medicines. Thus, this work considers the indicia of whether the pharmaceutical patent system's presence or absence is favourable to the availability of pharmaceuticals. This work is an inference from indicia and where reasonable a constructed comparison between a regime that is pharmaceutical patent free and a regime where pharmaceutical patents are available.

According to the First Optimality Theorem,[32] if an equilibrium exists at all, and if all commodities relevant to the costs or utilities are in fact priced in the market, then the equilibrium is necessarily *optimal* in the precise terms of Pareto.[33] Consumers and producers guide prices through pursuit of self-interest and thereby establish an allocation of the economy's resources such that no other allocation of resources can make all participants in the market better off. The pharmaceutical patent intervenes in the establishment of Pareto-efficiency by blocking the effectiveness of the Invisible Hand supposition in favour of the patent holder and thereby to the detriment of all other participants in the market. The detriment is visible, but tolerated because there is a presumption that this is the only way to stimulate pharmaceutical research and development.

The most obvious result of the pharmaceutical patent's intervention in the establishment of competitive preconditions for the supply of pharmaceuticals is a reduction in welfare below that which can be obtained from existing technologies and resources.[34] Clearly if future technologies are dependent on the price of current technologies, then the pharmaceutical patent may constitute a tool for attaining future

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[32] It should be noted that there is another fundamental theory of welfare economics, that is more expansive than a Pareto efficient allocation of resources. This second theorem holds that any efficient allocation of resources is sustainable through competitive equilibrium. Since both theories support our point then Pareto, the narrower theory, was chosen as if it applies so too does the more general theory.

[33] This is necessarily theoretical, because a precise statement of Pareto must be written mathematically.

[34] Efficient uptake of technologies and productive research organisation is the focus of Chapter 5.

pharmaceutical technologies. However, there is no indication that the pharmaceutical patent is the only method for obtaining the capital necessary to achieve future technologies or most importantly that it facilitates the acquisition of future pharmaceutical technologies. Thus, we have two main points of inquiry. Firstly, is there indication that the pharmaceutical patent is the most advantageous method, with respect to future welfare, of obtaining future pharmaceutical technologies? Secondly, is it necessary to find the capital for the invention of pharmaceuticals in the future in the price of present pharmaceutical technologies? Both questions go to the root of the pharmaceutical patent system's validity as a desirable facilitator of pharmaceutical invention.

We can see this clearly in the arguments purportedly used for the protection of pharmaceutical inventions through patents, which follows the syllogism.

- Pharmaceutical innovation is desirable.
- Pharmaceutical innovation can only be realised by private enterprise.
- Pharmaceutical innovation has to be funded through the sales and manufacture of pharmaceuticals.
- Without a promise of profit, investors would not speculate on the activity of pharmaceutical companies.
- Without investors pharmaceutical companies would not invest in pharmaceutical innovation.
- Pharmaceutical patents provide a promise of profit to investors.

- Dissemination of pharmaceutical knowledge is desirable.
- The patent, by the requirement of a sufficient specification[35], facilitates technology transfer.
- Trade secrets and other forms of protection either prevent the dissemination of know-how, or provide insufficient lead-time for investors to realise a return on their investment.

Thus, pharmaceutical patents results in pharmaceutical innovation.

This is the core of most statements concerning the necessity of the pharmaceutical patent for pharmaceutical innovation to occur. As exemplified by the U.S. International Trade Administration (U.S. Department of Commerce) in 2004:

> "To encourage the continued development of new drugs, economic incentives are essential. These incentives are principally provided through direct and indirect government funding, intellectual property laws, and other policies that favor innovation. Without such incentives, private corporations, which bring to market the vast majority of new drugs, would be less able to assume the risks and costs necessary to continue their research and development." [36]

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[35] §14(3) Patent Act 1977

[36] U.S. Department of Commerce International Trade Administration. Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation [December 2004], vii

Statements such as this are taken as the most important assessment of the pharmaceutical patent innovation regime. This is especially the case when dealing with the general public and where the negative impacts the pharmaceutical patent system are represented and therefore seen as localised phenomena and not a system of problems resulting from the pharmaceutical patent regime. For instance it is rarely publicised that - unfortunately the majority of

> "[pharmaceutical r]esearch spending is misdirected into products which add little therapeutic value to the medicine chest; and high prices for patented drugs are preventing access to life-saving drugs and distorting international trade."[37]

The problems or failings of the present system to provide availability and access are too rarely recognised. This results from our dependence on institutions (companies rather than the NIH), which have evolved in symbiosis with the pharmaceutical patent regime's artificial scarcity. We rely on these institutions that require monopolies to carry out pharmaceutical innovation and which conduct that research according to their own agenda. In consequence being aware of the situation, we should not expect efficient research efforts, or treatments for severe diseases that affect poor populations. What we can expect is that, if we

[37] Hollis A. An Efficient Reward System for Pharmaceutical Innovation. (2005) Online document. At 1. Available at: <http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf> (Last Accessed: 1st July 2009)

are shareholders of these institutions, the value of our investment will grow.

i.5. **Accessibility**

However, when we or those close to us are unwell and there is no cure or the remedy is beyond our purchasing power, then we question the system: Why should it be so expensive? Why are substantial funds allocated to cosmetic therapies[38] or lifestyle drugs rather than to chronic or mortal diseases? Indeed why should we pay for the future development of cosmetic pharmaceuticals, amongst other things, in the cost of chemotherapy drugs we purchase now?

By accessibility we are referring to the opportunity for as many people as possible to benefit from existent medicines. In other words, by

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[38] The usual distinction between cosmetics and drugs is the (USA) Federal Food, Drug, and Cosmetic Act §201(i). Which defines cosmetics by their intended use, as "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body...for cleansing, beautifying, promoting attractiveness, or altering the appearance."

Drugs are defined in §201(g), as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals."

UK law suggests a similar intention for the definition as the USA wording, but the wording is more precise. The Cosmetic Products (Safety) Regulations 2004, consider cosmetics to be "[a]ny substance or preparation intended to be placed in contact with any part of the external surfaces of the human body (that is to say, the epidermis, hair system, nails, lips and external genital organs), or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours except where such cleaning, perfuming, protecting, changing, keeping, or correcting is wholly for the purpose of treating or preventing disease."

accessibility we are considering the degree to which supply of a therapy approaches demand.

Consider that approximately 20 to 30 per cent of women with breast cancer have amplification and over expression of the HER2 gene.[39] In HER2-positive metastatic disease trastuzumab (Herceptin) is observed to achieve a clinical response in approximately 35% of patients as first line treatment[40] and significantly prolongs survival when used in combination with Docetaxel[41] and Paclitaxel[42].[43] Patients with HER-2 positive invasive breast cancer who receive trastuzumab treatment have a 50 per cent decrease in the risk of breast cancer recurrence compared with patients

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[39] Slamon DJ, Clark GM, Wong SG, *et al.* Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. Science 1987 Jan 9; 235 (4785): 177-82.; Ross JS, Fletcher JA. HER2/neu (c-erb-B2) gene and protein in breast cancer. Am J Clin Pathol. 1999; 112 (suppl 1):S53-S67.; Harries M, Smith I. The development and clinical use of trastuzumab (Herceptin). Endocr Relat Cancer 9: 75-85, 2002.

[40] Vogel, C. L., Cobleigh, M. A., Tripathy, D., *et al.* Efficacy and safety of trastuzumab as a single agent in first-line treatment of HER2-overexpressing metastatic breast cancer. J Clin Oncol 2002; 20:719-726.

[41] Extra J-M., Cognetti F., Maraninchi, D., *et al.* Long-term survival demonstrated with trastuzumab plus docetaxel: 24-month data from a randomised trial (M77001) in HER2-positive metastatic breast cancer. American Society for Clinical Oncology (ASCO) 2005; Abstract 555.

[42] Slamon, D. J., Leyland-Jones, B., Shak, S., *et al.* Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. (2001) 344 *NEJM* 783-792

[43] National Cancer Research Institute. 'UK Clinical Guidelines for the Use of Adjuvant Trastuzumab (Herceptin®) With or Following Chemotherapy in HER2-positive Early Breast Cancer.' (14 December 2005). Available at: <http://www.dh.gov.uk/assetRoot/04/12/63/84/04126384.pdf>

who receive the same chemotherapy without trastuzumab.[44] However, A 150mg vial of Herceptin powder costs the NHS £407.40 GBP and a private buyer considerably more. 2mg per kg of the patient's body weight are required each week for the course of the treatment.[45] In 2005 the annual cost of Herceptin treatment was around £20,000 GBP per person[46] and who should pay for provision of the drug has raised some controversy.[47] Roche, who market Herceptin internationally, reported a 48 per cent increase in Herceptin sales for 2005 with Herceptin sales generating 2.15

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[44] National Cancer Institute. 'Herceptin® Combined With Chemotherapy Improves Disease-Free Survival for Patients With Early-Stage Breast Cancer.' Available at: <http://www.cancer.gov/newscenter/pressreleases/HerceptinCombination2005> (Last Accessed: 1st July 2009); Piccart-Gebhart M, Procter M, Leyland-Jones B, et al. A Randomized Trial of Trastuzumab Following Adjuvant Chemotherapy in Women with HER2 Positive Breast Cancer. New England Journal of Medicine 353:16 2005.

[45] MIMS May 2005, 351

[46] BBC.co.uk. 'Drug refusal "a death sentence"' Available at: <http://news.bbc.co.uk/1/hi/health/4677086.stm> (Last Accessed: 1st July 2009)

[47] Trastuzumab has continued to demonstrate significant improvement in disease free and overall survival in women with surgically removed, high-risk HER-2/neu-positive breast cancer. However, Trastuzumab is expensive, it is additive, and although it produces statistically significantly improved therapeutic outcomes compared to other pharmaceuticals for treating breast cancer, those other pharmaceuticals are cheaper. Thus, in most countries, including those where pharmaceutical prices are substantially controlled (including the UK), Trastuzumab is not considered cost-effective. For a good review consider Neyt M., Albrecht J., Clarysse B., Cocquyt V. Cost-effectiveness of 'Herceptin: A standard cost model for breast-cancer treatment in a Belgian university hospital.' (2005) 21 *Int J. of Technology Assessment in Health Care*.132-137. (Belgium follows UK pharmaceutical pricing.) The significant exception is Canada where Trastuzumab is considered cost effective. Hedden L., O'Reilly S., Lohrisch C., Chia S., Speers C., Kovacic L., Taylor S., Peacock S., 'Assessing the real-world cost-effectiveness of adjuvant trastuzumab in her-2/neu positive breast cancer.' (2012) 17(2) Oncologist. 164-171. However, Canadian drug practice guidelines limit Trastuzumab to one treatment cycle. Thereafter recurring breast carcinomas can only be treated with Trastuzumab at the patient's own expense.

billion Swiss francs (£0.94 billion GBP[48]). [49] Together with oseltamivir (Tamiflu), Herceptin sales were responsible for a large portion of Roche's 2005 profits.[50] By 2009 the annual cost of Herceptin treatment had risen to around £87,000 GBP per person.[51] Its high price is morally repugnant considering the input of government funds into the breakthrough research and some phase trials.[52]

By 2006 the price of prescription drugs for the treatment of cancer increased by nearly 16% from the 2005 prices.[53] However, cancer drugs are not the only pharmaceuticals to have undergone a phenomenal price increase.[54]

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[48] 1 Switzerland Francs = 0.435518 GBP. Mid-market rates as of 26 February 2006 21:39:29 UTC

[49] Roche Annual Report 2005, Part2 : Financial Report. Page 6. http://www.roche.com/fb05e.pdf; Greil, A. 'Roche Posts Strong Sales, Operating Profit for 2005.' DOW JONES NEWSWIRES, 1February 2006. Available at: <http://www.natap.org/2006/newsUpdates/010206_03.htm> (Last Accessed: 1st July 2009)

[50] Roche Annual Report 2005, Part 2: Financial Report. Page 6. Available at: <http://www.roche.com/fb05e.pdf> (Last Accessed: 1st July 2009)

[51] MIMS May 2010, 357

[52] See, Love, J., 'NIH funded research involving trastuzumab (marketed by Roche under the trade name Herceptin)' Knowledge Ecology International 13th December 2010. Available at: <http://keionline.org/node/1031> (Last accessed 22 February 2011)

[53] Szabo, L., 'Prices soar for cancer drugs' (10 July 2006) *USA TODAY*. Available at: <http://www.usatoday.com/news/health/2006-07-10-cancer-costs_x.htm> (Last Accessed: 1st July 2009)

[54] Government Accountability Office (USA), Brand-Name Prescription Drug Pricing: Lack of Therapeutically Equivalent Drugs and Limited Competition May Contribute to Extraordinary Price Increases [Government Accountability Office, December 2009, Washington] 9. Congressional investigators found that amongst the 416 branded medicines they reviewed from 2000 to 2008, 357 increased in price between 100 to 499 per cent and 26 pharmaceuticals underwent price increases that exceeded 1,000 per

"...drug makers have typically defended high prices by... the cost of developing new medicines. But executives... are now using a separate argument - citing the inherent value of life-sustaining therapies. If society wants the benefits, they say, it must be ready to spend more for treatments..."[55]

i.6. **Incentive as Impunity**

The vast profitability of pharmaceuticals creates considerable expectation amongst shareholders, whom are the principal concern for all companies. As a result of the specialist knowledge, research and clinical trailing required to arrive at a pharmaceutical product, coupled with the way the present investigative and regulatory system interlinks with these process there is a large degree of trust in the data that is provided by parties with a

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cent. Note: the report is focused on Branded rather than patented medicines and some of the medicines considered were out of patent. However all of the pharmaceuticals exceeding 1,000 increases achieved those increases whilst under patent. In particular the nine drugs that achieved 2,000 per cent price increases between 2000 and 2008 were under patent.

"...price increases for common brand name and specialty prescription drugs continued to increase substantially despite a negative rate of general inflation for all consumer goods and services. In contrast, prices for common generic drugs have declined, albeit at a slower rate than in the previous year." at page 5 in, AARP Public Policy Institute, Rx Watchdog Report: Drug Prices Continue to Climb Despite Lack of Growth in General Inflation Rate (2009). E-Publication. Available at: <http://assets.aarp.org/rgcenter/ppi/health-care/i36-watchdog.pdf> (Last Accessed: 15 January 2010)

[55] Berenson, A., 'A Cancer Drug Shows Promise, at a Price That Many Can't Pay' (15 February 2006) *New York Times*. Available at: <http://www.nytimes.com/2006/02/15/business/15drug.html> (Last Accessed: 1st July 2009)

great bias in the outcome. In consequence, this engenders vast risks, questionable decisions and secrecy with deplorable consequences. The vast risk, however, is most poignant for the person taking the medicine and economically perhaps the insurer.[56]

For example, for years Merck insisted that the cardiovascular risks posed by its arthritis drug,[57] Vioxx, were small. Vioxx was a blockbuster drug with annual sales of $2.5 billion USD. All of this was despite the fact that Merck's researchers had reported, in internal company e-mails and documents, that Vioxx increased the risk of cardiac events.[58] It was not until August 2004, when Food and Drug Administration (FDA) and other researchers[59] reported the increased cardiovascular risk posed by Vioxx

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[56] Art 7(e) European Council Directive (EEC) 85/374 imposes strict liability for defective products, through the enabling act §4(1)(e) of the Consumer Protection Act 1987; see *European Commission v United Kingdom* (Case C-300/95). The 'defence of the state of scientific and technical knowledge at the time when the product in question' is retained as an objective defence. In contrast liability in the USA for pharmaceuticals is absolute on the part of the producer. However, considering the burdens this has placed on the insurance sector there has been a swing towards the European standard of strict liability and the former USA position. See Priest, G. L. 'The Current Insurance Crisis and Modern Tort Law' (1987) 96 Yale Law Journal 1521 at 1589; *Olson v. Artic Enter.*, 349 F. Supp. 761, 765 (D.N.D. 1972).

[57] *Drug, medicine* and *pharmaceutical* are used synonymously. Drug does not refer to illegal narcotic substances taken otherwise than medicinally.

[58] Mathews, A. W.; Martinez, B., "Warning Signs: E-Mails Suggest Merck Knew Vioxx's Dangers at Early Stage; As Heart-Risk Evidence Rose, Officials Played Hardball; Internal Message: 'Dodge!'; Company Says 'Out of Context'" Wall Street Journal (Eastern edition), November 1, 2004: A1

Martinez, B. 'Merck's Woes Grow As Credit Rating Is Put on Watch' The Wall Street Journal. November 2, 2004: A3

[59] Memorandum from David J. Graham, MD, MPH, Associate Director for Science, Office of Drug Safety to Paul Seligman, MD, MPH, Acting Director, Office of Drug Safety

and suggested that Vioxx could be responsible for as many as 27,000 heart attacks, that Merck withdrew its drug.[60] Unfortunately, this is not an isolated occurrence.[61] It would be in the interest of society, i.e. natural persons, if all data on a medicine being administered or about to be administered to people were made available to the public. Unfortunately, such a requirement might allow competitors to develop competitive treatments based on the same chemical or substantially improve the chemical's performance, and might also reduce the size of a market by preventing companies from selling drugs to people who do not need them.[62]

Surprisingly drugs are too frequently sold to people who do not need them.[63] The FDA approved Neurontin for the treatment of epilepsy.

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entitled, "Risk of Acute Myocardial Infarction and Sudden Cardiac Death in Patients Treated with COX-2 Selective and Non-Selective NSAIDs," September 30, 2004

[60] Cafferty, P., Families USA, Big PhRMA Behaving Badly: A Survey of Selected Class Action Lawsuits Against Drug Companies [Families USA, January 2005, Washington] 2

[61] For example, when Eli Lilly's internal Zyprexa documentation was ordered disclosed following many thousand of time bared legal actions and a class action, the documents show that Lilly had promoted a drug against the advice of their experts, whom warned about its toxic effects, in particular Zyprexa's propensity to induce acute weight gain triggering metabolic syndrome and diabetes. See *UFCW Local 1776 and Participating Employers Health and Welfare Fund v. Eli Lilly and Co.,* No. 05-CV-4115, (U.S. District Court, Eastern District of New York, Brooklyn. 25 August 2005); The grounds of the suit were Racketeer Influenced and Corrupt Organizations (Federal District Court Fillings and Dockets. Available at: <http://dockets.justia.com/docket/court-nyedce/case_no-1:2005cv04115/case_id-247732/> (Last Accessed: 1st July 2009)

[62] In 2005 Pfizer withdrew Bextra and agreed to pay $2.3 billion USD for the fraudulent marketing of Bextra and three other drugs. See, Harris, G., 'Pfizer Pays $2.3 Billion to Settle Marketing Case' (3rd September 2009) *New York Times* B4

[63] For an interesting example of drugs that have been marketed for people to whom they convey no therapeutic benefit consider, Pfizer's medicine Lyrica designated as a

However, Parke-Davis[64] may have considered the epilepsy market too small for Neurontin to generate desired profits. Thus, Parke-Davis surreptitiously promoted Neurontin for many other conditions including Lou Gehrig's disease, bipolar disorder, seizures, attention deficit disorder, drug and alcohol withdrawal seizures, migraine headaches and restless leg syndrome.[65] Minor considerations, such as the placebo being more effective than Neurontin, could be ignored where off-label uses increased Neurontin sales by 90 per cent to over $1 billion USD per annum.[66] Where use of a medicine for a specific condition is not approved by the FDA it is contrary to USA law to misbrand a drug,[67] *id est* include information about a drug's unapproved uses,[68] which would include advertising off-label uses to consumers. Physicians, however, are able to prescribe a drug for

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treatment for Fibromyalgia, a pain condition that is unresponsive to traditional analgesia medicines, such as asparin. Fibromyalgia is a disease whose existence is questionable. See Berenson, A., 'Drug Approved. Is Disease Real?' (14 January 2008) *New York Times*. Available at: <http://www.nytimes.com/2008/01/14/health/14pain.html?> (Last Accessed: 1st July 2009)

[64] Which was acquired by Pfizer in the purchase of Warner-Lambert in 2000. See, Pfizer History. Available at: <http://www.pfizer.com/about/history/pfizer_warner_lambert.jsp> (Last Accessed Accessed: 1st July 2009)

[65] Farrell, G., 'Pfizer settles fraud case for $430 million' (13 May 2004, updated 14 May 2004) USA Today. Available at: <http://www.usatoday.com/money/industries/health/drugs/2004-05-13-pfizer_x.htm> (Last Accessed: 1st July 2009)

[66] Pfizer's reported revenue for 2001 on Neurontin sales was $1.75 billion USD. Which placed it as Pfizer's 4th best selling drug. In 2002 Pfizer's reported revenue for Neurontin sales was $2.27 billion. Reports available at: <www.pfizer.com/files/annualreport/2001/financial/financial2001.pdf> and <www.pfizer.com/files/annualreport/2002/financial/financial2002.pdf>

[67] § 331(a); § 352(a); see Kordel v. United States , 335 U.S. 345, 348-50 (1948)

[68] 21 U.S.C. §§ 331(z) Prohibited acts; 360aaa Requirements for dissemination of treatment information on drugs or devices; *et sequentia*.

off-label uses.[69] Aware of this, Parke-Davis concealed and misstated clinical information concerning the ability of Neurontin to treat off-label conditions. Furthermore, it sponsored ghost written medical articles, and paid millions of USD to physicians to promote Neurontin.[70]

> "Warner-Lambert's promotional efforts were a highly organized and deliberate attempt to circumvent federal restrictions on marketing,"[71]

In January 2011, Pfizer was ordered to pay damages of $142.1 million USD for the illegal promotion of Neurontin for unapproved uses.[72] Surprisingly taking account of Pfizer's payouts for improperly marketing off-label uses from August 2008 to February 2011, including the $2.3 billion USD settlement in 2009,[73] these fines are less than 0.3 per cent of

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[69] Physicians may prescribe legal drugs for any purpose that they consider appropriate, regardless of whether the drug has been approved for that purpose by the FDA. See Citizen Petition Regarding the Food and Drug Administration's Policy on Promotion of Unapproved Drugs and Devices, Request for Comments, 59 Fed. Reg. 59,820, 59,821 (1994).

[70] Cafferty, P., Families USA, Big PhRMA Behaving Badly: A Survey of Selected Class Action Lawsuits Against Drug Companies [Families USA, January 2005, Washington] 1

[71] Associate Attorney General McCallum, reported in: Anonymous 'Pfizer to Plead Guilty to Illegal Marketing' (14 May 2004) *Los Angeles Times* C-3

[72] Feeley, J., Lawrence, J., 'Pfizer to Pay $142.1 Million Over Neurontin Marketing' (28th January 2011) *Bloomberg*. Available at: <http://www.bloomberg.com/news/2011-01-28/pfizer-ordered-to-pay-142-1-million-in-damages-over-neurontin-marketing.html> (Last Accessed 12th March 2011)

[73] Pfizer's $2.3 billion USD settlement of criminal and civil damages for illegally marketing Bextra amounted to less than three weeks of Pfizer's sales. See, Harris, G., 'Pfizer Pays $2.3 Billion to Settle Marketing Case' (3rd September 2009) New York Times B4

the revenue those products generated.[74] With an estimated net profit margin of between 16.82 and 14.84 per cent[75] in amoral terms it is easy to see the incentive for expanding markets beyond those who can benefit from medicines.[76]

i.7. **Property as Incentive**

Illicit practices are frequent in the pharmaceutical industry and, where substantial profits are involved, a fine or compensation can be little deterrent.[77] Perhaps further expansion of criminal sanctions to corporate law imposing culpability on the directors, chairman and chief executive officers of companies for the *manslaughter* and disability engendered by their company's behaviour might be appropriate.[78] Fines against the large

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[74] Some of these fines derive from the companies acquired by Pfizer after the illegal marketing practices began.

[75] EBIT Financial Analyses Center, Pfizer Profitability Analysis from December 2007 to December 2011.

[76] For more examples see, Evans, D., 'Pfizer Broke the Law by Promoting Drugs for Unapproved Uses' (9th November 2009) Bloomberg. Available at: <http://www.bloomberg.com/apps/news?pid=newsarchive&sid=a4yV1nYxCGoA> (Last accessed 22nd November 2009)

[77] It is difficult to find an example of where a pharmaceutical company is fined and where the fine is greater than the profits that the illegality engendered. 90 per cent of profits seems to be the largest penalty relative to profit publicly reported. The fines amounted to $634.5 million USD. Reported in: Meier, B., 'Big Part of OxyContin Profit Was Consumed by Penalties' (19 June 2007) *New York Times*. Available at: <http://www.nytimes.com/2007/06/19/business/19drug.html> (Last Accessed: 1st July 2009); Also reported at: Lohr, K., and Siegel, R., '$634 Million Fine, No Jail For OxyContin Executives' (10 Spetember 2008) NPR. Available at: <http://www.npr.org/templates/story/story.php?storyId=12131233> (Last Accessed: 1st July 2009)

[78] Corporate manslaughter as a doctrine has grown significantly in importance over the last three decades, and has been formalised into some legal systems through legislation.

pharmaceutical companies probably do not make economic sense; as such actions are demanding on government (or state and federal budgets) and add to the cost of health care as the pharmaceutical company recoups its costs through other product monopolies, some of which will be financed by government and insurance companies. In consequence it could be inferred that it is the consumer who loses out three-fold, that is from the cost of the government/consumer action, the harm of the illegal practice and the fine.

If society has a normative morality, which the existence of legislation aimed at safety suggests, then the pharmaceutical patent as an incentive to self-interest is in contention with that morality. This can be seen through Hume.

Hume held self-interest to be the motive for inventing property and the principal reason for human action.[79] In Hume's opinion the mutual interest of individuals, and thus society, lay in the formulation of strategies that channel passions in directions deemed socially constructive. Through social rules, conventions and customs that are internalised to a society by

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For example, in the UK: Corporate Manslaughter and Corporate Homicide Act 2007. However, the effectiveness of enacted corporate manslaughter provisions curbing dangerous illegal practices, in the presence of the large incentives available from pharmaceutical profits, is unlikely and remains to be demonstrated.

[79] Hume, D., *A Treatise of Human Nature: Being An Attempt to introduce the experimental Method of Reasoning into Moral Subjects*. Book III: Of Morals, Part I: Of virtue and vice in general, Section II : Of the origin of justice and property.

its members, can activity be directed towards socially useful objectives.[80] Without a concerted construction of a social order Hume considered that there would be murderous chaos.[81] By contrast, Rousseau recognised the need for social order,[82] but was also a passionate advocate of individual freedom. He rejected the notion of final sovereignty of the individual will and saw legislation as the product of the general will of the moral person rather than an aggregation of separate wills.[83] Thus, according to Rousseau civilisation, most notably the introduction of property is responsible for introducing evil into the world.[84] Hume shared Rousseau's view by holding that the human nature is a vessel of strife; a conflict of humanity on the one hand and 'avarice and greed' on the other.[85] This conception should be held in mind throughout the thesis as the problems

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[80] Hume, D., *A Treatise of Human Nature: Being An Attempt to introduce the experimental Method of Reasoning into Moral Subjects.* Book III: Of Morals, Part I: Of virtue and vice in general, Section II : Of the origin of justice and property.

[81] See Hobbes, who held that since there are no natural bonds of unity between individuals orderly life is only possible when all become subject to a supreme and absolute authority. *Leviathan.* Pt. Ch 13.

[82] For different reasons than Hobbes, in that Rousseau considered by giving oneself to all, one gives oneself to no one. Thus, each member of a sovereign becomes an indivisible part of the whole, whereas, Hobbes' absolute *Leviathan* exists as a separate body politic from those whom it governs.

[83] *Du Contrat Social*, Books I-II

[84] Both Russeau and Hume's writings indicate a link between ethics and feelings. Kant rejects their position by advocating objective 'pure moral law,' which is independent of all inclinations or feelings. The difficulty with Kant's proposition is the question of identifying the 'pure moral law.' Kant contends that only by rationality devoid of all sentiment and feeling can the 'pure moral law' be found. The difficulty I see with the Kantian perspective is proving rationality can be pure. After all, how were the first principles of rationalism derived?

[85] Hume, *Enquiries concerning human understanding and concerning the principles of morals*, (Re-printed) [Clarendon Press, 3rd Ed., 2002, Oxford]

of the patent system are raised and the interests of the parties resisting improvement to the availability and accessibility of medicines are identified. Indeed pharmaceutical innovation and the pharmaceutical patent present a clear instance of the conflict between societal morality and avarice. Moreover, if social morality ought to be indicated by legislation then considering the extent of legislators' vested interests in property rights over pharmaceutical inventions there is a serious need for political reform to allow legislation to converge with morality. Rousseau's view of civilisation is not entirely pessimistic. He believed that the product of the general will of the moral person, i.e. civilisation, could be a progressive force capable of elevating the ethical life of the individual. Thus, it can be hoped that the current political bias towards avarice and greed is transient.

i.8. **Without Incentive**

It is possible that there are many medicines that we do not have as a consequence of channelling pharmaceutical innovation through the patent system and thus the creation of artificial scarcity. The artificial scarcity, or in the case of most pharmaceuticals a monopoly, permits inefficient methods of innovation to be sustained. The monopoly distorts allocation and increases expense. In a very simplistic description, if the total money available for innovation within the system had been put into research in the

absence of monopolies, i.e. in a system of greater efficiency, it follows that more innovation would result.[86]

In some areas a comparatively small investment might yield considerable gains to human longevity and quality of life. For the diseases and conditions endemic to the World's poorest populations there are in many cases no available medicines. Between 1975 and 1999, about 1393 *new chemical entities* (NCEs) were marketed.[87] Only 13, less than 1% of these medicines have been for tropical infectious diseases.[88] Moreover, most of these 13 were developed to satisfy military or veterinary applications of interest to developed nations.[89] Only three were the result of a genuine

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[86] Evidently more capital in the absence of improved or stable efficiency does not guarantee greater quantities of useful research. It has been shown however that historic lessons applied even within the constraints of the patent system can generate efficiency gains. Thus although we cannot use increases in research funding within the USA to demonstrate that more investment in research and development means more NCEs, we can use European data. See Light, D., 'Global Drug Discovery: Europe Is Ahead' (2009) 28(5) Health Affairs 969-977. By historic lesson we refer to the change in research paradigm of the Nineteenth Century German Dyestuff Industry and the move from the highly skilled individual researcher to the collaborative efforts of many less experienced researchers. See Section 1.2.1 New Research Paradigm.

[87] Torreele, E. (Free University of Brussels, Belgium) "crisis of neglected diseases" conference 14 March 2002 New York, USA. See, Nelson, K. 'Stimulating research in the most neglected diseases' (2002) 359(9311) Lancet 1042; Smith, D., Binet, L., Bonnevie, L, Hakokongas, L., Meybaum, J., Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases' [DND Working Group, 2001, Editions Européennes, Brussels, Belgium] 11

[88] Trouiller, P., Olliario, P., Torreele, E., Orbinski, J., Laing, R., et al. 'Drug Development for neglected diseases: A deficient market and a Public health-policy failure' (2002) 359(9324) *Lancet* 2188-2194

[89] Torreele, E. (Free University of Brussels, Belgium) "crisis of neglected diseases" conference 14 March 2002 New York, USA. See, Nelson, K. 'Stimulating research in the most neglected diseases' (2002) 359(9311) Lancet 1042; Smith, D., Binet, L., Bonnevie,

effort to create drugs for neglected diseases.[90] The diseases of the world's poorest people seem to have little significance in the scheme of current innovation priorities. A survey in 2000 by the Pharmaceutical Research and Manufacturers of America (PhRMA) indicates that out of the 137 medicines in development for infectious diseases, sleeping sickness and malaria were only mentioned once.[91] In Africa over 60 million people are at risk from sleeping sickness and 500,000 are afflicted.[92] The disease is spread by the bites of infected tsetse flies and prevention technologies have not improved since before the fourteenth century. Prevention still '...depends largely upon avoiding the bites of tsetse flies.'[93] Who pays for the innovation of pharmaceuticals for the poorest populations and how that research ought to be undertaken is of considerable controversy.[94] Whilst

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L, Hakokongas, L., Meybaum, J., Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases' [DND Working Group, 2001, Editions Européennes, Brussels, Belgium] 11.

[90] Above.

[91] Smith, D., Binet, L., Bonnevie, L, Hakokongas, L., Meybaum, J., 'Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases' [DND Working Group, 2001, Editions Européennes, Brussels, Belgium] 12

[92] Smith, D., Binet, L., Bonnevie, L, Hakokongas, L., Meybaum, J., 'Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases' [DND Working Group, 2001, Editions Européennes, Brussels, Belgium] 8

[93] Wyatt, G., 'Sleeping Sickness' in Dawood, R. (ed.) *Traveller's Health: How to Stay Healthy Abroad* [Oxford University Press, 3rd Ed., 1st Reprint, 1992, Oxford] 132-133

[94] Increasingly over the last decade there have been initiatives by governments, industry, and organisations such as the World Health Organisation, World Bank and United Nations Development Program to stimulate interest in tropical disease research. Jamison, T., Breman, J., Measham, A., Alleyne, G., et al. (Eds.) *Disease Control Priorities in Developing Countries* [The International Bank for Reconstruction / The World Bank, 2006, 2nd Ed., Washington DC] 146. In the USA, the Food and Drug Administration (FDA) Amendments Act of 2007 introduced drug vouchers for companies that developed pharmaceuticals for infectious diseases that disproportionately affect poor populations in

this thesis addresses the issues of accessibility of medicines in the least economically wealthy countries, it is beyond the scope of this thesis to resolve all the issues concerning availability of medicines within those countries.[95] Although it is hoped that the suggested reforms in Chapter 5 will facilitate the establishment of local pharmaceutical research that would prioritise local diseases.[96]

So far we have defined our essential terms and raised the moral issue of how the pharmaceutical patent system skews legislation and innovation initiatives from morality towards self-interest.[97] However, we have not illustrated the cost of that self-interest. We shall do that now with a few examples.

i.9. **Health is Important**

Kaletra is a protease inhibitor that can be used to treat people with HIV. In 2002, Abbott, Kaltera's owner, was rapidly losing share of the protease inhibitor market to competitors. Norvir, another of Abbott's drugs, was

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developing countries. A voucher entitles the company to one expedited FDA review of another of its new drug applications.

[95] It is notable that pharmaceutical industries have seeded and developed more quickly in countries where pharmaceutical patents were weak, unenforced or inexistent. See, Boldrin, M., and Levine, D., 'The Case Against Intellectual Monopoly, Chapter 9' 3-5

[96] Even if disease endemic to the poor people were not the subject of research, pharmaceutical manufacturing capability may develop locally. Consider the situation in India prior to 2003. See, Lanjouw, J. O., 'The Introduction of Pharmaceutical Product Patents in India: "Heartless Exploitation of the Poor and Suffering?"' (1998) NBER Working Paper No. W6366: at 9.

[97] Examples of the vested interests of significant political figures and parties are given in Section 3.3.11. Hired Help Or Insiders.

beset with very serious side effects if used by itself as a protease inhibitor. However, it was found that when administered concurrently in small doses with other protease inhibitors that the combination dramatically improved the antiviral effect against even very resistant HIV strains. As a result, Norvir quickly become an important component in most protease inhibitor therapies. Which Abott saw as an opportunity to use Norvir to raise the cost of Kaltera's competitor medicines, thereby improve the attractiveness of Kaletra. Abbott implemented its strategy in December 2003,[98] when it raised the wholesale price of Norvir from $205.74 to $1,028.71 USD for 120 100mg capsules, a 500 per cent price increase.[99] The results were dramatic.[100] Table 1. presents the price increases of annual Norvir doses required in conjunction with other protease inhibitors.[101]

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[98] A useful collection of documents relating to Norvir is available at the Consumer Project on Technology. Available at: <http://www.cptech.org/ip/health/aids/norvir.html>

[99] Which would no doubt have a great impact on profits. See The Advocate, 'Industry analysts say Norvir price hike will double profits.' June 10, 2004. Available at: <http://www.advocate.com/new_news.asp?ID=12732&sd=06/11/04> (Last Accessed: 1st July 2009)

[100] See <http://www.cptech.org/ip/health/aids/norvir.html> (Last Accessed: 1st July 2009)

[101] Pharmaceutical prices outside the USA are more constrained because of price controls. Nevertheless there was widespread fear that a European price increase would follow the American one.

TABLE 1. Annual increase in the price of Norvir, as a booster for protease inhibitor therapies, following Abbott's 500 per cent Norvir price increase.[102]

Manufacturer	**Therapy**	**Annual price increase / United States Dollars**
Abbott	Kaletra	0
Boehringer-Ingelhein	Tipranovir	$12,000
Bristol Myers-Squibb	Atazanavir	$3,120
GlaxoSmithKline	Lexiva	$6,258

Kaletra's appeal with regard to pricing was considerably improved against competitor therapies. Many patients unable to afford the new prices were forced to switch from competitors' therapies to Kaletra.[103] Abbott increased its profits. However, changing an antiviral therapy in mid-course can have serious health risks, as well as undermining the effectiveness of a treatment.[104] In November 2004 the Illinois state court dismissed a class

[102] Alcorn, K., 'Ritonavir price increase: what are the consequences in 2004? Consequences for competitors,'18 December 2003. Avaiable at: <http://www.aidsmap.com/en/news/1E63C821-275E-45C2-95BC-6F6B99F38D54.asp> (Last Accessed: 1st July 2009); Cafferty, P., Families USA, Big PhRMA Behaving Badly: A Survey of Selected Class Action Lawsuits Against Drug Companies [Families USA, January 2005, Washington] 2

[103] "Price of AIDS Drug Soars Fivefold" Seattle Times, 5 January 2004.

[104] For example see, Levin, L., 'Changing antiretroviral therapy in paediatric patients' (2005) 6(4) *Southern African Journal of HIV Medicine* 38-42

action challenging the price increase,[105] holding that the patent for Norvir essentially entitled Abbott to charge any price it wished.[106]

i.10. **Research is Important**

Perhaps, commercial research and development and clinical testing are not the most effective method of generating and enabling access to new medicines. If the majority of funds, after manufacture, obtained from the sale of a pharmaceutical were re-allocated to research and development and clinical testing then there may be an argument for the present innovation regime. However, since there is substantial allocation of funds to activities unconnected to research and development and clinical testing that significantly increase the cost of a medicine, and therefore access to that medicine, there is a strong argument for regime change.

"In 1994, estimates of [research and development] spending as a percentage of sales were 12 - 19 per cent in the pharmaceutical sector, compared to an overall U.S. industrial average of 3.5 percent."[107]

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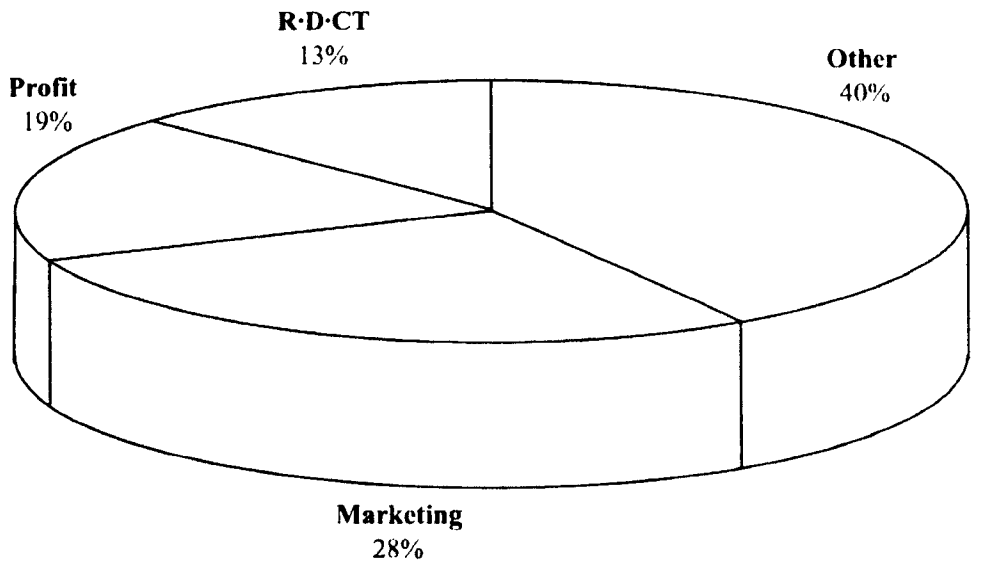
[105] Nelson, R., 'Debate over the ritonavir price increase gains momentum: Critics seek to reverse the fivefold price hike through legal action and boycott of Abott's products' (24 April 2004) 363 *The Lancet* 1369

[106] *Gingreau v. Abbott Laboratories*, No. 04 CH 8202, Memorandum and Order (Cook County Circuit Court, Nov. 12, 2004). This is interesting because the price difference of Norvir between Abbott's Kaletra and when used in combination with competitor therapies could have constituted monopoly leveraging with respect to 15 U.S.C.§2 Sherman Act. Following Schor v. Abbott Laboratories, No. 05-3344 (7th Cir. 2006) and the Supreme Court decision in Pacific Bell Telephone Co v. Linkline Communications Inc. (2009) this is no longer likely.

FIGURE 1. Pharmaceutical company distribution of revenue from 2000 to 2004[108]



Where R·D·CT represents research, development and clinical testing

Figure 1. Depicts a historical relative allocation of revenues by several of the world's largest pharmaceutical companies.[109] As will be seen

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[107] The Boston Consulting Group, Sustaining Innovation in U.S. Pharmaceuticals: Intellectual Property Protection and the Role of Patents (Jan. 1996) at 22. Requested from: http://www.bcg.com/

[108] Data derived from the USA Securities and Exchange Commission (SEC) filings for the companies: Pfizer Inc, Johnson & Johnson, Merck & Co. Inc., Abbott Laboratories, Bristol-Myers Squibb Company, Wyeth, and Eli Lilly and Company. Sectors represent the mean expenditures by these companies over a four year period.

[109] My assessment is supported by Gagnon and Lexchin, who used 2004 data sourced from the market research company CAM (part of the Cegedim Group) and the consulting group IMS Health on the companies Merck, Pfizer, Bristol-Myers Squibb, Eli Lilly, Aventis, Sanofi-Synthelabo, AstraZeneca, and Wyeth to compare marketing and research allocations. See, Gagnon, M-A., Lexchin, J., 'The Cost of Pushing Pills: A New Estimate of Pharmaceutical Promotion Expenditures in the United States,' (2008) 5(1) PLoS Med. Available at: <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0050001> (Last Accessed 7th April 2010). Another report using 1996-2004 data that considers revenue

research, development and clinical testing has the least allocation of revenues. Marketing receives at least twice the allocation of revenues as research, development and clinical testing.[110] Revenue allocations to Research and Development within the large pharmaceutical companies may be further reduced by the dearth of new blockbuster drugs as companies direct more resources to diversifying assets, purchasing companies or patents and rent-seeking behaviour. For example in February 2011, Pfizer reduced its research budget to 6.5 billion USD, which is estimated to be between 10 to 11 percent of Pfizer's 2012 revenue.[111]

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allocation to more activities is, Lauzon, L-P., Hasbani, M., 'Analyse économique: industrie pharmaceutique mondiale pour la période de dix ans 1996-2005. Montreal : Chaire d'études socio-économiques de l'UQAM, 2006. Available at: <http://www.cese.uqam.ca/pdf/rec_06_industrie_pharma.pdf> (Last Accessed: 13th February 2011)

[110] 2005 to 2010 data is not included due to a discontinuity in the trend data resulting from the increased tendency of pharmaceutical companies to outsource research and to purchase smaller pharmaceutical companies with marketable product portfolios. As a result this data may be unreflective of current revenue allocation. To produce an equivalent table for the period 2005-2010 requires data that is not available from the USA Securities and Exchange Commission (SEC) filings for the companies: Pfizer Inc, Johnson & Johnson, Merck & Co. Inc., Abbott Laboratories, Bristol-Myers Squibb Company, Wyeth, and Eli Lilly and Company. Further complications include the creation of subsidiaries as unlimited companies, which can be used to effectively hide financial information. For example, Janssen Pharmaceutical, a subsidiary of Johnson & Johnson, which has been re-registered as an unlimited company. Carswell, S., 'Janssen move keeps financial affairs private' (16th August 2008) Irish Times. Available at: <http://www.irishtimes.com/newspaper/finance/2008/0816/1218748038117.html> (Last Accessed: 1st July 2009).

[111] Pfizer Press Release 1st February 2011: Pfizer Reports Fourth-Quarter and Full-Year 2010 Results; Provides 2011 Financial Guidance and Updates 2012 Financial Targets. Available at: <http://www.pfizer.com/news/press_releases/pfizer_press_releases.jsp#guid=201102010

i.11. **Others can do it**

In addition to the cost of pharmaceuticals a substantial proportion of the breakthrough science, and development of new drugs is achieved by government, university, non-profit, and public/private groups. However, the structure of the pharmaceutical market, the requirements for the presentation of data for safety approval, and the cost of litigation contrive to place the majority of new drugs in the hands of private pharmaceutical companies. Given, the tendency of private research funds to be allocated to research on pharmaceuticals with relatively little incremental therapeutic value, but large profitability, publicly underwritten research remains extremely important. However, if government, university, non-profit, and public/private groups assign pharmaceuticals with great therapeutic value into private hands then many potential users will be excluded from life saving medicines developed by public funding.

In 1967 a team working at the Research Triangle Park, in the USA, isolated an active ingredient from the bark of the Pacific Yew tree, *Taxus Brevifolia*. Assays of this active ingredient lead to the important results

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06166en&source=RSS_2011&page=17> (Last Accessed: 13th February 2011); Cressey, D., 'Pfizer slashes R&D - Drug-maker plans to cut jobs and spending as industry shies away from drug discovery' (2011) 470 *Nature* 154-155. Available at: <http://www.nature.com/news/2011/110209/full/470154a.html> (Last Accessed: 13th February 2011)

published by Wanni, *et al.*, in 1971.[112] The active ingredient Dr. Wall named Taxol.[113] It was to become an extremely effective anticancer agent. Public funding underwrote a substantial part of the Taxol research and the USA's National Institutes of Health (NIH), a publicly funded body, sponsored the three phase clinical trials necessary if the chemical was to have therapeutic application.

In January 1991, during Phase III of its clinical trials the USA government signed a *co-operative research and development agreement* (CRADA) with Bristol Myers-Squibb for taxol. The CRADA granted Bristol Myers-Squibb the exclusive rights to all NIH funded Taxol research. In return Bristol Myers-Squibb agreed to provide the NIH with 17 kilograms of Taxol and use its 'best efforts' to commercialise Taxol. Bristol Myers-Squibb promptly entered into another CRADA with the USA Secretary of Agriculture granting Bristol Myers-Squibb exclusive rights to harvest Pacific Yew trees from Forest Service lands. The USA Department of the Interior entered a similar CRADA with Bristol Myers-Squibb for Pacific Yew trees on Bureau Land Management lands. By August, Bristol Myers-Squibb had also established a contract with Hauser, the former government contractor, in which Hauser agreed to supply bulk Taxol to Bristol Myers-Squibb for about $0.25 USD/mg.

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[112] Wani, M. C., Taylor, H.L., Wall, M. E., Coggon, P., McPhail, A. T. Plant antitumor agents. VI. The isolation and structure of taxol, a novel antileukemic and antitumor agent from *Taxus brevifolia*. (1971) 93(9) J Am Chem Soc. 2325-2327.

[113] Robinson, J., Prescription Games. [Simon and Schuster, 1st Ed., 2001, London] 108

By 1993, Bristol Myers-Squibb was demanding a wholesale price of $4.87 USD/mg, which was about 10 times the price the NIH had been paying its contractor, and 19.5 times the amount Bristol Myers-Squibb was paying Hauser for bulk Taxol. Added to the mark-up by distributors and doctors this meant that some patients were paying more than $8 USD/mg for Taxol; 32 times Hauser's bulk supply rate. With its Taxol market exclusivity due to end in 1996 Bristol Myers-Squibb sought to prolong its control through a diversity of means. In 1997 two of these came to fruition when Bristol Myers-Squibb was awarded an exclusive right to a method of administering Taxol[114] and Taxol orphan designation[115] for Kaposi's sarcoma indications.[116]

Orphan designation brought Bristol Myers-Squibb three major advantages: it granted Bristol Myers-Squibb seven years of marketing exclusivity for the orphan drug product;[117] tax incentives for clinical research undertaken; and funding to defray costs of qualified clinical testing expenses incurred in the development of the orphan product.[118]

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[114] USA Patent 5641803

[115] Orphan Medicinal status is available to medicines capable of providing benefit to especially rare conditions termed orphan diseases. It grants tax incentives and clinical research subsidies, as well as extended patent protection, data exclusivity extension and marketing rights. Regulation (EC) No 141/2000.

[116] Susannah Markandya, S., Love, J. 'Timeline of Paclitaxel disputes.' 23 August 2001. Available at: <http://www.cptech.org/ip/health/taxol/taxol-timeline2001.html> (Last Accessed: 1st July 2009)

[117] Orphan Medicinal status marketing exclusivity is for 10 years in the European Union. Article 8(1) Regulation (EC) No 141/2000.

[118] USA Orphan Drug Act 1983

In September 2000, Bristol Myers-Squibb quoted $6.09 USD/mg as the Red Book average Taxol wholesale price. Less than a month earlier a Taxol producer had revealed that manufacturing Taxol cost $0.07 USD/mg. For the same year Bristol Myers-Squibb reported annual Taxol sales of $1.592 billion USD.[119] Given these figures it has been estimated that Bristol Myers-Squibb earnings on Taxol were $4 to $5 million USD per day.[120]

i.13. **Where To Go**

The commercial regime of pharmaceutical innovation is in contrast to the 'open source culture' in other fields that have clearly demonstrated the possibility of organising the work of thousands of collaborators and organisations across the globe to create and run large projects successfully. World health for both the rich and the poor may benefit from a global 'open source' research and development and clinical testing network.[121] High purchase costs may yield high profits to the patent holder, but pursuit of profit engenders many problems. This thesis is essentially concerned with the misallocation that limits pharmaceutical availability and pharmaceutical access. At the root of the resource misallocation, and the key inhibitor of 'open source' pharmaceutical

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[119] BMS SEC 10-K form for the year 2000. Available at: <http://www.sec.gov/Archives/edgar/data/14272/000001427201500006/r10k1231.htm> (Last Accessed: 1st July 2009)

[120] Susannah Markandya, S., Love, J. 'Timeline of Paclitaxel disputes.' 23 August 2001. Available at: <http://www.cptech.org/ip/health/taxol/taxol-timeline2001.html> (Last Accessed: 1st July 2009)

[121] This is discussed in Chapter 5

research is the pharmaceutical monopoly, of which the pharmaceutical patent is a key component.[122]

ii. **Objectives and Parameters**

Our objective is to persuade that the patent system for pharmaceutical innovation poses significant problems for the availability, accessibility and safety of medicines. It will become clear that the adjustive purpose[123] of the pharmaceutical patent misallocates resources and retards innovation and availability of pharmaceuticals. It will also become apparent: that pharmaceutical patents impose a chaotic regime of drug development that is detrimental to global health strategies; that the pharmaceutical patent encourages development of drugs that sell in preference to drugs that pose therapeutic advances; that the pharmaceutical patent, i.e. innovation as property, is contrary to the objective of pharmaceutical innovation, and

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[122] A criticism of the patent-is-monopoly arises from a perceived discrepancy "between theory and reality." It is suggested that a patent cannot generate a monopoly in reality because "hundreds of patents related to the very same topic would emerge in most cases." For pharmaceuticals this objection is difficult to sustain: Firstly, few chemicals posses bioequivalence and even when they do present differing responsivity in patients. Secondly, the "hundreds of patents" is the norm in the context of pharmaceuticals. Because of the potential value, both strategic and monetary in potential products there is a strong interest in firmly closing off a "topic" to competition. Almost all of the significant patents will be held by relatively few firms and either by the corporate architecture of those firms or by their contractual undertakings will effectively be held by one hand. If the significant patents are distributed amongst competitive firms this is manifested on the market by the presence of me-toos. For an objection to the patent-is-monopoly consider, Pretnar, B., "Two sources of persisting patent controversy." 2005. Working Paper. Available at: <http://www.intertic.org/Policy Papers/Pretnar.pdf> (Last Accessed: 2 December 2009)

[123] The patent restricts the application of patented knowledge, permitting the patent holder to demand rents for employment of the knowledge. Such rents would not otherwise be available.

thus is an inappropriate response to externalities; that the patent function statements are incoherent; that the patent system is an unnecessarily expensive method of generating innovation; and that recovery of innovation costs through the price of a manufactured drug is not a necessary condition of pharmaceutical innovation.

We also search for justifications for the continued use of the present pharmaceutical patent system, which we identified above as a perceived dependence on a private pharmaceutical industry to innovate medicines. This perception must have an origin, either in history,[124] practicality[125] or doctrine.[126]

On the subject of doctrine, as this is a legal thesis and we have already mentioned the economic properties of a right over the use of knowledge (patent) it is time to introduce the legal notion of a patent – the *actio ius ius ad rem.* In the Hohfeldian[127] sense the imposition of a patent grants the patent holder a right and imposes a duty on everyone else. The right granted to the patent holder is a quasi-property right in the inventive step of the patented pharmaceutical. The duty imposed on everyone else is to respect the patent holder's ownership of the inventive step. As a result the patent holder may have a degree of control over all pharmaceuticals

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[124] Sections 1.1 to 1.3

[125] Sections 1.4 to 1.5

[126] Chapter 2

[127] Hohfeld, W. N., Fundamental Legal Conceptions as Applied in Juridical Reasoning and Other Legal Essays. Cook, W. W. (Ed.) [Yale University Press, 4th Printing, 1966, New Haven] 36 *et sequentia.*

incorporating the patented inventive step (product patent) and specified methods of utilising or producing the pharmaceutical (process patent). [128] The control exerted is an *actio ius ius ad rem*, a right over the *ius utendi fruendi abutendi*. Thus, the patent is not a right over a physical or material object, but a right over a right, and is applicable whenever the patent imposed duty is breached, i.e. the patent is infringed.

iii. **Background Theory**

Surprisingly, the classical literature on patents is remarkably thin and of limited utility. As Priest quite bluntly and succinctly comments. 'The ratio of empirical demonstration to assumption in this literature must be very close to zero.'[129]

The literature referred to is that of: Bentham (1795);[130] Say (1834);[131] Mill (1862);[132] Clark (1907);[133] Taussig (1915);[134] Pigou (1920);[135] Plant

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[128] A clear practical example is Abbott's use of Norvir, see Gingreau v. Abbott Laboratories (2004); Schor v. Abbott Laboratories (2006).

[129] Priest, G. L., What Economist's Can Tell Lawyer's About Intellectual Property: Comment on Cheung. (1986) 8 *Law and Economics* 19

[130] Bentham, J., The Works of Jeremy Bentham. Volume 3. Bowring, J. (ed.) [William Tait, 1843, Edinburgh]

[131] Say, J. B., A Treatise on Political Economy: Or the Production, Distribution, and Consumption of Wealth. Prinsep, C. R. (trans.) [Grigg and Eliot, 6th American Ed., 1834, Philadelphia]

[132] Mill, J. S., Principles of Political Economy with some of their Applications to Social Philosophy Ashley, W. J. (ed.) [Longmans, Green and Co., 7th Ed., 1909, London]

[133] Clark, J. B., Essential of Economic Theory [Macmillan, 1st Ed., 1927, New York]

[134] Taussig, F. W. Inventors and Money-Makers [Macmillan, 1930, New York]

[135] Pigou, A. *The Economics of Welfare* [Macmillan, 1924, 2nd Ed., London]

(1934); [136] and Arrow (1962).[137] This literature despite its empirical shortcomings still forms recurrent bedrock in contemporary pharmaceutical patent debates. Thus, it has instructive advantage with regard to later material and reveals many of the difficulties that patent debates conceal.

The core of Bentham, Say, Mill and Clark's conviction regarding patents was the 'something-for-nothing thesis.'[138] As Clark states,

> 'If the patented article is something which society without a patent system would not have secured at all – the inventor's monopoly hurts nobody... his gains consist in something which not one loses, even while he enjoys them.'[139]

Bentham's view, later also articulated by Say, Mill, and Clark, was that the patent system was indispensable to innovation, because an 'inventor who has no hope that he shall reap will not take the trouble to sow.'[140] The patent was a way to grant the inventor a necessary reward for their labour. We might notice a similarity with Locke's notion that since a person's labour is their own then the product of that labour is also theirs. However,

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[136] Plant, A., 'The Economic Theory Concerning Patents for Inventions,' (1934) N.S. 1 *Economica* 30-51

[137] Arrow, K. J., "Economic Welfare and the Allocation of Resources for Invention," R. R. Nelson (eds.) *The Rate and Direction of Inventive Activity: Economic and Social Factors* [Princeton University Press, 1st Ed., 1962, New York]

[138] Cheung, N. S., Property Rights and Invention. (1986) 8 *Law and Economics* 5-18

[139] Clark, J. B. Essentials of Economic Theory [Macmillan, 1st Ed., 1907, New York] 360-361

[140] Bentham, J., The Works of Jeremy Bentham. Volume 3. Bowring, J. (ed.) [William Tait, 1843, Edinburgh] 71

Locke was concerned with rights over real property, not rights over the rights over property.[141] Bentham as an advocate of the patent system considers that intellectual labour should yield material fruit as physical labour yields material fruit. However, the direct fruit of innovation is immaterial and Bentham neglected to notice that through the patent the material advantage gained by the inventor must arise from the material labour of others. The difficulties arising from treating real and intellectual property in the same fashion continue today.

Say concerning the patent system stated that, '[p]rivelages of this kind no one can reasonably object to; for they interfere with, nor cramp any branch of industry, previously in operation. Moreover, the expense incurred is purely voluntary; and those who incur it, are not obligated to renounce the satisfaction of any previous wants.'[142]

Plant remarked on this short-sightedness of the something-for-nothing thesis by noting Say and Clark's failure in considering that patents draw scarce resources into the acquisition of patents.[143] He also noted that patents increase the scarcity of resources.

> "Patents ... make possible the creation of scarcity of the products appropriated which could not otherwise be maintained. ...[W]e

[141] Locke, J. P., Two Treatises on Government Laslett, P. (ed.) [Cambridge University Press, 1st Ed., 1988, Cambridge]

[142] Say, J. B., *A Treatise on Political Economy* [1834] [Augustus M. Kelley, 1964, New York] 182

[143] Plant, A., Economic theory concerning patents, (1934) N.S. 1 *Economica* 30, 40-41

might expect that public action concerning private property would normally be directed at the prevention of the raising of prices, in [the case of patents]...the object of the legislation is to confer the power of raising prices by enabling the creation of scarcity."[144]

With retrospective acuity we may remark that Clark also tentatively noted patents lead to an overall increase in the scarcity of resources.[145]

If innovation would not occur in the absence of a patent then a patent is a required, if not necessarily sufficient, condition to that innovation. Thus, to have innovation one would have to have a patent system. However, if innovation occurs in the absence of a patent system then the patent system is not a necessary condition of innovation. Taussig believed innovation would occur in the absence of a patent system, as history demonstrated, thus proposed that the patent system was a contrivance that gained nothing and thus was a huge mistake.[146]

"One thing stands out conspicuously...," he wrote. "...[T]he race of contrivers and inventors does obey an inborn and irresistible impulse. Schemes and experiments begin in childhood, and persist

[144] Plant, A., Economic theory concerning patents, (1934) N.S. 1 *Economica* 30, 31

[145] Clark, J. B. Essentials of Economic Theory [Macmillan, 1st Ed., 1907, New York] 265-266

[146] Taussig, F. W. Inventors and Money-Makers [Macmillan, 1930, New York] 18

so long as life and strength hold. It matters not whether a fortune is made or pecuniary distress is chronic."[147]

Taussig considered it humankind's nature to invent, thus humankind would invent even in the absence of a patent system. Humankind's invention prior to 1471, and for the majority of the world until the last two decades, provides plenty of support for Taussig's view. Moreover, some of the most significant modern inventions were created without the intention of securing patent monopolies.[148]

Pigou also held that since the majority of invention is spontaneous, encouragement to invent is superfluous. Though he also suggested that the patent system can focus invention towards that which society desires.[149]

Plant certainly recognised the effect of patents in channelling resources. He warned that the channels which the patent's artificial monopoly encouraged diverted scarce resources to what was deemed patentable and most profitable under the patent rules.[150] What Plant does is to

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[147] Taussig, F. W. Inventors and Money-Makers [Macmillan, 1930, New York] 21

[148] For example, penicillin, polio vaccine and the internet

[149] Pigou, A. C., The Economics of Welfare [Macmillan, 4th Ed., 1932, London] 185

[150] Plant, A., Economic theory concerning patents, (February 1934) *Economica* 30, 31. This statement aptly describes the allocation priorities of resources into pharmaceutical innovation under the current patent system. See, Mannan, A., and Story, A., 'Abolishing the Product Patent: A Step Forward for Global Access to Drugs.' In Illingworth, P., Cohen, J., and Schuklenk, U. (eds.) The Power of Pills: Social, Ethical and Legal Issues in Drug Development, Marketing and Pricing Policies. [Pluto Press, 2006, London] 179-189

recognise that although each patent creates scarcity each patent does not necessarily create a reward.[151] In consequence there would be a rush to invent those things that were most profitable, with many allocating resources to that same endeavour, but only one able to benefit. Given a finite pool of resources, multiple expenditure on the same purpose would reduce the resources available for other purposes. Furthermore, if rapid expenditures of resources are more wasteful than more steady approaches to innovation then the resource pool will be further depleted for other projects.

Arrow, building on the work of Hotelling[152] and Samuelson,[153] considered that although property rights for ideas may be useful they are inferior to direct government investment in inventive activities. His conclusion stemmed from a belief that with or without a patent system there would be under investment in some areas of innovation that are simply not profitable. Other writers have suggested that public policy actions can have a strong effect on the rate of technological progress in the pharmaceutical industry.[154]

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[151] Plant, A., Economic theory concerning patents, (February 1934) *Economica* 30, 38

[152] Hotelling, H., The General Welfare in Relation to problems of Taxation and of Railway and of Utility Rates. (1938) 6 *Econometrica* 242-269

[153] Samuelson, P. A., The Pure Theory of Public Expenditure. (1954) 36 *Review of economics and statistics* 387-389

[154] Adrian Towse (ed.), Industrial Policy and the Pharmaceutical Industry [Office of Health Economics, 1st Ed., 1995, London]

Studies have suggested that the pharmaceutical industry, more than any other industry, places the highest importance on patents.[155]

" In addition, typical drug innovation today costs companies almost a half-billion dollars and requires more than a decade of research, testing, and FDA marketing approval time to get to the market. Finally, since many new compounds can be copied at a fraction of the original cost, without adequate and effective protection of intellectual property rights, through patents, trademarks, and proprietary business information protection, it would be illogical for investors to sink money into new drug discovery and development. The consequences? Since industry--not academia or government--is responsible for the large majority of new drug discoveries,[156] there would probably be far fewer research projects and products in the future to help prevent strokes, cure cancer, Alzheimer's disease, heart disease, and serious infectious diseases such as AIDS."[157]

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[155] Levin, R., Klevorick, A. K., Nelson, R., Appropriating the Returns from Industrial Research and Development (1987) *Brookings Papers on Economic Activity* 783-820; Cohen, W., Nelson, R. R. and Walsh, J. P., Appropriability Conditions and Why Firms Patent and Why They Do Not in the American Manufacturing Sector. Working Paper [Carnegie-Mellon University, 1997, Pittsburgh]

[156] Whilst technically true, this statement is in fact misleading. Industry is responsible for the majority of NCEs that receive market approval each year, however as will be described in Chapter 3, almost all of the NCEs that pose significant therapeutic breakthroughs originated from research conducted in publicly funded or charitable research institutions.

[157] Bale, H. E. (1997) Patent Protection and Pharmacutical innovation. *New York University Journal of International Law and Politics*. 95-107

Without patent protection, or an institution which protected innovators, then imitators would be able to free ride the innovator's research and development and clinical testing by duplicating the innovative pharmaceutical compound for a fraction of the innovator's cost. Edwin Mansfield from a survey of the research directors of 100 U.S. corporations, across twelve industries, concluded that out of all the industries that completed questionnaires the patent was most important to pharmaceutical companies.[158] He suggested that 65 per cent of pharmaceutical inventions would not have been introduced by the pharmaceutical industry in the absence of patent protection. For the other eleven industries he studied, this percentage was only 8 per cent. Whilst being nearly 30 years old and thus not necessarily reflective of how today's pharmaceutical CEOs would complete a questionnaire, Mansfield's research is still mentioned in the context of pharmaceutical innovation and pharmaceutical patents and must be mentioned. What the survey showed was that the pharmaceutical industry placed more importance on pharmaceutical patents than other industries according to their directors. It did not show that pharmaceutical innovation was greater in a system with pharmaceutical patents.

However, pharmaceutical research companies' interest in monopolising therapeutic markets is easily understood. It is suggested that

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[158] Taylor, C.T., Silberston, Z.A., The Economic Impact of the Patent System. [Cambridge University Press Cambridge, 1st Ed., 1973, England]; Silberston, Z.A., The Economic Importance of Patents (The Common Law Institute of Intellectual Property, 1st Ed., 1987, London]; Mansfield, E., Patents and Innovation: An Empirical Study. (1986) 32 *Management Science* 175.

pharmaceuticals are expensive to innovate, and that a medicine that is approved for the market will have cost $802 million USD.[159] Industry explains that this is because less than 1 per cent of compounds examined in pre-clinical trials make it into human testing. Then only 20 per cent of compounds entering clinical trials are approved for treatments.[160]

Moreover, the cost of pharmaceuticals is suggested to increase rapidly as research and development and clinical testing costs are held to have increased at an annual rate of 7.4% above general inflation when compared to the pharmaceutical introduction costs of the 1980s. It is suggested that a major factor in the increase is the significant increase during the 1990s in the size and number of clinical trials compared with an earlier period.[161]

Since life has greater value in the contemporary world than in passed ages past pharmaceuticals have greater significance than ever before. It is

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[159] DiMasi, J. A., Hansen, R.W., Grabowski, H. G., The Price of Innovation: New Estimates of Drug Development Costs [Tufts University Centre for the Study of Drug Development, 1st Ed., 2002, Boston]

[160] DiMasi, J. A., Success Rates for New Drugs Entering Clinical Testing in the United States (1995) 58 *Clinical Pharmacology and Therapeutics* 1–14. There may be significant cost inflation in the model arising from the data used. The data on which DiMasi bases his findings are not publicly available.

[161] DiMasi, J. A., Hansen, R.W., Grabowski, H. G., The Price of Innovation: New Estimates of Drug Development Costs [Tufts University Centre for the Study of Drug Development, 1st Ed., 2002, Boston]; For newer and older reports respectively, see DiMasi, J. A., Hansen, R.W., Grabowski, H. G., The price of innovation: new estimates of drug development costs (2003) 22 *Journal of Health Economics* 151-185; DiMasi, J. A., Hansen, R. W., Grabowski, H. G., Lasagna, L., The Cost of Innovation in the Pharmaceutical Industry. (1991) 10 *Journal of Health Economics* 107–129.

undeniable that medicines are important determinants of longevity and quality of life. Thus, we are increasingly willing to dedicate more of our labour to their purchase.

> 'It is hard to think of many industries that have contributed as much to human welfare as the pharmaceutical industry.'[162]

However, although the pharmaceutical industry may have made an important contribution to world health, is it more than would have been achieved in the absence of the pharmaceutical patent? Is it more than would have been achieved through another mechanism? There are an overwhelming number of indicia suggesting that the present system of pharmaceutical innovation holds back pharmaceutical progress. These indicia will be presented in detail in Chapter 3. They are in summary,

- Less than a fifth of revenue is invested in research and development.
- Knowledge is a public good, thus it is very expensive and difficult to keep others from using it.
- There is a correlation between an increased use of intellectual property rights and a decline in inventive activity.

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[162] Levy, R., Wickelgren, A., Competition Policy Issues for Regulators: A U.S. Perspective on Pharmaceutical Industry Cases Before the Federal Trade Commission. Kettler, H. (ed.) Consolidation and Competition in the Pharmaceutical Industry [Office of Health Economics, 1st Ed., 2001, London] 106–117.

- When a pharmaceutical is patented, there will usually be 40-50 patents registered. These patents act as deterrents to future market entrants and innovation.
- Intellectual property is expensive.
- Profit is the purpose of a company, thus the most profitable objective is pursued.
- Monopolies are less productive and far more expensive than competition.
- Modern technologies for data collaboration and information sharing are not used.
- Safety issues are masked within the system.
- Clinical trials and or the data generated by them are not impartial.
- Empirically profits always outweigh penalties and pharmaceutical companies are frequently convicted of racketeering and misleading public authorities.
- The majority of therapeutic breakthroughs originate in publicly funded or subsidised research institutions.
- Many diseases and conditions are neglected as they are considered unprofitable.

It is likely that the price the pharmaceutical patent system of innovation levies on 'human welfare' is greater than its contribution. The problem of reduced availability of medicines is further exacerbated by the limitations on accessibility that the pharmaceutical monopoly permits. If a medicine is

available but access is denied, when that access might be achieved through competition, ethical justification is difficult.

> "Moreover even if we could determine on principle what is the product of any one's labor it would be very doubtful morality if one could keep it all when others, the sick, the infant, or the very aged, were to perish because of the exercise of this right."[163]

iv. **Methodology**

This thesis questions the boundaries of knowledge; especially natural and social science distinctions that conceal the *conventionally decidable* nature of conclusions in both domains. Knowledge types are suggested as ontological (foundationalism), rationalism (epistemological) and empiricism (epistemological). Rationalism (logic) and empiricism (coherentism) are identified as intersubjective methods of establishing conventions. The reconsideration of the institutions of objectivity are an important part of the methodology of this thesis as many of the key theories relating to pharmaceutical patents are embedded in foundationalism guised as objectivity.

> 'The world must be understood culturally in terms of the significance it is given by social groups who perceive, categorise and act upon it according to socially conventional structures of language and meaning. Human beings never speak in the name of the real, or

[163] Cohen, M. R., Positivism and the Limits of Idealism in the Law (1927) 27(3) *Columbia Law Review* 240

grasp the world objectively, because the realities we recognise are shaped by the cultural contexts that enable our very cognisance of the world itself. Cultural categories provide the very possibilities for perception. What we experience as social reality is a constellation of cultural structures that we ourselves construct and transform in ongoing practice."[164]

Indeed for intellectual property there is no other way to understand its value other than as it arises out of cultural categorisation. Bereft of physical identity, we struggle to perceive its value in real terms. For it has none, save that which it is accorded by our cultural descriptions of our existence.

By creating conventions we rely on and format the interchange of experience between people, or between our senses and our actions. Providing that the outcome of the combination is predictable or consistent then we treat the information or experience as a truth. Thus, the object of conventional truth becomes a quasi fact, given the status of fact or truth until inconsistent with convention or experience. Through the method of convention we can build on quasi facts, hereafter facts, and share information described in terms of conventional truth. As a result we are for the most part comprehensible to one another and seemingly disconnected objects and impenetrable mysteries sometimes become an interconnected and comprehensible system.

[164] Coombe, "Objects of Property and Subjects of Politics," in Law and Anthropology: A Reader. Falk, S. (Ed.) [Blackwell, 1st Ed., 2005, London] 112-113

One set of intersubjective tools is economics. Like any wisdom generating tool, no matter how sophisticated, economics can only be applied to a model and that model is only a caption or reality. Use of the economist's tools can generate very useful insights into the deployment of resources and it would be foolish not to consider their import in a study concerning an institution that has been a subject of economic writing for nearly three hundred years. Indeed, the principal system adopted for the examination of intellectual property has been economic theory. There are however, a number of pitfalls in employing economics. These potential difficulties arise from the construction of economic theory and are contained in the constituting assumptions. To apply economic theory we must move from reality into a model, and then we must understand that model in terms of the categorisations of economic theory. To do otherwise is to render fact incomprehensible to our analysis.

For example, in economics law is an instrument of securing economic gain.[165] As a result the power relations engendered by law are transformed into terms comprehensible to an economic model. Far more than law and far less law are incorporated into the economic analytic framework than a law model. The transformation of secondary and higher orders of perception involves reducing empirical observation with at least three categories of assumptions the majority of which arise from the theorist's primary perceptions.

[165] This observation is applicable to descriptive economics, economic theory, and applied economics.

The first set of assumptions concerns the behaviour of individual human beings. The second set concerns the physical structure of the world and the third relates to the economic and social institutions. Like any set of conventions, such as physics or mathematics, economics is a simplification, a skeleton or framework that helps us understand the complexity of our world. In Rosemary Coombe's words, it is a 'cultural categorisation.'[166]

Evidently, assumptions must play a decisive role in the outcome of all models and it is extremely important to identify the assumptions involved. Identifying the propositions comprising syllogisms is an important part of how this thesis approaches the theories, sometimes disguised in economic terms, concerning pharmaceutical patents.

Sensitivity to foundationalist assumptions arising from my methodology required me to adopt a novel perspective when examining literature on patent theory. Literature considering the availability of resources for pharmaceutical innovation often considers the patent as synonymous with invention. Thus, the patent is an end in itself rather than simply a means to an end. However, all laws are a means to an end. Law is constructed of rights, which exist, but are not self-existent: it is the imposition and the observance of a right that gives rights their *esse*. Human beings,

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[166] Coombe, "Objects of Property and Subjects of Politics," in Law and Anthropology: A Reader. Falk, S. (Ed.) [Blackwell, 1st Ed., 2005, London] 113

however, are an end in themselves and never a means to an end.[167] Therefore, this investigation of the patent's effect on pharmaceutical innovation differs radically from previous works as it focuses on the human being as an end and considers the patent and the non-health interests bundled into the fabric of the patent institution as subservient to human health.

v. **Plan**

The project is directed towards identifying the incidence of the patent on:

a) pharmaceutical knowledge assembly, and

b) access and utilisation of pharmaceutical technologies.

Chapter 1 – The objective of this chapter is to demythologise the pharmaceutical patent. To do this the chapter is divided into two parts. The first part provides a history of the patent for inventions and the pharmaceutical industry's origins and development. The second part details the factors that distinguish pharmaceuticals from other types of inventions and explains the factors involved in the existence of pharmaceutical patents and their use as exclusionary tools.

The chapter shows that modern patents on pharmaceutical inventions arose, not out of their favourable stimulation of innovation, but rather from

[167] According to Kant's moral philosophy [hu]mans possess moral dignity because they are an end in themselves.; "The production of wealth is but a means to the sustenance of man; to the satisfaction of his wants; and to the development of his activities, physical, mental, and moral." Marshall, A., *Principles of Economics* [Macmillan and Co. Ltd., 9th Ed., 1961, London] 173

national protectionism and then reinforcement through the political lobbying of an industry grown powerful and dependent on them. The second part demonstrates a feedback or feed through relationship between the patent and the pharmaceutical industry; in that the particular characteristics of the pharmaceutical patent are largely the product of industrial design, and that the pharmaceutical industry as presently constituted is a product of the patent system. This is necessarily described by a characterisation of patent life cycles and the significance of each stage on a pharmaceutical patent owner.

Chapter 2 – This chapter's objective is an examination of the theoretical coherence of patent doctrine. It is based on material that has gone through a number of expansions, which began with a mathematical investigation of legal relations within patent doctrine to which economic theory and philosophical considerations were applied. The symbolic logic has been relegated to footnotes, but not removed because of its succinct explanatory power of complex relations.[168]

It is the most theoretical chapter of the thesis and can seem a dense as it is a distillation of formidable numbers of papers, all of which are found within the bibliography. We categorise the justifications from patent literature into four function statements - Invention Incentive, Disclosure

[168] A key to both the definitions and a brief summary of the symbolic logic terminology used are presented for your convenience in the appendices. To increase accessibility and to make the chapter readable, rather than requiring study, only the bare minimum of symbolic description been retained.

Incentive, Investment Incentive, Organised Derivative Innovation. Each of which we explain and then analyse. Our analysis considers the components of each function statement particularly the assumptions on which the function statements are based. We then test coherence between the function statements on the basis of their underlying assumptions.

We find that foundationalism guised as objectivity has become deeply entrenched in patent discourse and that many of the function statements are incoherent. These findings are significant for the rest of the thesis as arguments for pharmaceutical patents typically rely on patents simultaneously satisfying several function statements.

Chapter 3 – The objective of this chapter is to build on the theoretical revelations of chapter 2 by providing practical examples of how the pharmaceutical patent system of innovation is problematic and the reasons why. It describes the empirical indicia of the pharmaceutical patent system's poor productivity in delivering new medicines, and also the pharmaceutical patent system's incidence on access to medicines. Empirical examples are given for the problems that the misallocation of resources by the patent system creates.

The examples reinforce that the core assumption of pharmaceutical innovation is that the cost of research, development and clinical testing must be recouped through the cost of accessing medicines. The chapter

illustrates why linking pharmaceutical innovation to the price that can be recovered from one of its products is undesirable for both the assembly of pharmaceutical knowledge (availability) and the use of pharmaceutical knowledge (accessibility). Moreover, the chapter reveals the parameters within which change to the pharmaceutical patent occurs and the power relations determinative of that change. It is shown that regulation is determinative of industry structure and funds from industry flow into the political machinery and lawyers that are ultimately responsible for the laws that govern access to medicines and knowledge about them: Misallocation of resources begets further misallocation of resources and thus the system propagates and entrenches itself.

Chapter 4 – The objective of this chapter is to consider proposals for reform of our method of encouraging pharmaceutical innovation. There are a lot of proposals for patent reform and supplementary pharmaceutical innovation incentives to the pharmaceutical patent incentive. However, many share common themes or merely require additional funding to be invested in parallel incentive schemes. We consider the more detailed proposals that seek to address the problems of the current patent system and where they share common traits categorise them which permits a more detailed analysis than would have otherwise been possible.

Our criteria for assessing the proposals are the proposal's likely incidence on accessibility, availability and safety of medicines. We find that the majority of the proposals aim to remedy or curtail a particular symptom the

pharmaceutical patent system of innovation's malaise, but ignore or exacerbate others. Which reveals how complex reform has to be if a pharmaceutical patent is retained, but the problems are addressed.
We also notice, with respect to pharmaceutical knowledge assembly and use of that knowledge, that almost none of the proposals try to employ historic lessons about pharmaceutical innovation or modern systems of organisation and knowledge exchange. Thus, the proposals tend to eschew considerable potential for pharmaceutical invention.

Chapter 5 – Is a response to the perceived failings of the proposals in chapter 4. Its objective is to envisage, based on historic lesson and modern systems of organisation and knowledge exchange, a system of pharmaceutical innovation that approaches optimum availability and accessibility. It does not take into account the strong interests of the political elite in maintaining the profitable misallocations of the current patent system. Thus, it is less constrained than the proposals of chapter 4. Nevertheless the proposal is otherwise pragmatically based. It begins with a brief description of legislative changes and then explains how the removal of patent rights and exclusory rights in conjunction with organised knowledge exchange can lead to greater availability, accessibility and safety. It draws on historic examples and current information exchange technologies.

The mechanism suggested is a decoupling of the pharmaceutical product from pharmaceutical research and development. This would involve

abolishing patents for pharmaceuticals, or hereafter not granting them and extinguishing exclusory rights like market or data exclusivity. Research would be placed into an open global database in author attributed entries. Funding for that research would come from savings on the price of medicines. It is unclear if this degree of funding will be sufficient to meet societal needs. However, even with savings on accessibility and no increase in spending this level of funding could be the same as the current allocations to research and development by Industry and government. Moreover because the cost of accessing pharmaceutical knowledge is decreased and available expertise is increased drug discovery should be swifter and cheaper. Moreover, many of the institutional structures for the research (Universities) and clinical testing (teaching hospitals) are already in place and already significantly subsidised by governments. Use of these institutions would provide a larger, cheaper workforce and provide education and employment advantages. Industry funding to these institutions would have to be replaced, but there may be sufficient savings in accessing medicines to satisfy the loss of industry funding.

Since manufacturers are able to compete to produce pharmaceuticals then we would expect the development of more pharmaceutical industries, including within less wealthy populations, and a greater diversification and expansion in the numbers of manufacturers. This should lead to better stability and supply of medicines, and remove inefficient producers from the market. Since safety is desirable then we do not suggest any changes to product liability or tort, but we do suggest a good practice requirement

for pharmaceutical manufacturers that requires a detailed disclosure of manufacturing processes and quality controls. These changes could be easily incorporated into the pharmaceutical manufacturer's licence that is currently required in the European Union and USA.

CHAPTER 1

THE PHARMACEUTICAL PATENT

Patent law, as originating from statute, applies to a broad spectrum of technologies and with little exception statute initially treated the different areas of technology with uniformity. However, the different technology areas can display highly diverse characteristics.[169] These differing characteristics have been increasingly recognised and patent law has been modified through many vehicles; including patent regulations, decisions in patent cases, and the economics of patent practice. Thus, there is a growing divergence in the real characteristics of patent law between some technology sectors.

Formally, that is by statute or by case law, there is no definition of a pharmaceutical patent as distinct from patents in other technology areas. Nevertheless, statutes (as amended), treaties and some case law do

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[169] For example, the rapidity and expense of innovation, but also consider differences in the desirability of competitive pursuit of a better product. With respect to healthcare a tiny difference in quality has a significant effect on consumer choice. With respect to physician performance indicators see, Cheng, S..-H..; Song, H..-Y., Physician performance information and consumer choice: a survey of subjects with the freedom to choose between doctors (2004) 13(2) *Quality & Safety in Health Care* 98-101.
This is also illustrated through consideration of tool setting costs. With mechanical technologies, because of the interface of the component that is the subject of the patent with other components the high aggregate cost of tool sets in creating the finished ensemble that employs a mechanical patent is very high with respect to the cost of raw materials. Thus, where the embodying result of the patent requires this high initial investment in aggregate tool setting, combined with the costs associated with assembly of the embodying product there is an interest for the manufacturer of a product to have a time lag between each successive competing innovation so that they may recoup the cost of tool setting and enter into profit. The same is true in the manufacture of pharmaceuticals, but with pharmaceuticals it is important that the market prefers medicines of the highest quality and performance. In the case of mechanical inventions it may not be the case that the latest product of highest quality is available, the performance indicators may not be significantly different.

indeed treat pharmaceuticals differently from other technology areas. (For example, a longer patent term is available for pharmaceuticals.[170]) Furthermore, there are two other very strong reasons for lifting this narrowed group of patents, relating to pharmaceuticals, from patents in general. As will been seen, both the role that pharmaceuticals play in society and the legal framework surrounding the creation of pharmaceuticals and their use, are different from many other technology areas.

Pharmaceutical patents have not always been singled out for different treatment and this has come as a relatively recent phenomena. In the first part of this chapter (1.1) we briefly outline the history of the patent thereby demonstrating how its present form grew out of national protectionism, opportunism by patent practitioners and the burgeoning socio-political dominance of large concerted industry. One of those quickly growing industries comprised the pharmaceutical companies and the origins and growth of the pharmaceutical industry are described (1.2). The Second part of this chapter examines the factors, both socially (1.3) and legally (1.4.) that can be used to distinguish pharmaceutical patents from the patents of other technology sectors. More importantly this second part provides useful background information on the social issues and legal frameworks surrounding the use, development, marketing and exploitation of medicines (1.5). As a result the chapter is mostly descriptive but

[170] Patents (Supplementary Protection Certificates for Medicinal Products) Regulations 1992, S.I. 1992 No. 3091, reg. 5

provides a useful background for the later theoretical and empirically based chapters.

1.1. **The Origins and Evolution of the Patent for Invention**

Monopoly grants encompassing an industry or commodity are a very old institution. The grant of protective monopolies or franchises was practised in Western Europe as early as the Fourteenth Century.[171] Monopoly grants gave a power to both the grantor and the grantee. On one hand, the grantor gained the advantage of another award; one that they may give as a reward for service or to favourites, or sell or rent for profit.[172] Moreover, the grantor also gained a powerful tool of censorship against activities they wished policed or limited.[173] On the other hand, the grantee received an incentive to perform a specific function, which was generally lacking in society and would benefit the ruling class.

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[171] For evidence of its frequency in England see the Calendar of Patent Rolls. Amongst the records the most striking examples are the protections offered to clothiers and those engaged in the textile industries. Amongst these is the broader framing of the monopoly grant to Johanne Kempe of Flanders in 1331(*Calendar of Patent Rolls* 5 Ed III, p. I, m. 25), by statute in 1337 to 'all clothworkers.' Like grants to Kempe's were issued in 1336 (*Calendar of Patent Rolls* 10 Ed. III, Dec. 12) and 1368 (*Calendar of Patent Rolls* 42 Ed. III, p. I)

[172] Machlup, F., An Economic Review of the Patent System: Study of the Subcommittee on Patents, Trademarks, and Copyrights of the Committee of the judiciary (1958) US Senate, 85th Congress, 2nd Session, Study Number 15, Washington: United States Government Printing Office 2

[173] Cornish, W., Intellectual Property: Patents, Copyright, and Allied Rights [Sweet and Maxwell, 4th Ed., 3rd Impression, 1999, London] 340

An English franchise dated 1st May 1291[174] reads,

> "...[T]hat men may have the greater will to labour in the making of cloth in England, Ireland, and Wales, We will that all men may know that We will grant suitable franchises to fullers, weavers... who work in this mystery so soon as such franchises are asked of us."[175]

A particular form of the protective monopoly grant or franchise is the patent for invention; though, as will be seen, that the monopoly be addressed to inventors or limited to their inventions were not necessary conditions for this patent to be granted.

1.1.1 **From Italy**

The origin of patents for invention is attributed to fifteenth century Renaissance Italy. Where in 1421, the State of the Republic of Florence made the first known grant of a monopoly in an invention to an inventor.[176] The monopoly, bestowed on Filippo Brunelleschi architect of the cupola of the Cathedral Santa Maria del Fiore,[177] was granted for the invention of 'some machine or kind of ship' beneficial to the interests of 'merchants and others.' The text of the patent holds that Brunelleschi refused to disclose

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[174] From internal evidence the 'Athenaeum' suggests that the document more likely dates from the 1st of May 1327.

[175] Hist. MSS. Comm. Xiv, pt. Viii, 7

[176] New Encyclopædia Britannica, [1987, 15th Ed., Chicago, Auckland, Geneva, London, Manila, Paris, Rome, Seoul, Sydney, Tokyo, Toronto] Volume 26, Macropædia, 200

[177] Prager, F. D., and Scaglia, G., *Brunelleschi: Studies of his Technology and Inventions* [MIT Press Cambridge, Massachusetts, 1st Ed., 1970) 111-123

his machine to the public unless he was granted a prerogative so that he could reap the 'fruit of his genius.' The lords considering the potential benefits for both the State and Brunelleschi created and conveyed a right to Filippo 'so that he may be animated more fervently to even higher pursuits and stimulated to more subtle investigations,' as well, we presume disclose his invention. For three years the right enabled Brunelleschi to burn any other ship on any water within the Republic of Florence that had, held, or used in any manner his design.[178] History does not recall whether Brunelleschi exercised the power afforded by his patent, or whether the monopoly term was extended over the seven more years it took the eminent inventor to realise his invention. It does, however, inform us, without reason, that the *Badalone* or *acque vola* sank in May 1428 without completing the invention's 'claim.'[179] Nevertheless, Brunelleschi's patent is interesting since it is the first record of a monopoly addressed to the originator of an invention rather than a *mere* importer of an invention.

The number of patent grants in the State of Florence is not clear though the award of prerogatives to inventors continued. Indeed, half a century following Brunelleschi's patent, Venice seeing the prosperity of the Florentine Republic was quick to establish many of the institutions it

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[178] Prager, F. D., "Brunelleschi's Patent," (1946) 28 *Journal of the Patent Office Society* 109-135, 109

[179] Prager, F. D., and Scaglia, G., Brunelleschi: Studies of his Technology and Inventions [MIT Press Cambridge, Massachusetts, 1st Ed., 1970] 111-123
For a good, though brief account see
<http://www.stanford.edu/~broich/tamingnature/brunelleschi.htm> (Last Accessed: 1st July 2009)

deemed the root of Florence's success. Amongst these institutions was the award of patent monopolies for inventions. Thus, in 1474 the Republic of Venice passed, as far as we know, the World's first patent ordinance, which granted an inventor a ten-year monopoly in the exploitation of their invention.[180] This patent law ensured the monopoly by conveying to the inventor a right to destroy objects incorporating their idea. An important objective of the legislative act was to attract foreign inventors, including Florentine engineers.

With the Reception of Roman law well underway and the technical superiority of reasoning thereby available[181] it is appealing to think of the early patent system as an entity of noble intellectual birth. Moreover, given the proximity of Florence and Venice to Bologna it is more than likely that both affluent city-states had access to the *doctores*. However, the part played by the law masters of the era remains uncertain and it is highly probable that the idea of monopoly grants to inventors was a progeny of the existent grants of land and mineral rights prevalent at the time being extended to a newly growing mercantile class of trade folk. In short the patent was at its debut guided by pragmatism rather than a superiority of reasoning based on the intrinsic nature of (*European*) human society.

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[180] Mandich, G., Venetian patent (1450-1550) (1948) 30(3) *Journal of the Patent Office Society* 166-224. Provides a list of Venetian patents from 1475 to 1549. The list is also presented on-line at Wolfgang Pfaller's website. Available from: <http://www.wolfgang-pfaller.de/venpat.htm> (Last Accessed: 1st July 2009)

[181] There was much potential for the development of an incentive system from the available texts of the day. See Stein, P., *Roman Law in European History* [Cambridge University Press, 1999, Cambridge] Part III, 43-52

Targeted as the patent grants were on attracting those skilled in particular crafts for the pragmatic benefits conferred on a state's ruling classes,[182] the intellectual justifications for patent grants would be invented later.

1.1.2. **Migrating Know-How**

During the next century, or so, the practice of granting patents spread from the Italian City States to other Western European countries.[183] It is clear that European progress in the manufacturing arts was a product of the slow migration of superior technological achievements from the advanced civilisations of the East;[184] civilisations to whom the notion of patent grants for inventions were alien. The patent or monopoly grant was a way of stimulating a more rapid acquisition of the industrial arts by attracting those skilled in respective crafts to settle in the franchise granting state. An examination of early patent grants is exemplary of this and little importance is placed on the idea of the 'inventor' as the first originator of an invention. The essential requirements for a grant to be made were the importance of the industry and that the invention was new within that kingdom.[185] Geographically isolated, technological migration to England

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[182] For example in 1507, the Council of Ten, Venice, granted an exclusive twenty-year privilege for the introduction of the 'secret art' of mirror making to the city state. Nesbit, A., *Glass. With numerous woodcuts* [Chapman & Hall,1878, London] 90

[183] In 1467, a monopoly was granted in Berne for the manufacture and sale of paper. See Kohler, J., *Handbuch des deutschen Patentrechts in rechtsvergleichender Darstellung* [Verlag, 1900, Mannheim] 21, citing: Zeitschrift für schweizerisches Recht, N. F. xv, pp. 6 ff.; also see Renouard, A-C, *Traité des brevets d'invention* [Guillaumin, 1844, Paris] 79-80

[184] Prager, F. D., and Scaglia, G., Brunelleschi: Studies of his Technology and Inventions [MIT Press Cambridge, Massachusetts, 1st Ed., 1970] 141-142

[185] In England for examples see: *Calendar of Patent Rolls* 5 Ed. III, p. I, m. 25; 10 Ed. III, p. I; 42 Ed. III, p. I; 18 H. 6. Franc. 18. m. 27. We might draw parallels with this notion of

from the East was slower than on the Continent. As a result throughout the Middle Ages the English industrial achievements were considerably inferior to the Continental Kingdoms[186] and the Low Countries.[187] Thus, to increase the rapidity of industry skilled immigration it was during this period that England began to make patent grants for inventions.

1.1.3. **In England**

The first record of a patent grant to the introducer of a *newly* invented process in England dates from 1440.[188] It was granted to John of Sheidame for the introduction of a method of manufacturing salt on a scale previously unattempted in England, Ireland, Wales and Scotland.

During the Tudor period (1485–1603) the patent system became a tool of the Crown for encouraging skilled foreign artisans to enter into Crown service.[189] As clandestine negotiations replaced open letters and monopolies of production permitted the hoarding of skills essential to fledgling industries the objective of entering knew knowledge into the crafts and artisans of England underwent a radical change. Moreover, some royal patent privileges were granted, not to convey exclusive rights,

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'inventor' to the Patent laws of certain modern countries, For example Japan – see Japanese Patent Law Act 1959. Consolidated English translation is available at WIPO

[186] The disparate nations today subsumed into the modern France, Germany, Italy and Spain

[187] Wyndham Hulme, E., 'The History of the Patent System under the Prerogative and at Common Law' (1896) 12 L.Q.R. 141, 141

[188] 18 H. 6. Franc. 18. m. 27

[189] Wyndham Hulme, E., 'The History of the Patent System under the Prerogative and at Common Law' (1896) 12 L.Q.R. 141, 144

but to permit the addressee to do that which was otherwise prohibited.[190] Royal patent privileges were also increasingly used to award lucrative monopoly rights to court favourites and those capable of buying royal favour.[191]

In England during the reign of Elizabeth I (1533-1603), her minister, Lord Burghley (1520-1598), granted a series of patents with a view to encouraging foreign inventors to import their inventions and work them in England. Realising the potential of letters patent to unfetter manufacture from local custom and the jurisdiction of the established trades, the letters patent also served to diversify and establish new industries, in some cases ousting former local monopolies.[192] Industry, however was rapidly outgrowing local regulation and against the will of Parliament becoming national.[193] Thus, national policy for regulation was needed, but this brought about resistance. Nevertheless, England with its

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[190] Malapert, F., *Notice historique sur la legislation en matière des brevets d'invention* (1878) 3 *Journal des Economistes* 100; see Machlup, F., An Economic Review of the Patent System: Study of the Subcommittee on Patents, Trademarks, and Copyrights of the Committee of the judiciary (1958) US Senate, 85th Congress, 2nd Session, Study Number 15, Washington: United States Government Printing Office 2

[191] Machlup, F., An Economic Review of the Patent System: Study of the Subcommittee on Patents, Trademarks, and Copyrights of the Committee of the judiciary (1958) US Senate, 85th Congress, 2nd Session, Study Number 15, Washington: United States Government Printing Office 2

[192] Price W. H., The English Patents of Monopoly [Harvard University Press, 1913, Cambridge] 6

[193] For example, 5 Eliz. c. 4, statute of apprentices; For earlier statutes against migration of artisans from towns to the countryside see: 14 & 15 Hen. VIII, c. 1, country weavers are not permitted to deal with foreigners; 14 & 25 Hen. VIII, c. 3, the protection of Norwich artisans against neighboring competition. 21 Hen. VIII, c. 12, the protection of Bridport

"... fair degree of economic unity, with the narrower guild regulations and local exclusiveness already declining, with a sovereign who in practice was well-nigh absolute, who surrounded herself with ministers possessing at least the best practical economic ideas that the time afforded, and who was interested in the industrial.."[194]

was well placed to lay the seed for the development of a national patent policy.

However, Elizabeth I also continued the use of letters patent as a form of political capital to privilege favourites and assuage creditors.[195] Moreover, whilst the original patent grants had conveyed a ten-year privilege, the duration had gradually grown becoming twenty, twenty-one, and thirty. Worse yet for the burgeoning desire for greater liberty in commerce, some monopolies to favoured individuals[196] became renewable.[197]

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artisans against neighboring competition; 25 Hen. VIII, c. 18, the protection of Worcester artisans against neighboring competition; 5 & 6 Edw. VI, c. 24, the protection of Norwich artisans against neighboring competition; 2 & 3 Ph. & M. c. 7, the weavers' act.

[194] Price W. H., The English Patents of Monopoly [Harvard University Press, 1913, Cambridge] 7

[195] See starch patents: Pat. 3 Eliz. pt. 9 (15 April 1588); Pat. 36 Eliz. pt. 13 (6 July 1594), and Pat. 4o Eliz. pt.16 (20 May 1598); and their enforcement: Hist. MSS. Com. Cal. Salisb. Pap. v, at 532 & 533

[196] See Pat. September 1, 1585, which granted the lucrative monopoly on salt manufacture to Thomas Wilkes. Hughes, E., The English Monopoly of Salt in the Years 1563-71 *English Historical Review* (1925) 40 (159) 334-350

Considerable pressure eventually persuaded even the "illustrious"[198] and "well-neigh absolute"[199] Elizabeth I, on 28 November 1601, to issue the Proclamation concerning Monopolies.[200] The proclamation was directed at the reform of "many abuses and misdemeanours committed by patentees of certain privileges and licenses, to the general good of all her Majesty's loving subjects."[201] The reform was in effect the annulment of all the letters patent Elizabeth I had granted. The proclamation commands that no assistance be given to enforce the letters patent she had granted and that instruments that had been issued for enforcement of patents granted prior to the proclamation also be ignored.[202]

Elizabeth I continued to grant monopolies as privileges to political creditors until the end of her reign.[203] James I, In spite of his proclamation on 7 May 1603 suspending all letters patent, and his speech at the opening of Parliament the following year,[204] followed his predecessor's trend granting creditors monopolies through letters patent as an exercise of his

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[197] Wyndham Hulme, E., 'The History of the Patent System under the Prerogative and at Common Law' (1896) 12 L.Q.R. 141.

[198] Cornish, W., Intellectual Property: Patents, Copyright, and Allied Rights [Sweet and Maxwell, 1999, London] 111

[199] Price W. H., The English Patents of Monopoly [Harvard University Press, 1913, Cambridge] 7

[200] Brit. Mus. Proc. Coll. (G. 6463-388)

[201] Price W. H., The English Patents of Monopoly [Harvard University Press, 1913, Cambridge] 156

[202] Proclamation concerning Monopolies 1601, Brit. Mus. Proc. Coll. (G. 6463-388) paragraph 7

[203] *Darcy v. Allin* (1602) 11 Co.Rep. 846

[204] Parl. Hist. i, pp. 977 ff.

prerogative powers. This was to end with the Statute of Monopolies in 1624.

In the second session of Parliament, January to May 1606, patents of monopoly were a major cause of parliamentarian concern[205] resulting in the Petition of Grievances.[206] Before the issue of the patents of monopoly was brought to a confrontation, James I dissolved Parliament. By this time there was much uncertainty and speculation as to the value of a patent. After all James I had made strong declarations of his unwillingness to grant new patents and yet continued to do so; that the courts of common law had been set to administer some patents, but not others; commingled with the murky legacy of patents of monopoly from Elizabeth I's day. By 1614, following the loss of a £100,000 pounds per annum revenue, James I found himself short of funds.[207] To replenish his monies he embarked on a series of patent of monopoly grants. The result was an incredible failure, with losses of many thousands of pounds in schemes such as the alum and glass monopolies, that made no net profit.[208] Whilst other schemes such as the licensing of inns, of ale-houses, the gold and silver thread

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[205] Journals of the House of Commons, 9 April 1606

[206] See Journals of the House of Commons, 9 April 1606 316-318; State Papers (Domestic) 7 July 1610; Russell, C., Unrevolutionary England, 1603-1642 [Hambledon Press, 1990, London] 44-46

[207] Prothero G. W. *Statutes and Constitutional Documents Illustrative of the Reigns of Elizabeth and James I 1558-1625* [Oxford University Press, 1894, Oxford] at lxxxiii

[208] Gardiner S. R. *History of England 1603-42.* volume 4 [Camden Society, 1893, London] 21; Somers, Tracts, ed. Scott, W., [, ii, pp. 364-400, and Sloane, 2904; Harl. 3796; State papers (Domestic) 27 August 1619

monopoly, and subsidy of the new draperies yielded a mere nine to fifty pounds per annum[209] depending on the account.

1.1.4. **New Statute**

When in 1621 a new Parliament had to be called, the abusive monopolies were at the forefront.[210] By the end of the year a bill against the monopolies had already been put before both Houses.[211] The Lords rejected the bill. But threw it out, not because of its objective, but rather due to its language which was deemed unflattering of the king.[212] A joint committee of both Houses drew up another bill that was finally passed by both Houses in May 1624. The Statute of Monopolies[213] brought a radical change to the allocation of monopolies, their durations and the right by which they were granted and challenged.

Until the Statute of Monopolies, in spite of James I's contrivances to distance himself from the grant of some patents, all patents had stemmed from the prerogative power of the monarch. The Statute changed that, subjecting "forever hereafter" the force and validity of patents of monopoly

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[209] Gardiner S. R., History of England 1603-42. volume 4 [Camden Society, 1893, London] 33

[210] Gardiner S. R. History of England 1603-42. volume 4 [Camden Society, 1893, London] 33-35

[211] Journals of the House of Lords December 1, 1621

[212] Journals of the House of Lords December 3, 1621

[213] 21 Jac. I, cap. 3. A. D. 1623-24. An act concerning monopolies and dispensations with penal laws and the forfeitures thereof.

to the common law.[214] Moreover, the Statute declared the duration of patents was limited to a

> "...term of fourteen years... to be made of the sole working or making of any manner of new manufactures within this realm, to the true and first inventor and inventors of such manufactures ..., so as also they be not contrary to the law nor mischievous to the state, by raising prices of commodities at home, or hurt of trade, or generally inconvenient, the said fourteen years to be accounted from the date of the first letters patents "[215]

Considering James I belief in the absolute power of kings,[216] that the monarch was dependent on parliament to raise funds, and the potential power and wealth that the ability to grant monopolies brought the king, then the Statute of Monopolies was also a measure weakening the monarch. However, the Statute of Monopolies is far more significant than an attrition of prerogative powers, it set the foundations for a modern law of patents. Monopolies in manufacture and craftsmanship were now the sole purview of the first person to petition as inventor.[217] Gone were the monopolies renewable *add infinitum* that served as barriers to industry and in their place, the monopolies on new arts and crafts were limited to a term corresponding to two terms of apprenticeship. There were substantial

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[214] Statute of Monopolies 1624, §II

[215] Statute of Monopolies 1624, §VI

[216] See Tanner, J. R., *Constitutional Documents of the Reign of James I: A. D. 1603-1625* [Cambridge University Press, 1930, Cambridge] 4-22

[217] See §7(3)Patents Act 1977

derogations and exceptions,[218] but §VI, Statute of Monopolies 1624, would be of significant effect in determining the parameters of new patent grants.

1.1.5. **Protectionism**

The Eighteenth Century was an era of strong national protectionism with increasing competition in international trade, each nation's technological secrets were their advantage and so many regimens attempting to prevent technology transfer were put in place.[219] The industrial driving force however, and the source of England's prosperity was the wool trade. In 1700, cloth constituted approximately 70 per cent of English exports. It continued to comprise more than half of England's exports until the 1770s.[220] Without the strength of the wool trade and the protectionism afforded it,[221] the British industrial revolution might have been impossible, or very nearly so.[222]

Patents on the other hand although they had served to attract new methods of manufacture and new industries, were as Britain was becoming more technologically advanced in comparison to other nations,

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[218] See Statute of Monopolies 1624 §§: V, VII, IX, XI, XII, XIII, XIV

[219] Mantoux, P. *The Industrial Revolution in the Eighteenth Century* [MacMillan Company, 1961, New York] 237-238

[220] Musson, A., *The Growth of British History* [BT Bratsford Ltd, 1978, London] 85

[221] Chang, H-J., Kicking away the ladder: Development strategy in historical perspective. [Anthem Press, 2004, 1st Ed., 2nd Reprint, London] 19-24

[222] Davis, R. English Foreign Trade, 1700-1774 (1962) 15(2) *Economic History Review* 285-303

becoming a hindrance.[223] Towards the end of the 18th Century the courts began to impose a requirement that patentees make a sufficient statement[224] about their invention in return for the upholding of their monopoly.[225] Around this time there was a realisation that patents could be used to glean information about the technical specifications of an invention and thereby permit competitors to improve their own methods. The requirement for an adequate description of the invention became more of an issue within the courts, with competitors claiming that the specification was inadequate or that the invention was useless. Whilst disclosure of a specification may have been useful to some members of an industry, they also made prevention of technology export more difficult.[226]

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[223] Boehm, K., *The British Patent System*, Volume I: *Administration* [Cambridge University Press, 1967, Cambridge] 22-26; also see Boldrin, M. & Levine, D. K., *Economic and Game Theory: Against Intellectual Monopoly* [e-publication 2008] available at: <http://levine.sscnet.ucla.edu/general/intellectual/againstnew.htm> (Last Accessed: 1st July 2009) Chapter 1. Appraises the use of patent monopoly by Watt and its effect on the technological advancement of steam engine technology. "...[T]he evidence suggests that Boulton and Watt's patent retarded the high-pressure steam engine, and hence economic development, of about 16 years." At 15

[224] *Liardet v. Johnson* (1780) 1 Y. & C.C. 527. The defendant claimed that they had not infringed the plaintiff's patent on a method of making of stucco, because the specification did not properly describe the making of stucco. The case came before Lord Mansfield, who left deliberation of whether stucco could have been made by a workman from the specification.

[225] Adams, J., Intellectual property cases in Lord Mansfield's court notebooks (1987) 8(1) *Journal of Legal History* 18-24

[226] Cornish, W., *Intellectual Property: Patents, Copyright, and Allied Rights* [Sweet and Maxwell, 4th Ed., 3rd Impression, 1999, London] 112

1.1.6. **Patent Reform**

For patents to become workable significant changes were needed; the difficulties in obtaining patents, the uncertainty of a patent's validity, the difficulties in deriving revenues from a patent, and the demands of the manufacturing industry, needed to be addressed. In 1883 substantial changes were made to the English patent system:[227] Fees were reduced, a modern patent office was introduced in place of the Commissioners and applications were examined for formal defects and sufficiency of description.[228] There was however, great reluctance in England to introduce a patent administration who would examine applications with respect to the prior art, even though this had been done by the USA patent office since 1836.[229] Moreover, patent texts became available, suggesting that the concept of patent law had moved from sporadic and obscure acts to an accessible body of law that could begin to take a more concrete and coherent form.[230] With the ratification of international treaties[231] requiring a reciprocation of patent protection[232] the utility of the patent as an

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[227] Patents, Designs and Trade Marks Act 1883

[228] Patents, Designs and Trade Marks Act 1883

[229] Cornish, W., *Intellectual Property: Patents, Copyright, and Allied Rights* [Sweet and Maxwell, 4th Ed., 3rd Impression, 1999, London] 112

[230] For example, Terrell, T., *The Law and Practice Relating to Letters Patent for Inventions* [Sweet & Sons, 1889, London]; Frost, R., *A Treatise on the Law and Practice Relating to Letters Patent for Inventions* [Stevens & Haynes, 1891, London]. Patent texts were also appearing in other jurisdictions: Bert, E., *Brevets d'invention et marques de fabrique* (*Supplement au Genie Civil)* [Société des ingénieurs civils, 1891, Paris] (France); Walker, A. H., *Text-Book of the Patent Laws of the United States of America* [L. K. Strouse & Co., 1889, New York] (USA)

[231] Paris Convention for the Protection of Industrial Property, 20th March 1883

[232] Article 2, Paris Convention 1883: National Treatment for Nationals of Countries of the Union – the so-called principle of national treatment.

instrument of national market protectionism was almost ended.[233] These significant changes were supplemented by progressive administrative reforms that led to the creation of the Patent Office in 1852.[234]

Nevertheless, between 1883 and 1949, policy in the courts remained disfavourable to the grant of patent monopolies, as the monopolies were seen as being "generally contrary to the public interest."[235] However, from 1949 onwards the courts stance changed and policy once again became favourable to the grant of patent monopolies.[236] This substantial change in attitude may have been the intellectual result of several factors. In particular the economic conditions prevalent in a post war torn Europe, and the growth of large corporations with an expansionist agenda were most likely important. For the corporations provided employment and the potential of economic recovery, they also had the means to convey their desire through a language appreciated by the judges.

> "It was the patent profession rather than the corporations themselves who saw the potential benefits of the patent system to the corporate sector."[237]

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[233] Little effort was made to reduce the extra costs of infringement actions brought against infringers in other member states of the Convention, with respect to the costs that would be incurred if the infringement and patent holder were of the same jurisdiction.

[234] Bently, L., and Sherman, B., Intellectual Property Law [Oxford University Press, 2004, 2nd Ed., Oxford] 326

[235] *Obiter dicta per* Lord Salmon LJ, in *Ethyl Corporations Patent* [1972] RPC 169 at 193

[236] *Obiter dicta per* Lord Salmon LJ, in *Ethyl Corporations Patent* [1972] RPC 169 at 193

[237] Drahos, P; Braithwaite, J., *Information Feudalism: Who Owns the Knowledge Economy?* [Earthscan Publications Ltd, 1st Ed., 2002, London] 43

1.1.7. **Dominion Comes**

Patent professionals, perhaps foremost of which was Edwin J. Prindle (New York Bar, Secretary of the Patent Committee of the National Research Council, President of the New York Patent Law Association, Chairman of the Patent Committee of the American Chemical Society), who saw the patent system as a powerful and fundamental tool of business.[238] Prindle principally attributed the USA's ascent to global trade dominance as a result of the patent system.[239] He advised businesses that the patent was the most effective method of controlling competition,[240] and enunciated the disadvantages of not making use of the patent system.[241]

Corporations were quick to seize on a vehicle that could help them hold their lead-time and exclude others from what they perceived as their markets. In the larger corporations departments of intellectual property lawyers came into existence whose role was to strengthen the corporation through strategic management of intellectual property, to police the work of the corporation's research scientists so that none of their valuable

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[238] Drahos, P; Braithwaite, J., Information Feudalism: Who Owns the Knowledge Economy? [Earthscan Publications Ltd, 1st Ed., 2002, London] 44

[239] Prindle, E. J., 'The marvellous performance of the American patent system' (1927-28) 10 Journal of the Patent Office Society 255, at 258; Prindle, E. J., *Patents as a factor in manufacturing* [The Engineering Magazine: Works Management Library, 1908, New York] 13

[240] Prindle, E. J., *Patents as a factor in manufacturing* [The Engineering Magazine: Works Management Library, 1908, New York] 14, 81

[241] Prindle, E. J., *Patents as a factor in manufacturing* [The Engineering Magazine: Works Management Library, 1908, New York] 102

technologies could be taken up by competitors and to look for weakness and opportunity in their competitor's intellectual property.

It was not the patent system as such that gave the USA rapid global trade dominance, but rather the economic hardships the European powers suffered during World War I. Once the USA corporations had emerged onto these markets and begun to cater to the demands their reeling European competitors were unable to supply, the patent became an effective tool for baring competitor's recovery and preventing entry to the new technology markets the growing corporations were able to buy up or create.

Once this dominant equilibrium was established the patent served as a buffer between the market incumbent and any would be competition. Indeed the foresight of Prindle and his colleagues in promoting the use of intellectual property to business had placed USA business on a good footing to enter foreign markets with impunity. Cartels were illegal but the patent presented a legal means of dividing up markets. Moreover, it was a device recognised in most of the industrial nations, even if it had fallen into disfavour as it had in Britain. Corporations and the USA patent profession saw the opportunity to expand the benefits of their control and intellection property agreements were pushed into the international forum. Better still the problems of enforcement previously experienced by commodity cartels can now be dealt with in the public forum as government granted monopolies. The technology cartels having experienced the monopoly

power that their intellectual property walls granted, pressed for the establishment of international treaties favouring their interests. Europe, particularly Germany,[242] readily followed in the USA's wake. After all it had corporations of its own and the developing countries moving towards their own semi-liberation from colonial military dominance were rich with resources and ripe for technological feudalism.

1.2. **Rise of the Pharmaceutical Industry**

The pharmaceutical industry owes its origins to a chemical industry that developed out of the demands of other industries. The beginning of the chemical industry might be linked with the changes in philosophy and the development of an approach that could be termed scientific to the production of sulphuric acid, which occurred during the Eighteenth Century.[243]

By the Nineteenth Century, discoveries and dissemination of theories concerning organic compounds[244] were chiefly responsible for the rise of a

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[242] Despite the severe attenuation of its industrial power as a result of two world wars still retained its industrial expertise.

[243] Aftalion, F. A., *History of the International Chemical Industry*. Benfey, O. T. (Trans.) [University of Pennsylvania Press, 1991, Philadelphia] 10-11

[244] Laboratory synthesis of organic compounds that had previously only been obtained from the nature became possible. For example the industrial synthesis of ethanol: "By heating carbon (coke or charcoal) in the electric arc surrounded by an atmosphere of hydrogen acetylene C_2H_2 is formed. By an easy process acetylene can be made to combine with more hydrogen so as to produce ethylene, C_2H_4. Ethylene disolves in

new industry concerned with the manufacture of synthetic dyestuffs.[245] Driven by certain factors such as the demand for new and durable colours, the need to dispose of coal tar and trends in pure chemistry research, fashion and medicine, the industry grew quickly.[246]

1.2.1. **New Research Paradigm**

German dyestuff companies initially on no stronger footing than those in Britain and elsewhere realised the benefits of highly organised industrial research.[247] The degree of testing necessary to achieve a successful dye disfavoured the single chemist. A large team of unskilled chemists under the direction of a skilled chemist could, if working systematically, perform many more tests than a single far more skilled chemist ever could.[248] Once a candidate for a successful dye was discovered, its refinement and the careful organisation of its production could be passed on to a dedicated team of experienced scientists. Indeed with this model of

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concentrated sulphuric acid, and the compounds thus formed when mixed with water and distilled, yields alcohol, C_6H_2O. The alcohol formed is identical in every respect with alcohol produced by fermentation of sugar." Tilden, W. A., *Chemical Discovery and Invention in the 20th Century* [George Routledge & Sons Ltd, 1917, 2nd Ed., Revised, New York] 834

[245] Dutfield, G., Intellectual Property Rights and the Life Science Industries: A Twentieth Century History [Ashgate, Aldershot, 1st Ed., 2003] 73-87; For a detailed account see: Travis, A. S., The Rainbow Makers: Origins of the Synthetic Dyestuffs Industry In Western Europe [Lehigh University Press, 1st Ed., 1993, Lehigh]mm

[246] Travis, A. S. (Ed.). "150 Years of the Coal-Tar Dye Industry, 1856-2006," special issue of History and Technology, 22(2) (2006) 115-118, 131-224

[247] Drahos, P; Braithwaite, J., Information Feudalism: Who Owns the Knowledge Economy? [Earthscan Publications Ltd, 1st Ed., 2002, London] 40

[248] Beer, J. J., 'Coal Tar Dye Manufacture and the Origins of the Modern Industrial Research Laboratory' (1958) 49 *Isis* 123-131

industrial research and production the chemists came into contact with many more discoveries than a lone investigator could, and thereby gained experience phenomenally faster. To the rest of the dyestuff industry it seemed that within a relatively short time the German dye manufactures had the formulations for an enormous number of dyes and experts unmatched by any other dye producing nation. By combining this mode of research savvy with skilful use of secrecy and patents to maintain and prolong their lead-times German dye manufactures were able to dominate the global dye market.

1.2.2. **Dominating Colour**

Patents are likely to have played a key role in control of the organic dyestuff market, especially in the latter half of the nineteenth century. The German Patent Law of 1877[249] provided a common patent regime for the German states and equipped the burgeoning organic dyestuff manufactures with a process patent valid across the whole of Germany.[250] Between 1877 and 1904 approximately fifty per cent of the total number of chemical patents in Germany were related to the dyestuff industry. Out of the 12,128 chemical patents granted in Germany during this period,

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[249] The act was responsible for the creation of the *Kaiserliches Patentamt* (the Imperial Patent Office) in Berlin. Auspiciously, the first German patent granted was a process patent (product patents were not available under the Act) for a red ultramarine colour by the inventor Johann Zeltner of Nürnberger Ultramarin-Fabrik. Retrieved from Deutsches Patent und Markenamt history. Available at: <http://www.dpma.de/english/the_office/history/index.html> (Last Accessed: 1st July 2009)

[250] Marsh, U., Strategies for success: Research organisations in German chemical companies and IG Farben until 1936 (1994) 12(1) *History and Technology*: 223-232

approximately 3447 patents were for processes of bleaching and dyeing, and 3733 patents were related to processes for preparing colours, lacquers and varnishes.[251] Through these patents the German dyestuff manufacturers were able to systematically exclude competitors from German territories and influence the dyestuff trade in other countries.[252] In fact by the end of the Nineteenth Century ownership of sixty-six per cent of chemical patents in the USA were distributed between three German companies - Hoechst, Bayer, and BASF.[253] The world's dye market was also German dominated, with German firms controlling sixty per cent.[254]

As mentioned patents were not the only tool successfully exploited by the fledgling German chemical industry. Secrecy was also employed to advantage in the lengthening of lead times, and particularly potent where misleading patents were taken for processes that were in reality kept secret. Many German companies skilfully employed a combination of patents and secrecy against potential imitators.[255]

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[251] Haber, L.F., The Chemical Industry During the Nineteenth Century [Clarendon Press, 1958, Oxford] 293

[252] Liebenau, J., 'The management of high technology: The use of information in the German chemical industry, 1890-1930.' In Kudo, A, and Hara, T., (eds.) International Cartels in Business History [University of Tokyo Press, 1992, Tokyo] 65

[253] Liebenau, J., 'The management of high technology: The use of information in the German chemical industry, 1890-1930.' In Kudo, A, and Hara, T., (eds.) *International Cartels in Business History* [University of Tokyo Press, 1992, Tokyo] 65

[254] Muller Thurow, G., 'Industrialisation of Invention: a Case Study from the German Chemical Industry' (1982) 73 *Isis* 363-368

[255] Hounshell, D. A., and Smith, J. K., *Science and Strategy: DuPont R&D, 1902-1980* [Cambridge University Press, 1988, 1st Ed., Cambridge] 89-90

With dyestuffs composed of different compounds, as many of the compositional compounds as possible were patented. Those compounds, which could not be patented, were kept secret, as was the precise quantity of each compound in the dyestuff. Moreover, to further confound imitators misleading patents were registered. Sometimes an entire class of compounds would be patented, with only a few possessing the necessary properties for the dyestuff. Thus, imitators had a difficult and expensive task in discovering the correct composition of a marketed dye. Even when they were able to recreate a close imitation there was usually a significant delay between the availability of the original dye and the imitations. The most lucrative time for a new dye was its first entry to the market and the lead-time derived from this combination of patents and secrecy strengthened the profitability of new dyes. Typically those dyes whose composition remained undiscovered by imitators commanded prices of 40-50 per cent more than the standard colours of known composition.[256]

Traditionally doctors had produced their own medicines,[257] however as extraction of alkaloids became increasingly complex in the Twentieth Century[258] some chemical manufacturers saw the opportunity to produce

[256] Arora, A., 'Patents, licensing and market structure in the chemical industry,' (1997) 26(4-5) *Research Policy* 391-403

[257] Poynter, F. N. L., *The Evolution of Pharmacy* [Pitman Medical, 1965, London] 131-149

[258] Crellin, J. K., 'The Growth of Professionalisation in Nineteenth Century British Pharmacy' (1967) 11 *Medical History* 215-227

standard packages of chemicals from which doctors could continue to produce their medicines.[259]

1.2.3. **Dyes and Medicine**

The dyestuff manufacturers diversified their production by converting dye intermediates into chemicals that could be used to treat human conditions. Within the academic-industrial symbiosis dyes themselves also found a direct application to medical research with Paul Ehrlich's utilisation of dye tone changes to demonstrate reduction and oxidation in living cells. Ehrlich was thus able to develop a cellular surface model. Dyes found further application in medical research, as did the paradigm of research occurring in the German dyestuff manufacturers. Ehrlich's research team seeking a chemical that exhibited anti-microbial activity began a systematic screening of the chemical derivatives of atoxyl, a dangerously toxic chemical reported by Antoine Béchamp and used to treat skin illness.[260] Their coordinated examination of the biological activity of a lead compound through systematic chemical modifications was a first, and has since been the basis for most modern day pharmaceutical research. Arsphenamine, later trade named Salvarsan, was reported in 1908 by Jordan Wilson as a discovery resulting from the systematic screening method advocated by Ehrlich. An analogue of an azo dye and arsenic, Salvarsan is both a good example of the closeness of the dyestuff industry to the manufacture of medicines; and of the developing understanding of

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[259] Sneader, W., *Drug Discovery: the Evolution of Modern Medicines* [John Wiley, 1985, London] 41-42

[260] Ihde, A. J. *The Development of Modern Chemistry* [Dover, 1984, New York] 697-698

medicines, since it is an artificial chemical compound containing arsenic that does not produce the ordinary effects of arsenic poisoning, but is still toxic to *Spirochœta pallida*.

Until the mid Nineteenth Century the approach to drug therapeutics had remained entirely empirical. However, with the first chemical analyses of naturally occurring drugs the mechanism of drug action could be understood in physiological terms. What emerged was a new paradigm to the invention of medicines. Chemical and physiological knowledge, rather than trial and error, became the foundation of medicine development. As the eminent chemist Sir William Tilden noted in 1917,

> '...[t]he discovery of new remedies depends more and more on a combination of chemical and physiological knowledge.'[261]

1.2.4. **Consequence of War**

World War I instigated a significant change to the German domination of the synthetic dye industry in the United States. With the British blockade of Germany, German dye exports could not reach the USA which suffered a dye shortage. With the loss of German chemical products not only the USA was to suffer a shortage of chemicals, but also other countries such as Britain. Which caused recognition of the paucity of skilled chemists and

[261] Tilden, W. A., Chemical Discovery and Invention in the 20th Century [George Routledge & Sons Ltd, 1917, 2nd Ed., Revised, New York] 339

a renewed consideration of the academic-industrial symbiosis instituted in Germany at the beginning of the Nineteenth century.[262]

Unlike Britain, the production of organic chemicals in the USA prior to the war had been very limited, with most of the market supplied by European companies. For example, chemicals for use in university and industrial research laboratories were imported from Germany (Kahlbaum's Chemicals) and Great Britain (Boots Ltd.).[263] DuPont, a manufacturer of gunpowder and the largest supplier of gunpowder to the United States military, had been diversified after rulings against it under the Sherman Act.[264] It saw potential in the USA's dye shortage for the development of one of its diversified branches and found itself well placed in infrastructure and facilities to assume the supply deficit resulting from the German dyestuff manufacturers' inability to get their products to the USA's market.

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[262] Johnson, J. A., 'the academic-industrial symbiosis in German chemical research, 1905-1939' in Lesch, J. E. (Ed.) *The German chemical industry in the twentieth century* [Kluwer Academic Publishers, 2000, new York] 15-56; For a detailed treatment see Johnson, J. A., The Kaiser's Chemists: Science and Modernization in Imperial Germany [Chapel Hill Press, 1990, Chapel Hill]

[263] Fisher, H. L. "Organic Chemistry. 1876-1951," in "Chemistry: Key to Better Living," Diamond Jubilee Volume, American Chemical Society, Washington, DC. (1951) 52- 57

[264] 15 U.S.C. §1–7. The impact of the Sherman Act's provisions were significant for business, as hereto the objective of business had been to grow to monopolise markets and thereby control and direct trade. This was no longer overtly possible. 15 U.S.C. §1: "Every contract, combination in the form of trust or otherwise, or conspiracy, in restraint of trade or commerce among the several States, or with foreign nations, is declared to be illegal." And, 15 U.S.C. §2: "Every person who shall monopolize, or attempt to monopolize, or combine or conspire with any other person or persons, to monopolize any part of the trade or commerce among the several States, or with foreign nations, shall be deemed guilty of a felony..." For earlier UK control over monopolies see, 51 & 52 Hen. 3 Stat.1; 51 & 52 Hen. 3 Stat.6; 23 Edw. 3; 27 Edw. 3, Stat.2, c.25; 25 Hen. 8 c.2

Collaborating with a British firm that had taken over a confiscated Hoechst factory, DuPont quickly invested $11 million USD to develop expertise in the dyestuff manufacture.[265]

Moreover following World War I, Dupont's prosperity continued. As a result of the hyperinflation in Germany and also more directly from the war reparations[266] DuPont was able to obtain from the Chemical Foundation Incorporated non-exclusive licenses, on a royalty basis, for all German patents in the USA.[267] Thus, DuPont was well positioned to develop its global chemical presence. However Germany still possessed considerable chemical expertise and DuPont, despite the difficulties engendered by trade secrecy laws, undertook recruiting German chemists from their German companies by offering ten to fifteen times their salaries.[268] To further insulate the USA's markets from foreign companies, trade agreements and extremely high import tariffs[269] were put into place, thereby ensuring the growth of national corporations.

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[265] Hounshell, D. A., and Smith, J. K., *Science and Strategy: DuPont R&D, 1902-1980* [Cambridge University Press, 1988, 1st Ed., Cambridge] 94

[266] Treaty of Versailles 1919, articles: 231-248

[267] See Steen, K., 'German chemicals and American politics' in Lesch, J. E. (Ed.) *The German chemical industry in the twentieth century* [Kluwer Academic Publishers, 2000, New York] 334-345

[268] Hounshell, D. A., and Smith, J. K., *Science and Strategy: DuPont R&D, 1902-1980* [Cambridge University Press, 1988, 1st Ed., Cambridge] 96

[269] On the USA's import tariffs see Irwin, D. A., 'From Smoot-Hawley to Reciprocal Trade Agreements: Changing the course of US Trade Policy in the 1930s' in Bordo, M. D., Goldin, C. D., and White E. N. (eds.) *The Defining Moment: The Great Depression and the American Economy in the 20th Century* [Chicago University Press, 1998, Chicago] 327-333

The post war period 1916 to 1923 was also marked by substantial industrial support for the production of chemical literature and research organisations. Most importantly the emergence of industry funded organisations constituted of an academic-industry symbiosis.[270] Britain having found itself during the war short of trained chemists able to produce the essential intermediates it had previously imported from Germany for its industries undertook a serious program of chemistry instruction.[271]

As a result of these changes significant breakthroughs in knowledge occurred[272] and the synthetic dyestuff manufacturers, like DuPont, trading in the developing pharmaceutical market, were well placed to take advantage of the new knowledge.

Competition was eschewed in favour of cartels both national and global. These cartels employed contracts, patent licenses, and economic force to

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[270] Kohler, R., 'A Policy for the Advancement of Science: the Rockefeller Foundation 1924-1929' (1978) 16 *Minerva* 480-515; Johnson, J. A., 'the academic-industrial symbiosis in German chemical research, 1905-1939' in Lesch, J. E. (Ed.) *The German chemical industry in the twentieth century* [Kluwer Academic Publishers, 2000, New York] 16

[271] Matthews, L. G., *History of Pharmacy in Britain* (E. & S. Livingstone (Longman Books), 1962, Edinburgh and London] 118-127

[272] For example, the creation of organic compounds increased exponentially after Marcellin Berthelot demonstrated how, from starting with minerals, carbon can be combined step by step with hydrogen, oxygen and nitrogen to produce organic compounds. One example of the importance of Berthelot's work is the synthetic formation of ethanol, C_2H_6O. From his hypotheses Berthelot was able to design a synthesis.

maintain and increase their market shares and to deter competitors from entering the market.[273]

Following the miracle successes that Howard Florey and Ernst Chain were able to demonstrate from penicillin, the immediate benefit of penicillin to the war effort was realised. Fledgling pharmaceutical companies received enormous government funding in order to scale up their production facilities and create penicillin manufacturing plants. Ironically, Florey believed it would be inappropriate to patent penicillin.[274]

A sustained demand for penicillin arose from the civilian population, ensuring that penicillin manufacturers did not need to downsize. Moreover, with the reception of penicillin a burgeoning demand for more wonder drugs was stimulated.

The post war reception of science and technology was far more favourable than ever previously. Technology had provided the decisive elements to the engagements and thus was the key to future advantage. As such policy needed to be adapted to promote science and innovation, but it also

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[273] Good accounts of this period can be found in: Haber, L.F., The Chemical Industry During the Nineteenth Century [Clarendon Press, 1958, Oxford]; Haber, L.F., The Chemical Industry: 1900-1930 [Clarendon Press, 1971, Oxford]; Haynes, W., 1954, American Chemical Industry, Volumes 1-6 [Van Nostrand, 1954, New York]; and Hounshell, D. A., and Smith, J. K., Science and Strategy: Dupont R&D, 1902-1980 [Cambridge University Press, 1988, 1st Ed., Cambridge]

[274] Doherty, P., 'Howard Florey' (November 3, 1999) Time Magazine. Available at: <http://www.time.com/time/magazine/article/0,9171,33700,00.html> (Last Accessed: 1st July 2009)

had to favour the growth of national industries and favour national interests overseas.

1.3. Role of Pharmaceuticals in Society

Pharmaceuticals are intrinsically linked to the longevity and welfare of humans. As a result they are an important part of a complex web of interactions: both social and economic in nature. Linked to human health, pharmaceutical demand is generally irregular and unpredictable. This is especially illustrated by the dearth of vaccines at the outbreak of pandemics[275] and the number of medicines disposed of each year.[276] Moreover, pharmaceuticals are not necessarily available or researched even if large populations suffer from an illness or condition. This is illustrated by the observation that a large proportion of diseases, perhaps ninety per cent, occur in the tropics but only five per cent of global health resources and research investment are directed towards those diseases.[277] Within Healthcare the role a pharmaceuticals is diverse.

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[275] Lopez, R. A., and Zorzopulos, J., 'Vaccine shortage for pandemic influenza: Can it be solved?' (2006) 24(15) *Vaccine* 2701; Cinti, S., 'Pandemic Influenza: Are We Ready?' (2005) 3(3) *Disaster Management & Response* 61-67; Daems, R., Del Giudice, G., Rappuoli, R., 'Anticipating crisis: Towards a pandemic flu vaccination strategy through alignment of public health and industrial policy' (2005) 23 (50) *Vaccine* 5732-5742

[276] Jesson, J., Pocock, R., Wilson, K., 'Reducing medicines waste in the community' (2005) 6(2) *Primary Health Care Research and Development* 117-124

[277] Godal, T., 'Fighting the Parasites of Poverty: Public Research, Private Industry and Tropical Diseases' (1994) 264 *Science* 1864-1866 at 1864

Pharmaceutical therapies can substantially reduce or substitute for hospitalisation, surgical intervention and enable quicker recovery times.

1.3.1. **Subjective Effect**

Medicines can also very individualistic in terms of the pharmacodynamics and pharmacokinetics that a particular user might experience. This complexity arises because an individual may be more or less sensitive to a medicine's active ingredient. Which may result in a range of responses that differ from other people undergoing the same pharmaceutical therapy. A wide variance of differences can arise from particularly adverse reactions leading to death to complete unresponsiveness to the drug. The most likely explanation for these variances is the extent of our physiological and biochemical knowledge. Thus, over time as our knowledge of physiology and biochemistry improve the responsivity of given patient to a medicine should become foreseeable.

This difference in the performance of medicines is particularly visible when competing patented pharmaceuticals for the same condition are available on the market. Poignant examples of the variance in effectiveness of active ingredients that differ very minimally can be seen amongst statins.[278] Where it is critical the administration of a pharmaceutical will immediately exhibit effectiveness it is especially important that sufficient information is available to permit informed selection. Within the context of statins, post-acute myocardial infarction in elderly patients is extremely

[278] Franco, O., Peeters, A., Looman, C., Bonneux, L., 'Cost effectiveness of statins in coronary heart disease' (2005) 59 J Epidemiol Community Health 927–933

illustrative of this.[279] As such it is important that medicines are made available with sufficient information to allow informed choices to be made in their selection, whether this is by a qualified healthcare professionals or a health care professional in conjunction with the consumer.

1.3.2 **Patient Choice**

Unlike most other areas of consumerism, the patient (consumer) has little choice with regard to most contemporary pharmaceuticals and there are a number of ways in which this distinguishes pharmaceuticals as a product from other objects of consumerism. Unless a medicine is out of patent, or has been extremely successful economically and the originator did not tie down all opportunities for market entry, there will be no other medicines on the market with bioequivalence. Moreover, the person choosing the medicine is usually a physician and not the consumer.[280] Another factor is that in some cases the consumer pays indirectly through insurance premiums or national health contributions and these collective schemes will set choice limiting parameters for payouts.

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[279] Zhou, Z., Rahme, E., Abrahamowicz, M., Pilote, L., 'Survival Bias Associated with Time-to-Treatment Initiation in Drug Effectiveness Evaluation: A Comparison of Methods' (2005) 162 (10) *American Journal of Epidemiology* 1016-1023

[280] Since an institution or individual can be decisive in which medicines are purchased for a large number of people, incentives to that institution may play a larger part in product validation than the superiority or price of a medicine. For example see, US Department of Justice, 'U.S. Files Suit Against Johnson & Johnson for Paying Kickbacks to Nation's Largest Nursing Home Pharmacy,' (15 January 2010) Available at: <http://www.justice.gov/opa/pr/2010/January/10-civ-042.html> (Last Accessed 13th April 2011. Omnicare Inc. v. UnitedHealth Group Inc., PacifiCare Health Systems, Inc., and RxSolutions, Inc., d/b/a Prescription Solutions 629 F.3d 697 (7th Cir. 2011)

Legal access to pharmaceuticals is controlled by national policy, which is usually implemented for drugs which are not considered illegal or dangerously unviable, through two modes of distribution: prescription drugs and pharmaceuticals which can be purchased in licensed outlets and are referred to as over-the-counter medicines.

Prescription pharmaceuticals tend to be more expensive and newer than over-the-counter drugs. This is a result of two factors. Firstly prescription drugs tend to be more expensive because almost all the active ingredients of the prescription drug will be patented, whilst the patents on active ingredients of over-the-counter medicines will have expired or lapsed. Secondly, over-the-counter pharmaceuticals are usually weaker formulations of older prescription drugs that have been deemed safe and effective for over the counter sales.

1.3.3. **Safe Choice**

For safety reasons prescription medicines are only available for a specific person, specified by the prescription and by then by a label attached to the packaging of the medicine. The person to whom the prescription is addressed is not legally authorised to share their prescription medicine with anyone else. By doing so they not only initiate tortuous liability, they may also be committing a criminal act, and be guilty of breaching their license to use the medicine from the patent owners. However, Over-the-counter medicines that are purchased by one person may be utilised by

another providing that the instructions on the enclosed information are complied with.

There is a sensible reason for the restricted use pedantry on prescription medicines. Prescription formulations of medicines are invariably much more potent than their OTC counterparts. As a result misuse of prescription formulations of medicines poses a greater risk to the user than an OTC formulation. As a proportion of autopsies examination findings prescription medicines are responsible for three times as many deaths as chemicals classified in law as narcotics. For example, an analysis of 168,900 autopsies conducted in Florida in 2007 found cocaine, heroin and methamphetamines resulted in 989 deaths, whilst prescription medicines killed 3,071 people (2,328 by opioid painkillers and 743 by pharmaceuticals containing benzodiazepine).[281]

In the USA, the Food, Drug, and Cosmetic Act 1938 empowered the FDA to undertake some regulation of food, cosmetics and pharmaceuticals, but did not provide clear guidelines on which medicines could only be sold following recommendation by a qualified physician and which would be OTCs. Subsequent amendments in 1951 and 1962 required that medicines could only be categorised OTC *iff* they were effective and

[281] Gutierrez, D., 'Prescription Drugs Kill 300 Percent More Americans than Illegal Drugs' (November 10, 2008) *Natural News*. Available at: <http://www.naturalnews.com/024765.html> (Last Accessed: 1st July 2009)

safe.[282] Which is why for some prescription medicines a weaker OTC formulation is available.

Declassification presents serious health considerations, as there are no organized systems for reporting the side effects and adverse indications which over-the-counter medicines might cause. As a result regulatory authorities and pharmaceutical manufacturers have no expedient method or clear indication of how widespread adverse incidents of over-the-counter drugs are. Frontline practitioners, particularly physicians undertaking research involving some observation of the over-the-counter medicines, and thereby medical journal publications are usually the first indications that an over-the-counter medicine posses a health care risk.

Another aspect of pharmaceutical labelling is an expiry date indicating a time after which it is unadvisable for the medicine to be used. The expiry date, in addition to health warning, and listing contents are traits medicinal packaging shares with processed foods. In the case of medicines an expiry date exists because the active components of medicines may degrade with time.[283]

1.3.4. **Consequential Choice**

Pharmaceuticals possess another important characteristic that defines their role in society. It is the nature of pharmaceuticals to provide

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[282] Wax, P. M., 'Elixirs, Diluents, and the Passage of the 1938 Federal Food, Drug and Cosmetic Act' (1995) 122(6) *History of Medicine* 456-461

[283] Expiry dates may also serve the function of discouraging parallel importing.

satisfaction only in the event of a perceived reduction or elimination of illness. Moreover because of the complex web of interactions and dependencies in contemporary society the effects of a successful pharmaceutical therapy or the absence of such a therapy may have considerable effects for other human beings.

Indeed, not developing a cure for a debilitating or lethal ailment has economic ramifications to the productivity of an industrious individual. For society *in toto* prevention of a debilitating illness will have an economic significance as the debilitated individual will become partially or totally dependant on other providers. Death or debilitation of a friend or loved one is likely to have serious social effect, especially where those directly affected are aware that death or debilitation were likely avoidable. Caring for debilitated people, particularly by their friends or loved ones is well documented to cause psychological trauma.[284] Moreover, regardless of whether the carer is vocational or professional, caring results in a loss to net social productivity; as labour, and therefore productivity, must be diverted to care for the unnecessarily debilitated individual. Premature dead also present a grave attenuation of social productivity through loss of

[284] Most standard guides for carers include sections on how to deal with the physchological burdens of caring and how to recognise symptoms that they may be suffering as a result of their caring activities. There are a formidable number of publications on the subject, two recent journal publications are: Noble, A. J., and Schenk, T., 'Posttraumatic stress disorder in the family and friends of patients who have suffered spontaneous subarachnoid hemorrhage' (2008) 109(6) *Journal of Neurosurgery* 1027-1033; Barton, K., and Jackson, C., 'Reducing symptoms of trauma among carers of people with psychosis: pilot study examining the impact of writing about care giving experiences' (2008) 42(8) *Australian and New Zealand journal of psychiatry* 693-701

their skills and experience, as well as their contributions to social networks. Consider, for example that between 1996 and 1998

> "...insurers and health maintenance organizations spent 16.8% more on prescription drugs."[285]

Over a twelve-year period, encompassing 1996 to 2008, this rise has been around 27% depending on the source of data, despite a greater spending in volume on unpatented medicines.[286] This rise reflects only a small portion of the cost both socially and economically of having high prices with respect to the cost of pharmaceuticals. Where a pharmaceutical is too expensive or the success of treatment to low to meet insurers parameters, neither insurers nor health care organisations will pay for that pharmaceutical.

There are also the consequences for personal integrity associated with illness. Certain illnesses have a social impact and therefore although not life threatening or debilitating these illnesses can inflict serious social consequences again leading to a loss of social welfare and net productivity for a society.

Yet there is a cost involved in creating a cure and making it available to those who need it. The method of meeting those costs successfully and of

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[285] *Wall Street Journal*, 29 June 1999, B4

[286] Composite data, sources: National Association of Health Underwriters; America's Health Insurance Plans; Australian Health Insurance Association.

providing an infrastructure for research, development and education must be considered. There are decisions to be made about the priority of medicine development. There are a plethora of questions that need to be resolved on moral and practical levels: *W*ho, ought/can have access to a medicine? For example how much time or productivity does successfully treating an individual with a medicine save when without treatment that individual would otherwise be unproductive due to sickness or death? How can we ensure availability and accessibility of medicines? Or recognise when administering medicines will lead to a successful outcome? What is the economic cost of creating an accessible supply of medicines? What is the economic cost of limiting access to medicines? What is the social cost of limiting access to medicines? What is the most efficient manner to balance the social and economic costs of providing access to medicines? Is there a conflict between efficiency and equity? Is there a priority to the allocation of resources to medicines and if so then how can it be determined? What scheme of morality should we adopt for deciding answers to these questions? Indeed if there are answers then they will come from policy that must be decided from the prevalent relations and values within a society.

The pharmaceutical possessed of its own special niche in the life of humankind has been given a unique legal identity. These distinguishing characteristics are essential to an understanding of the complexity of issues surrounding pharmaceutical innovation and its relation to pharmaceutical patents in the present system.

1.4 **Characterisation of Pharmaceutical Patents**

The patent resulting from the agenda of patent lawyers, industry leaders and post-war national protectionism is a complex creation of political agenda and pragmatic, if policy driven, decisions by courts[287] and trend setting repeat players.[288] It is a legal creation. It is a construct that does not share the attendant natural characteristics of real property, such as the physical limitation of real property to be used by a physically limited number of persons. As a result the principal demarcation of what characterises a pharmaceutical patent comes from the interpretation of legislation and the appreciation of scientific literature, and by institutions qualified to award or rescind patents. Together these institutions decide what can qualify as a patent on pharmaceutical subject matter.

1.4.1. **Patentable Subject Matter**

In the United Kingdom only the UK Intellectual Property Office and the European Patent Office (EPO) have jurisdiction to grant patents. Patents granted by the EPO are treated as if issued by the UK Intellectual Property

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[287] For example consider, *Diamond v. Chakrabarty*, 447 U.S. 303. 100 S.Ct. 2204. 65 L.Ed.2d 144; discussed in, Lumelsky, A., '*Diamond v. Chakrabarty*: Gauging Congress's Response to Dynamic Statutory Interpretation by the Supreme Court' (2005) 39 (3) U.S.F. L. Rev. 641-692

[288] For example consider the frequency of mentions within the UK patent practice manual that are derived from cases involving the following companies: Bayer, Ciba-Geigy, Eli Lilly, Glaxo Group, Kirin-Amgen Inc, Merck & Co Inc, Merrell Dow Pharmaceuticals, Pfizer, and Schering. The UK Intellectual Property Office Manual of Patent Practice is available from: <http://www.ipo.gov.uk/p-manual-practice.htm> (Last Accessed 22 February 2010)

Office.[289] For the most part the shared jurisdiction to grant patents is unproblematic.[290] UK regulations, practice directions and statutory implementing amendments closely follow the frequent European regulations on patents. It is from these regulations that the scope of patentable pharmaceutical subject matter in the UK is defined.

At present pharmaceutical patents may be held on almost any chemical or biological material. There are procedural considerations such as the formalities of application, revocation or invalidated and up to date payment of renewal fees, but these are less interesting than the actual scope of what is legally, as opposed to administratively, permitted to be a valid pharmaceutical patent.

With respect to biological material[291] Patents Act 1977 Schedule A2, which implements Directive 98/44/EC, provides that although biological products and processes are not excluded from the class of patentable objects *per se*, certain biological subject matter cannot constitute a patentable invention. For example, the human body or the simple discovery of one of its elements[292] are not patentable *per se*, nor are animal and plant

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[289] Patents Act 1977, §77(1) as amended.

[290] UK patent decisions exert an important influence on other jurisdictions, especially the European Union. Consider 'purposive construction,' Lord Diplock in Catnic Components Ltd v Hill & Smith Ltd [1982] RPC 183, 243; Kirin-Amgen v. Hoechst Marion Roussel Limited [2004] UKHL 46; [2005] R.P.C. 9

[291] "...any material containing genetic information and capable of reproducing itself or being reproduced in a biological system." Directive 98/44/EC Art.2(1)(a)

[292] Patents Act 1977 Sch. A2 para. 3(a). See Directive 98/44/EC Art.5(1)

varieties.[293] However, the technical process used to isolate or produce elements from the human body, including genes, may be patentable. For example Nuclear Factor κB, which is a key regulator of the human immune response to infection, is patented.[294] Furthermore, with regard to the narrow scope given to the definition of 'variety' by the EPO it is possible through careful drafting of patent claims to in effect patent animal and plant varieties.[295] This will only be possible where the distinctive characteristic of the variety is the product of a patented modification or gene that is not naturally expressed. For example, a seed plant that is capable of reproducing the distinctive characteristic would not be capable of being a 'patented variety.'[296] The patent on the modification or gene that gives rise to the distinctive characteristic of the variety however would be valid. For a patentable 'animal variety' there is a further hurdle that the genetic modification of the identity of the animal is not 'likely' to cause the animal suffering without any substantial medical benefit to humans or the animal.[297] As such actual manifestations of animal and plant varieties that

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[293] Patents Act 1977 Sch. A2 para. 3(f). See Directive 98/44/EC Art.4(1)

[294] Garber, K., Patently absurd? (2006) 24 *Nature Biotechnology* 737-739

[295] European Directive 98/44/EC Art.4(1). Also consider the European Patent Convention 1973 (as amended and revised in 2007) which states in Article 53 "Patents shall not be granted in respect of biotechnological inventions which, in particular, concern: (d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes."

[296] Consider, Patent Act 1977 §60(5)(a)(b), or in a commercial context for plants §60(5)(g), or §60(5)(h) for an animals.

[297] European Patent Convention 1973 Article 53(d)

can legally only be obtained by licence from the patent holder of the genetic modification are relatively few.[298]

1.4.2. **Patent Strategy**

Pharmaceuticals are obtained either by extraction of chemicals from organisms, through chemical synthesis, or a combination of both. The biologically active substance is called the active ingredient. The active ingredient is the most important component of the medicine and the most valuable. Patents will be filed on as many different aspects of obtaining, refining, testing and administering an active ingredient as possible. If an organism is the source of a chemical or gene needed for the formulation of an active ingredient then it is advantageous if either the organism or the components essential to the creation of the desired extract within an organism can be patented.[299]

The method of extracting the desired component of the active ingredient from an organism might in some cases, where it is novel and capable of industrial application even on a small scale, yield other patents. The processes of combining chemicals are another possibility for a patent. The combinations of one, two or three chemicals might in itself seem *obvious*. Particularly, if the mechanism is one that is well documented. However, if there is a chain of reactions, which will of course involve specific conditions, such as temperature and pressure, then it is possible

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[298] Examples would include organisms incorporating genetic use restriction technology

[299] *Moore v. Regents of the University of California* (51 Cal. 3d 120; 271 Cal. Rptr. 146; 793 P.2d 479)

through careful drafting to remove most vestiges of obviousness. Furthermore, many reactions proceed more expediently in the presence of a catalyst. The use of that catalyst and all similar catalysts, even if well known, might be describable as finding a new application in the particular reaction at hand providing it is not explicitly documented in the *state-of-the-art*. Whilst not 'new' or 'novel' in the ordinary meaning of the English language, the new use might readily qualify as 'novel' in patent terms. As a general rule, the more well known the function of a catalyst is, then the tighter the claim needs to be and the more complex the specification. Sometimes a reaction or catalyst will be too well known to make patenting attempts economically viable.

There are other components of the pharmaceutical that are necessary for it to work. As we mentioned, methods of administering the active ingredients are also possible patentable components of a pharmaceutical. Active ingredients are generally incorporated into a vehicle, such as a liquid, crystal, or cream, so that the active ingredient can be injected, swallowed or applied. Depending on the importance of the vehicle, particularly with respect to its impact on the effectiveness of the active ingredient, as many aspects of the vehicle as possible will be patented. Patents on the vehicle may also be on the method by which it is synthesised, or on the way it is combined with the active ingredient. However, the majority of vehicles for pharmaceuticals are standard

formulations and thus, the opportunities for patents[300] as well as the scope of preventing the use of other vehicles, viable with the active ingredient, are very limited.

1.4.3. **Patent Form**

Having pointed out that there are many opportunities in the process of arriving at a medicine to register patents, let us consider the forms those patents can take. The patents that are obtained can be divided into three categories. These are the product, process and product-by-process patents.

A product patent means that the end result, the product, is patented. This type of patent is concerned only with the end chemical and not the process by which it is made. Product patents will be secured, where possible, on every reagent throughout every stage of the manufacturing process.

[300] Older formulations for vehicles fail to satisfy Patent Act 1977 §2. Since the claim in the application for new vehicles is as encompassing as possible it will generally be difficult to show later that a new use for that vehicle, as per Patent Act 1977 §2(6), has been found.

The process patent refers only to invention within the method or process by which a product is obtained. For a process patent to be valid only the process needs to be novel. The novelty of the product is irrelevant.[301]

A product-by-process patent is a patent where the claim on a product is made by virtue of the process by which that product is obtained. In the UK a distinction is drawn between two product-by-process patent claims: The first is where the patentee has defined the scope of the monopoly claimed by the process; in this case the monopoly is defined by claiming products made by a particular process. The second is where the patentee disclaims products which do not have the features of products made by the process which has been claimed; in this case the monopoly is defined by claiming products with features that result from the particular process used. Only the first type of product-by-process patent is considered permissible.

According to the Court of Appeal "...If a person invents a new method of extracting gold from rock, he can obtain a claim to the process and as Article 64(2) [EPC] makes clear, he can also monopolise the gold produced directly by the process."[302]

This is a very different position to the EPO, where a product-by-process patent will only be considered novel if the product itself is novel. The USA

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[301] *Kirin-Amgen Inc ("Amgen") v Transkaryotic Therapies Inc ("TKT") & Ors.* [2003] RPC 31

[302] *Kirin-Amgen Inc ("Amgen") v Transkaryotic Therapies Inc ("TKT") & Ors.* [2003] RPC 31, para 33

follows a similar line to the EPO, in that a product-by-process patent will only be valid in the product is new or that the particular product resulting from the process is expected to have imparted as a result of the process distinctive non-obvious characteristics.[303]

1.5. **Pharmaceutical Patent Life Cycles**

Now that it is clear how heavily staked with patents what we simply refer to as a 'patented pharmaceutical' is, let us consider how the patents on that pharmaceutical fit into the life cycle of the pharmaceutical. That is the stages through which a NCE goes from registration of the first patents, through development and clinical testing to the grant of market approval. Followed by the employment of different stratagems to prolong market exclusivity.[304] Which leads eventually to the expiry of the patent and other instruments of market exclusivity and the entry of generics to the market.

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[303] See Ex parte Gray, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989). Where the claim was directed to b-NGF produced through genetic engineering. Whereas the prior art had disclosed the human nerve growth factor b-NGF. Whilst the applicant questioned the purity of the prior art factor they failed to evidence concrete indication that the engineered b-NGF was not substantially the same whether isolated from tissue or produced through genetic engineering. Thus, the dispositive issue was held by the Board to be whether the claimed factor exhibits any unexpected properties compared with the factor disclosed by prior art.

[304] The period of market exclusivity is deemed the most significant part of a patented pharmaceutical's existence. As a result most works that discuss strategy and patent life cycles for pharmaceuticals will focus on prolonging the period of market exclusivity for the patented pharmaceutical.

Pharmaceutical patent life cycles are typically regarded as a tension between patented and generic drugs. As a pharmaceutical patent ends, the originator tries to extend their market monopoly against the entrance of a generic manufacturer. However, other patented drugs might also compete for the same market, during the life of the first comer's patented medicine and after its expiry. Which means that the pharmaceutical patent life cycle refers to a more convoluted and interesting series of events than a period when a pharmaceutical was in patent and a period when it was not.

1.5.1. **Terminology**

Since there may be many players, each of which enters the market at a different point in time and not necessarily through the same formalities, precise descriptive terminology has evolved. We will explain and use the terms as they are used and understood in the pharmaceutical industry.[305] Of course some of the terms have also been adopted by popular press and used in news articles with a variety of meanings and little consistency.

As stated earlier, a patented medicine *usually* precedes generic entrants to a new therapeutic area. There are occasions when unpatented medicines have created new therapeutic areas. However, the first medicine of a class must undergo full clinical trials to gain market approval and thus cannot be a generic medicine. This first medicine in a therapeutic area, patented or not, is termed an originator medicine.

[305] Based on my observations when conducting interviews, and as explained to me during informal discussion with industry representatives (2004-2005).

Originator is a term that is applied loosely to the patent holder of the originator medicine. Or if there was no patent on the medicine, whoever was responsible for attaining market approval is termed an originator. Subsequent entrants to the market that do not fit the legal requirements for being a generic are also termed originators, because they usually introduce another member of a chemical class or new chemical class into a therapeutic area. It is possible for same company to be both an originator and generic manufacturer in the same market.

Popular media and some journal articles tend to use the term 'branded' to signify originators and then consider all other market entrants as generics.[306] This is an incorrect usage of the term generic. Law through the different regulatory requirements that apply to a generic medicine defines the category of generic. When the MHRA or FDA approves a pharmaceutical, the medicine receives a non-proprietary name and optionally a brand or proprietary name.[307] Thus, the popular use of branded and generic distinctions arises from the fact that generic medicines must be labelled with the non-proprietary name of the medicine,

[306] For an example of confusion creeping into academic literature, consider: Cool, K., and Schendel, D., 'Strategic Group Formation and Performance: The Case of the U.S. Pharmaceutical Industry, 1963-1982' (1987) 33(9) *Management Science* 1102-1124

[307] Manufacturers of generic medicines, unless they are producing a medicine whose non-proprietary scientific name is well known, must expend resources in order to have consumers associate their product with its function. This is a small but effective tool in maintaining customer fidelity for originators and I am not aware of where a branded name has not been taken.

but lack the brand name.[308] E.g., generic versions of Zantac are labelled with the non-proprietary name Ranitidine.

There is a further objection to the loose employment of 'branded and generic' as categorisations. This finds its form within the incorporation of fallacies into statements and premises connected with appeals to emotion,[309] to pity,[310] and to force[311] depending on the perspective of the commentator.[312] The employment of 'patented and generic,' or 'originator and generic manufacturer,' facilitate eschewing the incorporation of these fallacies. Since originator and generic are terms employed within official pharmaceutical literature, such as the Official Journal of the European Union, they are the terms that we will use.

However, there are two other nominatives that are useful and part of pharmaceutical industry jargon. Drugs that follow an originator into a new

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[308] Medicine labelling requirements for the European Union are contained in Title V of Directive 2001/83/EC

[309] *argumentum ad populum*

[310] *ad misericordiam*

[311] *ad baculum*

[312] The fallacies of relevance are frequently used in popular press with the intention of portraying generics or 'branded' medicines as good or bad depending on the commentator's point of view. With respect to appeal to emotion and appeal to pity, as well as an clinician's perspective consider Eban, K., 'Are generic drugs a bad bargain? All of us want cheaper medicine - but not if it costs us our health' May 26, 2009 *Today MSNBC.com.* Available at: <http://today.msnbc.msn.com/id/30940044> (Last Accessed: 1st July 2009)
For an example of an appeal to force – 'pay up or there will be no more' - see: Public Citizen, Rx R&D Myths: The Case Against The Drug Industry's R&D "Scare Card" 2001. Available from Public Citizen at: <http://www.citizen.org/documents/ACFDC.PDF> (Last Accessed: 1st July 2009)

therapeutic area and are patented are referred to as *Me-too* drugs. These are distinct from medicines that follow the originator medicine, but are not patented which are termed *copycat*. Within the pharmaceutical industry copycat refers exclusively to medicines that do little more than copy an existent, usually out of patent medicine. As such all generic medicines are termed copycat medicines.

Deliberate misuse of a term can convey derogation to members of the industry, but would mostly go unnoticed by the media and general public. For example, referring to a me-too as a copycat would suggest that the work which went into engineering that drug was trivial, even though patenting might have required demonstration of significant therapeutic improvement[313] or another form of novelty.[314]

1.5.2. **Patent Thicket**

Now that we are clear on the terminology we can start describing the life cycle. The struggle for a particular pharmaceutical market begins with the illumination of that market. This usually occurs following the publication of scientific research paper or publication of a patent. Either publication will indicate the existence and potential profitability of a new market, or that a

[313] §2(6) Patent Act 1977

[314] Which would most likely be a *new* pharmaceutical that was not foreseen and closed off by the originator.

new mechanism or different application of an existing pharmaceutical works.[315]

Immediately after discovery of an interesting drug a company will employ a defensive patenting strategy where they patent around their invention tying down market entry and creating misleading impressions about their active ingredients to prospective reverse engineers. This strategy involves the investigation and patenting of all closely related groups of compounds whether or not these compounds are likely to be successful candidates.[316] As many aspects as possible important to the manufacture and use of the pharmaceutical are patented as well. Thereby creating further difficulty for competitors. These aspects can include:

"...

- basic composition, including new or alternative compounds;
- method of treatment, including new use of known compounds, different
- dosing, and therapies in combination with other drugs;
- synthetic production;
- formulation and drug delivery;
- prodrugs releasing active ingredient;

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[315] Lowe, D., Now Your Liver Doesn't Have to Make It For You (2008) Chemistry and Pharma Blog. Available at: <http://pipeline.corante.com/archives/me_too_drugs/> (Last Accessed: 1st July 2009)

[316] Smith, M. C. Principles of pharmaceutical marketing. [Haworth Press, 3rd Ed., 1983, Philadelphia] 173

- substances resulting from metabolism in body;
- different crystalline or hydrated structures;
- gene-markers showing response to drug therapy;
- ... devices ... for administering the drug."[317]

As a result, pharmaceutical inventions are regularly enclosed by 30 to 40 patents and sometimes more.[318] Where it is judged that the pharmaceutical product and potential competitor products are securely blocked from competitors and that the manufacturing processes for the medicine can be kept reasonably secret, key stages in the manufacturing process are kept secret and neither patented or publicised through research publications. These secret manufacturing stages will be patented, as the patents on the product near expiry. Thereby extending the monopoly on the product and maintaining some barriers to market entry by competitor molecules. Should another company discover the manufacturing process, then the company holding the patents on the pharmaceutical will, either immediately patent the manufacturing

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[317] European Generic Medicines Association, 'Pharmaceutical Patents' Available from: http://www.egagenerics.com/gen-phrmapatents.htm (Accessed: 7th February 2005)

[318] Patent Attorney Interview (2005); EGA FAQ available at: <http://www.egagenerics.com/FAQ-generics.htm> (Last Accessed: 1st July 2009) Sometimes a large number of patents are used in conjunction with secrecy in order that the product cannot be obtained even if each individual patent in the process is understood. Moreover, should the secret part of the information be disclosed the patents would provide a barrier to competitors entering the market. Moreover, once the patents on the disclosed information near expiry then some further information previously kept secret can be patented.

process,[319] or where the other company has sought to patent, either oppose registration of the patent or claim prior use exception.[320]

Good patenting strategy requires meticulous closing down of all possible points of entry for competitors, whilst providing the competitor with little or no guidance on how to obtain the pharmaceutical. A famous early example from the chemical industry is the Haber-Bosch process for the manufacture of ammonia, which was enclosed by over 200 patents. These patents covered the apparatus, temperatures, and pressures necessary to the process, but provided no details about the necessary catalysts or the preparation of such catalysts. Since the catalysts were critical to the process for synthesising ammonia the information disclosed in the patents was redundant to other industrial engineers trying to manufacture ammonia. Moreover, by keeping the catalyst information secret Haber-Bosch significantly increased their lead-time and the

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[319] Which might involve a claim under §37 Patent Act 1977

[320] For example see Genzyme's patents on the manufacturing of Cerezyme. Whereas, Genzyme's monopolies, patents on the product and their Orphan Status, have expired Genzyme still holds patents on the manufacturing methods until 2022. Would be competitors no longer barred by a monopoly on the chemical can not produce the chemical anyway, unless they can circumvent through alternative manufacturing processes the patents on Cerezyme's manufacturing. USA Patent number 5,549,892, on a method of treating a human subject with Gaucher's Disease expires 27 August 2013 (USA Patent and Trademark Office database); A patent on the process by which CHO cells are used to manufacture Cerezyme (pharmaceutical product patent filed in 1980 (USA Patent and Trademark Office database) was granted a patent in September 2002, which will last until 2022 and encompasses several chemical products also produced from CHO cells, including Cerezyme, Fabrazyme, Thyrogen, and Aldurazyme. (USA Patent and Trademark Office database; Genzyme Corporation 10-Q Securities and Exchange Commission Filing: 11 August 2005)

expense for competitors seeking to circumvent Haber-Bosch's patent rights.[321]

Once the patents are granted and the pharmaceutical is deemed secure, a company may, depending on the type and market presence of the company and the economic conditions, publicise the NCE to investors. Generally, when a company's development pipeline contains few prospects, potential new drugs are revealed very early. Possibly before clinical trials have even begun. Thirty years ago when large pharmaceutical companies had many more products in their development portfolios new medicines were not revealed until they were in the later phases of clinical trials, i.e. it was more certain that they might be viable.

1.5.3. **Supplementary Protection Certificate**

With the patents granted, attempts at regulatory approval can also begin. These are preferably run alongside research on the pharmaceutical. As the delay to market entry caused by conducting research required to gain market approval provides eligibility to a supplementary protection certificate (SPC).[322] An SPC can extend the life of a pharmaceutical

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[321] Haynes, W., *American Chemical Industry*, Volumes 2 [Van Nostrand, 1954, New York] 86-87

[322] European Regulation No. 1768/92/EEC instituted Supplementary Protection Certificates for pharmaceutical products. (UK implementation: S.I. 1992 No. 3091, Reg. 5). Subsequent additions and amendments, such as Regulation No. 1610/96/EC creating Supplementary Protection Certificates for plant protection products, were consolidated into a codified new Regulation No. 469/2009/EC which came into force on 6 July 2009. Whilst, the new Regulation No. 469/2009/EC is directly applicable in all European

product patent[323] by up to five and a half years. The term of a certificate is equal to the time between the filing date of the patent and the date that the pharmaceutical incorporating the active ingredient was granted market approval in the European Community less five years. For example, if there were a seven year interval between filing and market approval, then the patent on the active ingredient would be eligible for an SPC that prolonged its patent term by two years.

The supplementary protection certificate only enters into force after the product patent it concerns expires, and it is normally limited to a maximum patent extension of 5 years. Which would require a delay of ten years between the filing date of the patent and the date that the pharmaceutical incorporating the active ingredient was granted market approval in the European Community. However, the SPC can be extended by six months, to a maximum of five and a half years, if it relates to a product that was

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Member States, the Supplementary Protection Certificates and extended patents only have effect in the State in which they are granted.

[323] SPCs are only available for the active ingredient, or combinations of active ingredients for pharmaceuticals (Regulation No. 469/2009/EC Art 1(b)), or the active substance or combination of active substances of a plant protection product (Regulation No. 1610/96/EC Art 1.8). Plant protection products are medicines for plants construed in a much broader sense than we have defined pharmaceuticals. As such plant protection products include: chemicals that protect plants or plant products against harmful organisms, e.g. horticultural fungicides and insecticides; that influence plant life processes, but are not simply nutrients, e.g. growth regulators; that preserve plant products, but are not subject to Community law on preservatives; or that destroy undesired plants, plant parts, or prevent undesired plant growth, e.g. herbicides. Plant protection products other than this mention are not considered in this thesis.

delayed market approval because clinical trials for paediatric applications were conducted.[324]

In the UK, all medicines must be directly approved by the Medicines and Healthcare Products Regulatory Agency (MHRA),[325] which will then issue a 'marketing authorisation' and product licence specifically for the approved product.[326]

1.5.4. **Clinical Trials**

To gain market approval the MHRA requires results from 3 phase trials demonstrating that the advantages a product possess outweigh its disadvantages. The MHRA require that the design and conduct of the phase trials provide acceptable levels of protection for participants. However, when the phase trial data is submitted the research methodology is not examined by MHRA with the objective of ascertaining if there were acceptable levels of protection for participants. Since, what is deemed an acceptable level of protection for a participant establishes a basis for a *duty of care* and because of lower costs and penalties in the

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[324] Regulation No. 1901/2006/EC Article 36

[325] The MHRA is a new authority, established in 2003 to bring together the functions of both the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA).

[326] Within the European Union marketing authorisation can, depending on the subject of the application, be sought from the European medicines Agency (EMA) and is valid in all European Union and EEA-EFTA states. Application to the EMA is obligatory for medicines based on biotechnology, high-tech processes, or designated for treatment of HIV/AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions, and viral diseases.

case of negligence, the phase trial data is often gathered from amongst populations in countries with low GDP.

India is particularly attractive as it has the largest pool of patients suffering from diabetes, cancer, heart disease and many other diseases that are profitable research objectives. Moreover, India is stable, has extremely poor populations, and fewer restrictions on clinical testing than Europe or North America.[327]

The phase trials or clinical testing[328] consist of three stages that are designed to progressively test the effectiveness of a therapy and its safety.[329]

Phase I trials are usually conducted on a small group of healthy volunteers, and are designed to determine the pharmacokinetics and

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[327] Global consultants McKinsey & Co estimate that by 2010 about 1-1.5 billion USD will be spent on clinical trials in India and that by 2015 India's pharmaceutical market will reach $20 billion. See, Kumra, G., Mitra, P., Pasricha, C., 'India Pharma 2015: Unlocking the Potential of the Indian Pharmaceutical Market' (2007) McKinsey and Company Report. 10, 13 Available from: <http://www.mckinsey.com/locations/india/mckinseyonindia/pdf/India_Pharma_2015.pdf> (Last Accessed: 5 February 2010)

[328] With the increased public interest in pharmaceuticals there has been a growth in information available concerning the processes involved in their safety testing, regulation and approval. For example, for an account on clinical trials addressed to the general public see NIH, 'Understanding Clinical Trials.' Available at: <http://clinicaltrials.gov/ct2/info/understand> (Last Accessed: 1st July 2009)

[329] For a guide to clinical trials consider, Kerr, D., Knox, K., Robertson, D., Stewart, D., Watson, R., (eds.) *Clinical Trials Explained: A Guide to Clinical Trials in the NHS for Healthcare Professionals* [Blackwell Publishing Ltd, 2006, 1st Ed., Oxford]

pharmacologics of a drug. That is, dose dependent responses and early indications of effectiveness are sought.

Providing Phase I generates promising results, studies move to Phase II. Where data on the effectiveness of the drug in patients with a specific disease or condition are sought. This sample group usually consists of a few hundred individuals.

Phase III trials expand the Phase II through uncontrolled and further controlled trials amongst a much bigger sample group. The objective of Phase III is to generate additional data concerning effectiveness and safety, which is needed to evaluate the benefits and risks of the drug. The pharmaceutical manufacturer may eventually distribute selective data from Phase III to physicians.

The clinical trial data must also be accompanied by supporting documentation sufficient to assure the MHRA that the pharmaceutical company and any wholesalers are able to manufacture, distribute and supply the product to required safety and quality standards.

1.5.5. **Data Exclusivity**

Once the new medicinal product application is completed and approved by the MHRA,[330] the pharmaceutical product is considered to enter a period

[330] In the USA this is the FDA. Apart from duration Data Exclusivity is remarkably similar in the USA and Europe. However, in Europe in addition to domestic market approval

of data exclusivity.[331] Data exclusivity is available even if the applicant does not have a patent. The requirement for data exclusivity is that the new medicinal product application contains an active ingredient that has not been approved before by the MHRA.[332] Since new medicinal product applications require clinical trial data then the applicant will have also conducted trials on the pharmaceutical. The effect of data exclusivity is that during the specified period no applications for market approval can be referenced by the regulatory authority to the data in the originator new medicinal product application. The data exclusivity therefore, applies to both medicines that claim bioequivalence or bio-similarity[333] to the NCE and medicines that claim a new use for the NCE.[334] The period of data exclusivity is an exclusory regime almost disconnected from the patent system,[335] and although not a property right it does have important impact

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there is also the EMA's centralised process. Approval by the MHRA approves the medicine by the principle of mutual recognition across the whole of the European Union.

[331] Article 10 Directive 2004/27/EC

[332] If the active ingredient has only been approved in combination then it is still disqualified from Data Exclusivity.

[333] Article 10.4 Directive 2004/27/EC

[334] New use is considered a new invention in UK law §2(6) Patent Act 1977 as amended. A New Use requires clinical trial data to support the New Use, but certain pharmacological traits, such as toxicity for the same dosage and method of delivery, might be referenced to data submitted in an early application. That is, unless Data Exclusivity applies. In the USA new indications are covered by 21 U.S.C. §355(b)(2) and termed 505(b)(2) applications, see 505(b)(2) Drug Price Competition and Patent Term Restoration Act 1984 (USA). 505(b)(2) applications are only eligible for three years of market exclusivity.

[335] In the USA if the originator's patent on the FDA approved product is invalidated, then a second entrant (generic) can obtain a 'certification of patent invalidity' which reduces the 5 year period of data exclusivity by 1 year. 21 U.S.C. § 355(c)(3)(E)(ii)

on the introduction of cheaper bioequivalents to a market and therefore on accessibility.

Article 10 of Directive 2004/27/EC (amending Directive 2001/83/EC) harmonised EU data exclusivity to eight years with an additional two-years of market exclusivity.[336] An additional year of market exclusivity is available for NCE applicants providing that within the first eight years, the NCE applicant obtains authorisation for one or more new therapeutic indications, which are held to bring a significant clinical benefit in comparison with existing therapies.[337] Market exclusivity differs from data exclusivity in that during market exclusivity the MHRA can reference new application to the data in the new drug application for the relevant NCE. However, even if the MHRA finds concordance in the reference it will not issue regulatory approval until the expiry of the market exclusivity period.

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[336] Data Exclusivity was introduced to many countries by Article 39(3) TRIPs, which requires protection of 'data against unfair commercial use.' Whilst the UK and USA have developed extreme approaches to protecting data against 'unfair' commercial use, not all TRIPs signatories consider reference to originator test data an unfair commercial use. §55.2(1) Canadian Patent Act 1985 as amended provides an early working exception for a subsequent manufacturer to use a patented invention for the purpose of obtaining regulatory approval for a product. It states: "It is not an infringement of a patent for any person to make, construct, use or sell the patented invention solely for uses reasonably related to the development and submission of information required under any law of...a country... that regulates the manufacture, construction, use or sale of any product." However, to prevent copycat medicines being sold on the market before relevant patents have expired a Notice of Compliance is required. See, Canadian Patented Medicines (Notice of Compliance) Regulations [S.O.R./93-133] as amended. Consolidated text is available at: <http://www.wipo.int/wipolex/en/details.jsp?id=9380>

[337] This is known as the 8+2+1 formula

1.5.6 **Post Approval Monitoring**

Whenever a new medicinal product is marketed, then the person marketing that drug is required to set up a system to monitor the safety of the product on the market. At random intervals the regulatory authority may perform an inspection of the monitoring system. Monitoring systems are not required for older medicines, such as weaker formulations of prescription medicines that are sold as over-the-counter drugs.[338]

The MHRA can command the removal of a drug from the market, and order suspension of its manufacture if necessary. To assist in the gathering of post-approval data the MHRA requires that new chemicals and vaccines are labelled with a black triangle for up to two years following approval. The black triangle symbol must be displayed on all advertising material, product information, and prescribing manuals associated with the new medicine. This marking helps to make healthcare practitioners aware of the need to monitor the new medicine more carefully than older chemicals or vaccines and to report side effects to the MHRA. The objective of the black triangle and the feedback on the new medicine that the MHRA receives is to enable the MHRA to perform continuing assessment on the medicine and to take action if the chemical or vaccine is deemed to have too high level of side effects for its therapeutic benefit.

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[338] See MHRA Good Pharmacovigilance Practice. Available at: <http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodPharmacovigilancePractice/index.htm> (Last Accessed: 1st July 2009); MHRA, Good Pharmacovigilance Practice Guide [Pharmaceutical Press, 1st Ed., 2008, London]; NICE new medicine monitoring guidelines (2008). Available from: <http://www.nice.org.uk/guidance/index.jsp> (Last Accessed: 1st July 2009)

In other words, an assessment of whether the advantages outweigh the disadvantages of taking the drug. Potentially, the MHRA can require continued use of the black triangle in relation to a product until the MHRA is satisfied that the advantages outweigh the disadvantages of taking the medicine.

In some circumstances a medicine approved over two years ago may be required to display the black triangle if the combination of active ingredients is different, if it is being used in a new way, at a substantially different dosage, or for a different condition. Annually, the MHRA receives around 25,000 applications for changes to the use, or dosage, or method of application of a medicine.[339]

Where a medicine, post-approval, is deemed unsafe or there are serious concerns about the risks that it poses then the MHRA's Defective Medicines Report Centre will alert[340] healthcare authorities, NHS trusts, healthcare practitioners and wholesalers, professionals, hospitals, GP surgeries, and wholesalers notifying them of the risk and where necessary ordering the product recalled.

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[339] MHRA, Medicines and Medical Devices Regulation: What you need to know, 2008, at 8. Available at: <http://www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con2031677.pdf> (Last Accessed: 1st July 2009)

[340] The Defective Medicines Report Centre's alert has four classes, ranging from an immediate recall, because the product poses serious risk or danger of mortality (class 1) to the product poses not risk to patient safety, but there is a reason for caution (class 4).

1.5.7. **Evergreening**

Now that we have explained the patents that are available and some ways in which they can be extended, as well as how a medicine acquires and retains market approval in the UK, let us consider the strategies employed to maintain the patents and extensions, and to delay competition. Evidently policing of both patent applications and competitor medicines for infringement or discovery of information the originator wishes to keep secret are important. A pharmaceutical company will have employees or contract one of the many companies that watch patents to stand sentry over its patents. It will also use publicity and communications with health care practitioners to make its product well known. However, to ensure the high returns on its investment are prolonged as long as possible the pharmaceutical company also needs to utilise all the regulatory, marketing, and innovation encouragement schemes that are available.

Keeping market exclusivity requires the timely creation of market barriers and sufficient market uncertainty to delay or discourage competition. The general methodology of creating barriers to competition are:

- FDA for approval of a new chemical entity (five years),
- Reacquiring three-year regulatory data exclusivity through new indications and alterations to the active ingredient (three years),
- Paediatric exclusivity (six months) - paediatric studies that may reap six month regulatory patent extensions under a paediatric exclusivity (Note: multiple paediatric exclusivities may be possible

for the same pharmaceutical, but they must each be on a different active ingredient),

- Orphan drug status (up to ten years).
- Developing and seeking patent protection for product line extensions, which may include changes in form, dosage or strength that have convey significant therapeutic improvement (twenty years)
- Bioequivalence and pharmaceutical equivalence challenges against generic equivalence applications.
- Department for Environment Food and Rural Affairs (UK) or Environmental Protection Agency (USA) issues, British National Formulary (UK) or Pharmacopeia–National Formulary (USA) entries, and safety and labelling issues.

The term used to describe these attempts to prolong a pharmaceutical's monopolistic existence is Evergreening. The European Generic medicines Association states, evergreening,

> "...aims to prevent or delay competition from generic medicines by extending market protection through patents on minor changes to the original product."[341]

Indeed,

[341] EGA FAQ. Available at: <http://www.egagenerics.com/FAQ-generics.htm> (Last Accessed: 1st July 2009)

"...a patent on a new use ("indication"), formulation, salt or ester can block the registration or marketing of a generic medicine for treatments where the base patent has already expired."[342]

This is because, in addition to the new patent term for the sampled claims of the originator patent, the new patent will also reinstate data exclusivity for information that may have been contained in earlier drug approval applications.

In 2008, the Canadian Supreme Court faced with Evergreening addressed the issue directly. It concluded that,

"Evergreening is a legitimate concern and, depending on the circumstances, strategies that attempt to extend the time limit of exclusivity of a patent may be contrary to the objectives of the Patent Act. The Act aims to promote inventiveness by conferring exclusivity for a limited period of time while providing for public disclosure of the invention to enable others to make or use it after expiry of the period of exclusivity.

However, a generalized concern about evergreening is not a justification for an attack on the doctrine of selection patents for two reasons. First, a selection patent may be sought by a party other

[342] EGA FAQ. Available at: <http://www.egagenerics.com/FAQ-generics.htm> (Last Accessed: 1st July 2009)

than the... [originator]. In such a case, anticipation or obviousness may be an issue, but evergreening does not arise...

Second and more importantly, selection patents encourage improvements by selection. The inventor selects only a bit of the subject matter of the original genus patent because that bit does something better than and different from what was claimed in the genus patent."[343]

The Canadian Supreme Court's judgement follows the same patentee friendly course as the English courts in their recent decisions.[344] However, as yet the House of Lords has avoided addressing Evergreening directly.[345]

Minor changes to the product that may alter the effect of the active ingredient entitle the pharmaceutical to three years, in effect three *more* years, of data exclusivity. These minor changes can be effected through alterations in the strength of the dosage, the form in which it is taken, or the frequency with which it is taken.

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[343] *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, 2008 SCC 61

[344] Consider: *Actavis v Merck* [2008] EWCA Civ 444; *Conor v Angiotech* [2008] UKHL 49; *Dr Reddy's v Eli Lilly* [2008] EWHC 2345; *Generics (UK) v Daiichi* [2008] EWHC 2413; *Generics (UK) v Lundbeck* [2008] EWCA 311. However in *Actavis UK Limited v Novartis AG* [2010] EWCA Civ 82 the Court of Appeal upheld the High Court's finding (*Actavis UK Limited v Novartis AG* [2009] EWHC 41) of obviousness in the evergreening patent. Which may indicate a changing attitude to evergreening. But once again the court did not address evergreening directly.

[345] *Conor v Angiotech* [2008] UKHL 49

Moreover, changes in the time of administration and drug delivery systems might also have an impact on the active ingredient, as will changes in metabolites, intermediates, polymorphs and isomers. New pharmacokinetic data will also qualify for three more years of data exclusivity.

Maintaining data exclusivity is of great importance, because it prevents generic drug applications on the originator pharmaceutical from being considered by the regulatory authority, which can extend barriers to market entry after drug patents have expired.

1.5.8. **Generic Medicines**

Generic drugs are copies of originator drugs and should have exactly the same pharmacological effects as the originator medicine. Thus, at the same dosage and method of administration, the generic will poses the same effectiveness, safety, side effects and risks as the copied pharmaceutical. Generic medicines may even utilise the same chemical entity as the drug they are copying. Thus competitor manufacturers will, as the patent on the drug they are copying is expiring and providing the eight years of data exclusivity are still not in operation, make an application for regulatory approval.[346] The application is addressed to the

[346] In the USA the data exclusivity may soon be extended from 5 to 12 or perhaps 14 years, which would have ramifications for the UK data exclusivity term. Engelberg, A., Kesselheim, A., Avorn, J., 'Balancing Innovation, Access, and Profits — Market Exclusivity for Biologics' (2010) 361 N Engl J Med 1917-1919; Musselwhite, L., and

same authority from which the originator obtained approval. Thus, the authority is able to compare the data in the generic application with the data submitted by the originator, which the authority will have retained. In the UK this regulatory authority is the MHRA and in the USA the FDA.[347]

Originator pharmaceutical companies are popularly considered to be innovators, whilst generics are regarded almost as free-riders who make serious inroads into markets created and developed by the originator. Thus, the generic entrant is seen as inhibiting the research potential of the originator by reducing the originator's revenue and therefore the resources available for research reinvestment. This is an argumentum *ad populum*, as society has already defined the extent of the originator's privilege and originator's market behaviour often seeks to undermine the market control of originators in other therapeutic areas during the term of the patent privilege.

There is also a misconception, that once the first drug in a class creates a market that it is easy for subsequent drugs of the same class to also gain market entry. In some cases the cost of developing an unpatented competitor drug (Copycat) can be almost as expensive as the cost for the

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Andrews, J., 'Protect Pharmaceutical Innovation' (2010) 328(5984) *Science* 1354; Knowles, S., 'Fixing the Legal Framework for Pharmaceutical Research' (2010) 327(5969) *Science* 1083-1084

[347] The European Agency for Evaluation of Medicinal Products (EMEA) is also an important alternative for obtaining marketing authorisation for medicinal products in the European Union. Marketing approval by the EMEA is valid in all European Union Member States as well as European Free Trade Association Member States which comprises: Iceland, Liechtenstein, Norway and Switzerland.

first market entrant (originator). Whilst the second market entrant might substitute the assay of a broad range of molecules with reverse engineering and then a smaller assays of molecules, that second entrant must undertake phase trials as rigorous as the first market entrant. This is because even if there are drugs in the same chemical class as those included in the originator's patent thicket, these chemicals require market approval. Which is desirable to promote safety as not all chemicals in a class may actually work, or be considered sufficiently safe to use.

Where a would-be new entrant to a market may have reduced pre-approval costs is where the new entrant can show bioequivalance between their pharmaceutical and one already approved for the designated condition, which is termed a generic application.[348] In this case, in place of the three phase trials this generic entrant to the market needs only the data to demonstrate bioequivalence.[349] Since regulation only requires a minimum cohort of twelve people in the generation of bioequivalence data, [350] conducting bioequivalence tests is substantially cheaper than conducting clinical phase trials.

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[348] Termed an 'Application for generic medicinal product' in the UK and an 'Abbreviated New Drug Application' in the USA

[349] Placebo controls are not required to demonstrate bioequivalence. European Medicines Agency (Committee for Medicinal Products for Human Use) Guideline on the Investigation of Bioequivalence. (EMA, 20th January 2010, London) Available at: <http://www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/01/WC500070039.pdf> (Last Accessed: 21st May 2010)

[350] European Medicines Agency (Committee for Medicinal Products for Human Use) Guideline on the Investigation of Bioequivalence. (EMA, 20th January 2010, London) Available at:

However, originators will ensure that it is as difficult as possible for would be generic manufacturers to demonstrate bioequivalence. Data from the originator products, submitted to the regulatory authority, is never revealed to third parties, and so cannot be used by generic medicine researchers.[351] Thus, generic manufacturers do need to conduct research in order to produce enough bioequivalence data for the regulatory authority to be confidant that the generic product is sufficiently accurately described by the phase trailing of the originator data. Data exclusivity for the originator drug means that for eight years the regulatory authorities will not assess the safety and efficacy profile of a generic application and for two or three years after expiry of the data exclusivity period the generic applicant drug cannot be marketed. The most opportune moment for the generic manufacturer to begin establishing their bioequivalence data is strongly dependent on national provisions concerning data exclusivity.[352]

In the UK the bioequivalence study will assess indicators of the chemical's performance on volunteers, by monitoring the quantity of active substance in the body after application of the pharmaceutical. For a pharmaceutical to be considered a generic or reference medicine it must be bioequivalent.

<http://www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/01/WC500070039.pdf> (Last Accessed: 21st May 2010) at 8.

[351] EGA FAQ. Available at: <http://www.egagenerics.com/FAQ-generics.htm> (Last Accessed: 1st July 2009)

[352] §60(5)(b) Patents Act 1977. However, some countries may provide much less freedom for research than others. See Okuyama, S., Japanese courts find no "experimental use" haven for generic drug makers accused of infringing pharmaceutical patents (1997) 16(2) Biotechnol. Law Rep. 158-161

Which means that identical levels of the active substance must be observed in the body after application of the pharmaceutical as are found in the originator studies. In most cases almost identical levels of active substance between the originator chemical, already approved for the market, and the generic or reference medicine will deem the generic product as equally safe and effective as the originator chemical. However, there may be factors which require more information to be supplied to the regulatory authority. For example, if the method of delivery of the chemical is changed, if the method of manufacture or storage conditions differ, or if a specific property of the active chemical differs in some way from the originator.[353] Any of these factors will provide grounds for the originator, or another interested party, to challenge the bioequivalence of the generic applicants' data. Moreover, the originator knows the data they submitted and has access to the data submitted by the generic applicant, thus the originator has a strong tactical advantage in delaying the approval of generic products through bioequivalence challenges.

Usually originators will patent around their product to strengthen their monopoly. However, not all of the patented chemicals are submitted for regulatory approval and so are not protected by a period of data exclusivity. Thus, one strategy that can be advantageous to generic manufacturers is to utilise, as their active ingredient, a different salt than the one for which the originator received market approval, but which is out of patent. Such applications can present difficulties to regulatory

[353] European Medicines Agency, Post-authorisation Evaluation of Medicines for Human Use, London: 19 September 2006, Doc. Ref. EMEA/393905/2006

authorities, as the substituted salt may express similar activity levels to the originator chemical, but have other effects that are not clearly indicated in the bioequivalence data. [354] In such cases the regulatory authority will usually require further information to persuade them of the safety and efficacy of the substitute chemical.

Another technique that can be employed by generic manufacturers to enter the market earlier is to assert that an earlier patent necessarily anticipated the later one on which the originator company is now relying to maintain market monopoly or that the originators patents do not encompass the generic medicine. Other grounds of invalidity might also be raised, such as insufficiency. However, this can be both expensive and exceedingly risky. As this is usually contestation over access to a very proven and lucrative market the originator will invariably make a legal challenge against the generic manufacturer.

One such legal challenge is the USA the doctrine of constructive patent infringement. Which, if demonstrated, provides the originator with a ground to sue for declaratory relief. Although the originator need not initiate an action straight away, they could wait until there is actual infringement. Which might be more damaging to the generic

[354] Verbeeck, R.K., Kanfer, I., and Walker, R.B., Generic substitution: The use of medicinal products containing different salts and implications for safety and efficacy. European (2006) 28(1-2) *Journal of Pharmaceutical Sciences* 1-6

manufacturer's investment, than the pre-emptive strike.[355] In the UK where constructive patent infringement exists, but only to the extent that there is actual infringement and a party to the infringement has constructive notice of the fact and thus is culpable for the infringement, the originator must wait for the actual infringement.

Once the data establishing bioequivalence to the authority's satisfaction is established then the safety and efficacy of the generic product can be cross-referenced by the regulatory authority with the confidential information held on the originator chemical.[356]

Generic medicines, that have satisfied the regulator that they have bioequivalence with an originator chemical that has received regulatory approval, do not require further substantiation by clinical trial data.[357] This has an effect on the cost of the pharmaceutical, but it is not the most significant factor in the price determination of a generic medicine. The most important price determinant factor is that the generic will not be introduced into a market with a monopoly. There will be competition, and thus the price of the generic must be competitive.

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[355] Patently-O, Patent Law Blog, Pfizer Agrees Not To Sue Apotex on Zoloft. 27th September. Available at: <Patentshttp://www.patentlyo.com/patent/2006/09/index.html> (Last Accessed: 1st July 2009)

[356] EGA FAQ. Available at: <http://www.egagenerics.com/FAQ-generics.htm> (Last Accessed: 1st July 2009)

[357] This is the reason why applications for regulatory approval in the USA are termed 'Abbreviated New Drug Applications' because for the most part they are not required to include preclinical animal and clinical human test data to establish safety and effectiveness. See <http://www.fda.gov/cder/Regulatory/applications/ANDA.htm> (Last Accessed: 1st July 2009)

For a generic manufacturer to remain competitive they must dependably provide quality drugs and price them attractively. As such generics undergo frequent review and improvement.[358] This is consistent with the accepted paradigm, which holds that competition in technology markets has positive consequences for the price, quality and introduction rate of new products to the market.[359] This is especially the case when generic medicines are in strong competition with products from competing pharmaceutical companies.

The behavioural difference between generic drug owners and patented drug owners can be explained quite simply. For the patented medicine, if it has been well secured, then even without patent line extensions for 25.5

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[358] A line of investigation I pursued early in my research was whether the cost of tool setting for generic manufactures was lower than for patented medicine manufacturers? Both types of manufacturers have an interest in keeping their costs as low as possible, thus tool setting costs should be comparable. However, there are two indicators that these tool setting costs are not comparable. Firstly, there is the claimed minimum manufacturing costs for bulk chemicals. This was particularly evident between 1999-2002 in the context of access to antiretroviral drugs for poorer nations. Secondly, there is the strategic benefit in maintaining broader manufacturing facilities. This is particularly the case when manufacturing drugs that may be used during pandemics. Being able to increase production in a very short time is an important factor in Government contracts. Also designating pharmaceuticals for other conditions or altering the formulation to extend market exclusivity may require modifications to tool setting. Thus, long run costs are reduced if the future requirement is foreseen in plant development and initial tool setting. Unfortunately, I could not acquire the necessary data to analyse.

[359] Referring to methods of doing business, see: Surowiecki, J., Patent Bending, 14 July 2003 The New Yorker. Available at: <http://www.newyorker.com/archive/2003/07/14/030714ta_talk_surowiecki> (Last Accessed: 1st July 2009)

years[360] from the filing date there is no need to innovate or to improve the medicine as there are no alternatives for those who need the medicine. Indeed, it is possibly more important for an originator to channel resources into prolonging the life of their monopoly than trying to develop a truly *new* application or product.

For generic competitors to enter the market it might take much longer than 25 years.[361]

European Commissioner for Competition Neelie Kroes summarised the properties of generic medicines when remarking,

> "... longer protection acts as a disincentive to innovate... Health care systems throughout Europe rely on generic drugs to keep costs down. Patients benefit from lower prices... Moreover,

[360] The standard patent term is 20 years beginning with the date of filling (§25(1) Patent Act 1977). A supplementary protection certificate may add up to five years (formerly: S.I. 1992, No. 3091, Reg. 5; now covered in EC Regulation No. 469/2009). Clinical trial data submitted as a Paediatric Investigation Plan can entitle the applicant to a supplementary protection certificate of five and a half years (EC Regulation No. 1901/2006 Article 36; EC Regulation No. 469/2009 Article 13(3)). These three measures in conjunction, can bring the period of market exclusivity available up to 15.5 years. Which will be 15.5 years starting from the date when the pharmaceutical received its product licence from MHRA or ten years from when the patent application was filed.

[361] Submitting data that indicates that the medicine might have a use on an indication considered a rare disease (no more than 5 in 10,000 people) can convey 10 more years of data exclusivity (EC Regulation No. 141/2000 Article 8(1))

competition from generic products after a patent has expired itself encourages innovation in pharmaceuticals."[362]

The commissioner does omit one critical point, one that we have already mentioned. Generics almost invariably follow a patented medicine. The first drug in a new field of pharmaceutical therapies is almost always patented.[363]

[362] Anonymous, 'Competition: Commission fines AstraZeneca €60 million for misusing patent system to delay market entry of competing generic drugs' (15th June 2005) IP/05/737 *EUROPA (Rapid Press Releases)* Available at: <http://europa.eu/rapid/pressReleasesAction.do?reference=IP/05/737> (Last Accessed: 1st July 2009)

[363] There are extremely rare exceptions, such as penicillin or the early polio vaccines.

CHAPTER 2

PHARMACEUTICAL PATENT THEORY

"On a subject teeming with human significance rigorous logic is of the utmost importance."[364]

2.1. **Theoretical Framework**

Successful complete descriptions of the patent system's function have not previously been undertaken and antecedent literature treats the functions of the patent system as model incompatible objects. Innovation specialists have tended to focus on expanding the body of knowledge describing firm behaviour and research trends, but have neglected a rigorous, terminologically homogeneous, consolidation of existing function theory. Instead they have borrowed from patent theory desirable elements for their objective and ignored others. The unifying thread of economic modelling and analysis techniques does provide a *prima facie* thread of homogeneity. Unfortunately, due to the diversity of the patent genus[365] and the complexity of innovation functions, sufficient to predict with stability the comportment of the patent system, a straightforward aggregation of hypothesise yields unsatisfactory results. In this chapter we will demonstrate why.

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[364] Cohen, M. R., Positivism and the Limits of Idealism in the Law (1927) 27(3) *Columbia Law Review* 237-250, at 243

[365] TRIPS Article 27(1) sets the minimum parameters for patents of all signatories of the WTO. It states, '...patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application.'

2.1.1. **Justification By Contradiction**

The coherence and homogeneity problems of patent theory result from the absence of a linear development of patent justificatory ideology.[366] The most pervasive retrospective ideological assertion is that the patent system has throughout its existence been a utilitarian construct:[367] The action of granting a 'right to secure the enforcement power of the state in excluding unauthorized persons, for a specified number of years, from making commercial use of a clearly identified invention'[368] is morally right since it produces at least as much good, or utility, for the ensemble of people affected by the invention as any alternative action a community could perform in its place to obtain the invention. This assumption concerning the effectiveness and nature of the patent system, frequently the starting point for patent system analysis,[369] bears the hallmark difficulties of all utilitarian theory. Firstly, how can a utilitarian construct be

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[366] To suggest that there is would be to assume that words had kept their meaning, subjective and inter-subjective relationals remained unchanged, and that social demarche was intransient. As described above at 1.1, the patent system is rather the organic growth resultant of extensive lobbying; decisions of the courts, tribunals and interparty agreements; and national protectionism, than a sustained systematic progression.

[367] Merges, R. P.; Menell, P. S.; Lemley, M. A.; Jorde, T. M., (Edd.) Intellectual Property in the New Technological Age (1997) 135-137; Menell suggests that the "...principal system adopted for the examination of intellectual property has been economic theory: a particular instantiation of utilitarianism." Menell, P. S., '1600 Intellectual Property: General Theories,' (1999) 129-188, at 130. However, not all justifications are utilitarian. See Oddi, A. S., 'Un-Unified Economic Theories of Patents - the Not-Quite-Holy Grail,' (1996) 247-277

[368] Machlup, F., *An Economic Review of the Patent System*, Subcommittee on Patents, Trademarks and Copyrights, US Senate, 85th Congress, 2nd Session, Study Number 15 [United States Government Printing Office, 1958, Washington D.C.] 1

[369] Menell, P. S., 1600 Intellectual Property: General Theories (1999) 129; Fisher, W., Theories of Intellectual Property 1

formulated and evaluated? Secondly, is it desirable to adopt a utilitarian construct to stimulate new invention? An answer to the first question can be constructed from a careful analysis of the patent system's functions. A response to the second question can be obtained from an understanding of the essential nature of a given patent.[370]

This chapter is, therefore, a theoretical investigation of the statements about the patent system's function. These are statements that have been used to justify the imposition of a patent system on a community. The statements are problematic and hence it was considered clearer to label them as 'function statements' rather than 'functions', which would misleadingly presuppose the statements had been inferred from empirical support or possessed inherent coherence. It is the reason why we have maintained the cumbersome appellation of *function statement*.

2.1.2 **By Dogma**

It will become clear that the existing statements of the patent system's function are affirmed dogmatically, that is they are stated authoritatively and are not to be disputed or doubted. Thus, they provide no further authority to justify the function of the patent system that is not contained in the original dogma. Moreover, the original premiss are in many cases contradictory with the premiss of other function statements, suggesting

[370] Whether the patent system is utilitarian by virtue that it produces at least as much good, or utility, for the ensemble of people affected by the invention as any alternative action a community could perform requires an examination of empirical data and a detailed premonition of alternatives.

that even if the problem of dogma were ignored many of the function statements could not be a coherent justification for the patent system's existence.

2.1.3. **By Thread**

We have identified from patent literature that the patent has six main threads that are used to justify its existence. We have labelled these 'function statements,' and they are invention incentive, disclosure incentive, investment incentive, organised derivative innovation, property sovereignty, and knowledge feudalism. These function statements are not mutually exclusive and overlap does occur, particularly in conflicts between premiss. Other functions of patents for inventions that are *prima facie* different from function statements can be asserted, but these are either relevant only to specific aspects of patent legislation,[371] or are derivatives or compositions of the function statements treated here. Property sovereignty and knowledge feudalism are not overtly used statements and might not generally be considered desirable objectives for the patent to serve. Moreover, since property sovereignty and knowledge feudalism are more drawn from empirical observations than patent literature[372] they are more correctly treated in Chapter 3.

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[371] For example, consider the availability of SPCs for medicines, but not for any other area of patentable innovation where safety requirements must be demonstrated, before a product can enter the market. Within it we find the strands of premiss pharmaceutical innovation is more desirable than other forms of inventive activity, or that pharmaceutical innovation is more expensive than any other form of inventive activity.

[372] A significant exception is Drahos, P. and Braithwaite, J. *Information Feudalism: Who Owns the Knowledge Economy?* [Earthscan publications Ltd, 2002, London]

2.1.4. **Without Merit**

Amongst the other functions of patents for inventions that are not treated are those that are so entirely without merit that they deserve no treatment at all. The strongest amongst these is that a patent indicates that a pharmaceutical is safe. This is a misconception. For example, consider a patent awarded for a compound that improves the adherence of platelets to collagen fibres in the vascular endothelium by increasing effectiveness of the glycoprotein platelet collagen receptor. Even though that compound has been registered, it posses another hemostatic property, i.e. that it causes serious embolisation, that will prevent it from receiving a product licence and market approval.[373] Patent acquisition and market approval are independent processes, and neither process is an indication of the eligibility of the pharmaceutical for the other.

Some statements of the invention incentive function utilise the terms social benefit and social cost respectively to refer to resources derived from and required by the patent system. The terms are straightforward, but in most instances make an implicit assumption that the social benefit of a particular invention is strictly its final use value.[374] Thus, the social benefit of the patent system derives from the innovation that occurs over that innovation which would occur in the absence of a patent system. Hence, in some innovation incentive models the social benefit of the patent

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[373] The risks of the pharmaceutical are too great for the benefit that it conveys.

[374] McFetridge, D. G.; Rafiquzzaman, M., 'The Scope and Duration of the Patent Right and the Nature of Research Rivalry,' (1986) 104 on 'Postpatent Competition theory.'

system is the entirety of inventive activity, since in the respective innovation incentive function statement it is assumed that no innovation would take place without the patent for inventions. Since social benefit is not used consistently throughout the function statements its use will be avoided. The social cost of a patent is the use restriction imposed on the community by the patent holder by virtue of the patent. Though used with sufficient consistency by patent innovation literature to have enough homogeneity to form a workable definition it is too nebulous in its parameters to be used except in very general terms and its use will also be avoided.

2.2. **Invention Incentive Function Statement**

The first of the function statements, invention incentive, is the most well known function of the patent system and the subject of a very large body of empirical work.[375] The invention incentive function, or the theory of how the patent system provides an incentive, is best understood through the

[375] Nordhaus, W. D., *Invention, Growth and Welfare: A Theoretical Treatment of Technological Change* (1969); Kamien, M. I.; Schwartz, N. L., 'Market Structure, Elasticity of Demand and Incentive to Invent,' (1970); Kamien, M. I.; Schwartz, N. L., 'Market Structure and Innovation: A Survey,' (1975); Loury, G. C., 'Market Structure and Innovation,' (1979); Lee, T.; Wilde, L. L., 'Market Structure and Innovation: a Reformulation,' (1980); Kamien, M.I. and Schwartz, N., *Market Structure and Innovation* (1982). Rigorous explanative models of innovation utilising the innovation incentive statement in conjunction with empirical data significantly began with William Nordhaus in 1969. Today there are generally between thirty to forty important empirical studies of the patent system utilising the incentive statement accessible in English, French, German or Italian, across the breadth of patent technologies or patenting firms, each year.

assumptions (premiss) that comprise the canonical form of the invention incentive function statement.

2.2.1. **Premise 1: No Patent, No Invention**

The first assumption (φ^A)[376], presupposes the advantage of the patent system as a source of innovation incentive, compared to the absence of such a system. It holds that without the patent system, the incentive for innovation will be insufficient to meet minimal community requirements.[377] Announcing the winner of a race before a race begins might in some peoples' opinion defeat the purpose of the race. However, in this instance the premise (φ^A) serves as a reversal of the burden of proof concerning the effectiveness of the patent that is demonstrative of the political origins of the patent system.[378] It is a strong strategic position to take for those in favour of a patent system, as it places two difficult burdens on the critic if they are to falsify the innovation incentive advantages of having a patent system on the basis (of φ^A) that without the patent system, the incentive for innovation will be sufficient to meet minimal community requirements. Thus, it must be determined what are the minimal community

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[376] If you are not familiar with symbolic notation then these characters can be ignored as I have provided analysis and explanation in both forms. However, even if the symbolic syllogisms cannot be followed it does help to have a signifier for the exact premise close at hand. This will become clear as the discussion becomes more complex. If you are familiar with symbolic logic, you will see that only the main syllogisms are presented in symbolic form and these are relegated to the footnotes and then summarised in Appendix 1.

[377] The return expected by a community for the resources it sets aside for that purpose.

[378] Chang, H-J., *Kicking away the ladder: Development strategy in historical perspective.* [Anthem Press, 2004, 1st Ed., 2nd Reprint, London] 19-57

requirements for innovation and then demonstrate that those requirements are met in the absence of a patent system.

Prima facie, when the history of innovation prior to the Statute of Monopolies 1624,[379] or even the Venitian Patent Ordinance of 1474, is considered the premise (φ^A) might be falsified depending on the standard adopted for the minimum community requirements for innovation. If the standard adopted is too high then the patent system may fall foul of not satisfying the minimum innovation requirement of the community.

For example, if the minimum community requirement for innovation were considered to be cures to all diseases. Then evidently before 1624 there were diseases without cures. Thus, in the absence of the patent system innovation could not satisfy community requirements for innovation. However, maintaining the same minimal requirement for innovation it is clear that under the present day patent system innovation is unable to satisfy minimal community requirements. The standard then for innovation to be sufficient to meet minimal community requirements must be set equal or bellow what is achieved under the patent system.

However, it is also necessary to consider that the nature of innovation in the modern world[380] may have changed substantially from that of the pre-

[379] 21 Jac.1, c.3

[380] The period at which we assert the modern world to begin is only important when constructing a model for falsification. As a convention this work ties the modern world to

patent world. This could be in terms of the properties of an invention, the nature of inventor[381] and community expectation.[382] If this is the case, then inference from pre-patent innovation that invention will satisfy minimum community demands for innovation cannot be assessed. As even though the standard, which is to be applied for the required minimum of innovation, purports to be the same the social context has changed. Thus, the premise (φ^A), that without the patent system, the incentive for innovation will be insufficient to meet minimal community requirements, on the basis of historical anecdote is unfalsifiable.

We can explain this difficulty of 'proof' more formally. Proof as such does not exist, we rely on conventions for our intersubjective standards of objectivity. Proof in this case requires the establishment of such a convention. Thus, it is necessary to falsify the hypothesis (φ^A) that without the patent system, the incentive for innovation will be insufficient to meet minimal community requirements. Falsification of this hypothesis requires empirical study with a statistical significance indicative that more innovation takes place in the absence of a patent system than in the presence of one, or that the hypothetical standard set for minimum community requirements of innovation are met. Conducting a valid

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the rise of industrial innovation. For pharmaceutical innovation this is the early twentieth century, for biotechnology inventions this is the late twentieth century.

[381] Change in the paradigm of the individual inventor to the corporate and institutional inventor. See Noble, D. F, *America by Design* [Oxford University Press, 1979, 2nd Ed., Oxford] 67-109

[382] That community expectation is a product of the acts of market dominant forces is a difficult hypothesis to falsify.

empirical study to falsify the hypothesis (φ^A) is immensely difficulty. Which is why this reversal of the burden of proof is so powerful; for the patent critic to overcome it is extremely difficult, but it must be defeated before the premise (φ^A) can be overcome.

Technically this is a shoe that fits both feet. As indeed, it is a fallacy of relevance, present in a considerable volume of patent literature, to assert that for a given invention, innovation would or would not have occurred, but for a patent system. This is because, the interconnection of environmental, economic and psychological factors necessary for the realisation of an invention are so complex and tied to the specific *loci* - cultural, temporal and spatial characteristics and composition of an invention - that it would be an *argumentum ad ignorantiam* to assert by virtue of the realisation of a similar invention within or without a patent system that the given invention would or would not arise.

Furthermore, in the present world, which by virtue of TRIPS is to know at least as paper rules ubiquitous patent legislation, there are few if any legal enclaves of modern and patent free research and development. The award of software and business patents, as such, in the USA and the *prima facie* refusal of these enclosures of the public domain in Europe might appear to constitute a fertile field of examination. However, a comparative analysis of the effect of a patent system on either of these institutions would be inadequate for the purposes of ascertaining which inventions are most easily obtained in the absence of a patent system.

The reason being that the cross contamination of ideas and structures between each system and the component step nature of innovative activity (that is, each new inventive step is an inventive increment for future innovation) prevent the successful allocation of the necessary and sufficient intellectual breakthrough to the patent or non-patent granting system.

2.2.2. **Premise 2: No Rivalry**

The second assumption (φ^{B}) of the innovation incentive function statement is utilised implicitly and holds that inventors perform research leading to non-rivalrous inventive steps.[383] This premise (φ^{B}) serves two purposes. Firstly, it simplifies mathematical modelling by excluding competitive research and duplicate resource expenditure from innovation models. Secondly, it serves as a base for two *prima facie* persuasive statements: Firstly, the longer the duration of a patent the greater the magnitude of incentive and thus, the greater the number of potential inventors persuaded to innovate (φ^{B1}).[384] Secondly, the larger the breadth of entities capable of being patented the greater the domain of inventors to which the patent system provides incentive (φ^{B2}).[385] If the second premise (φ^{B}) is

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[383] Arrow, K. J., 'Economic Welfare and the Allocation of Resources for Invention,' (1962); Nordhaus, W. D., *Invention, Growth and Welfare: A Theoretical Treatment of Technological Change* (1969); Scherer, F. M., 'Nordhaus' Theory of Optimal Patent Life: A Geometric Reinterpretation,' (1972).

[384] Nordhaus, W. D., *Invention, Growth and Welfare: A Theoretical Treatment of Technological Change* (1969); Scherer, F. M., 'Nordhaus' Theory of Optimal Patent Life: A Geometric Reinterpretation,' (1972)

[385] Klemperer, P., 'How Broad Should the Scope of Patent Protection Be?' (1990)

unfalsified then its two related premiss (φ^{B1} and φ^{B2}) lead to a conclusion that the stronger the patent incentive, either by duration or breadth, then the greater the patent system's innovation incentive. However, the second premise (φ^{B}) is a denial of the classic description of human activity where economic actors pursue the most favourable product, spatial and physical attributes of a market. Innovators by their success either demonstrate the existence of a new market, or the weakness of market competitors.[386] Whilst some inventions, technological breakthroughs, do create new markets the majority provide improvements and compete to supply existing demands. An empirical assessment of the invention market will also suggest that where a particular inventive step, improvement or breakthrough, offers very large rewards compared to similar technology areas, that is where inventors have the appropriate resources to compete for equivalent inventive steps, then copy inventing will take place.[387] The rivalry to arrive first at the invention with the greatest reward is termed a *patent race* and is the subject of an economic theory that attempts to depict the dynamic incentives of the patent system.[388] It can be considered as a preferable, though limited, alternative to the second premise (φ^{B}) of the innovation incentive function statement.

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[386] Loury, G. C., Market Structure and Innovation (1979) 93(3) *The Quarterly Journal of Economics* 395-410 at 396-402

[387] Me-too pharmaceutical patents are an example, but inventing around is also a frequent occurrence with mechanical patents. On the 'overfishing' of limited technology 'pools' see Barzel, Y., 'Optimal Timing of Innovations,' (1968).

[388] Dasgupta, P. S.; Stiglitz, J. E., 'Uncertainty, Industrial Structure and the Speed of R&D,' (1980)

Patent race theory[389] is based on competition between actors to transform ideas into property. That is, the transformation of an inventive step into property that it is assumed will lead to a product that will reward the owner for their efforts. Thus, it has two significant components: a) the conditions an inventor has to satisfy to obtain a patent; and b) the value of the rents derived from the patent. Since acquisition of a patent is the end point for patent race theory, it is especially applicable to situations where the inventor lacks resources to undertake market supply of the invention, or where further development is necessary for the invention to be approved for the market (as is the case for pharmaceutical patents).[390] The patent is seen as a product destined to meet a particular demand and the competition arises from the anticipated benefit of achieving rents from first

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[389] Loury, G., 'Market Structure and Innovation' (1979) 93 *Quarterly Journal of Economics* 395-410; Dasgupta, P., Stiglitz, J., 'Uncertainty, Industrial Structure, and the Speed of R&D' (1980) 11 *Bell Journal of Economics* 1-28; Lee,T., Wilde, L., 'Market Structure and Innovation: A Reformulation' (1980) 94 Quarterly Journal of Economics 429-436; Reinganum, J., 'The Timing of Innovation: Research, Development and Diffusion' in Schmalensee, R., and Willig, D., (eds.) *Handbook of Industrial Organization* [North Holland, 1989. 1st Ed., Amsterdam] 849-908; Harris, C., Vickers, J., 'Racing with Uncertainty' (1987) 54 *Review of Economic Studies* 1-21; Segerstrom, P., Anant, T., Dinopoulos, E., 'A Schumpeterian Model of the Product Life Cycle' (1990) 80(5) *American Economic Review* 1077-91; Grossman, G., Helpman, E., 'Quality Ladders in the Theory of Growth' (1991) 58 *Review of Economic Studies* 43-61

[390] Some economists suggest that the patent reduces transaction costs of licensing the invention. See Arrow, K. J., 'Economic Welfare and the Allocation of Resources for Invention,' (1962); Merges, R. P., 'Expanding Boundaries of the Law: Intellectual Property and the Costs of Commercial Exchange: A Review Essay,' (1995); Arora, A.; Gambardella, A., 'The changing technology of technological change: general and abstract knowledge and the division of innovative labour,' (1994). However, even if the patent lowers licensing transaction costs obtaining a patent and restricting the embodiment of the respective inventive step incurs transaction costs. Coase, R. H., 'The Problem of Social Cost' (1960) 3 *Journal of Law and Economics* 1-44

supply of that demand. For society it allows a balance to be found between eliminating inefficient inventors and wasting resources in duplicatory competition. The optimum balance set by the length of the race and the prize rents should create dynamic efficiency: That is, static efficiency such as the accessibility of medicines are balanced by long run concerns such as the research and development of new medicines.

If a race is long with a large prize then it will stimulate inventors to work hard and will eliminate the most inefficient competitors. Elimination of the most inefficient competitors serves dynamic efficiency and thus contributes to welfare. However, the long duplicated expenditure of resources between competitors is wasteful.

In the context of pharmaceuticals, prizes can be extremely large for a few patents, which are embodied in market approved products, but the majority of pharmaceutical patents receive no rents. The objective of these no-rent patents is to waste competitors' resources. This is positive in the light that they will deter many inefficient competitors from the patent race with the large reward and present savings to society. However, it is disadvantageous to society as the resources deployed in the no-rent patents must be compensated by rent from the prize patent of the patent race. It is also disadvantageous as competitors who continue to compete must expend resources to navigate the no-rent patents. This situation is represented in most therapy areas. The first mover advantages mean that

in some cases the race leader can still win even if they are less efficient than competitors.

Since the prize is a large reward competitors may still continue to compete even after an inventor has obtained the prize.[391] In general this is undesirably wasteful to society, though in some circumstances the increased uptake of competing products may make contributions to welfare. For the competitors it may reduce the value of the available prizes to static efficiency leaving little or nothing to be invested in other patent races.

Although it is called patent race theory it can include the innovation activities of generic manufacturers. If improvement (insufficient to qualify as a new invention under § 2(6) Patent Act 1077) is a sufficient qualifying factor and market share is decisive of the winner, patent race theory readily accommodates generic medicines. Thereby, factors such as the price of the medicine, its quality and its availability become variables within patent race theory. Which already makes patent race theory more preferable to (φ^B) assuming non-rivalrous inventive activity.

Moreover, since innovation may be rivalrous the inventor may not be in a position to benefit from their inventive work.[392] Furthermore, increase in

[391] Me-too medicines for example the PDE5 inhibitor market

[392] This might be for one or more of several reasons, i.e. because an earlier patent anticipates the inventive step or that despite the technological merits of the inventive step the inventor lacks the resources to access the market.

the total inventive effort does not guarantee an increase of innovation output. Thus, the related premiss (φ^{B1} and φ^{B2}) of the second premise of the innovation incentive function statement, no longer state a reliable proportional relation between patent strengthening and innovation output. Rewards are considered to be greatest for first comers, thus inventors have an interest in investing their resources in order to be the first to patent the inventive step. In so doing it is likely that they will consume their resources faster and less efficiently than if their object were to achieve a particular inventive step in the absence of competition.[393] The result of achieving a particular invention faster and less efficiently is that the resulting product is more expensive as the inventor must recoup higher opportunity cost.

Moreover, even if a given inventor paces their research and development independently of competition and thus discovers the inventive step with economic efficiency there will be other potential inventors working on the same objective. These potential inventors must derive benefit from somewhere to repay their resource investment in unrewarded research. According to standard welfare economics this cost has eventually to be met by the community.

2.2.2.1 **Patent Race Alternative**

Patent race theory as a result can only describe an incentive for inventors who have sufficient resources not to be excluded from a market. As those

[393] Barzel, Y., 'Optimal Timing of Innovations,' (1968) 348-350

without resources to enter the market cannot compete. Remembering that licences are available for pharmaceutical products it is possible that they may join with another competitor or entrant to acquire sufficient resources to in effect enter the market. This is usually the case for university and government inventions.

As market share is decisive of the winner, a patent by itself may become less important than other strategic behaviours.[394] Subsequent patents, even though they are potentially weak because they lack an inventive step, may be required. Pharmaceuticals are a complex technology area in a mature industry where patenting standards can be surprisingly low.[395] In these circumstances we would expect patent ownership to be shared amongst competitors resulting in low incentives to innovate. However, although ownership of pharmaceutical patents tends to be shared they are not shared amongst competitors. The patents are shared amongst research entities, such as universities or the NIH, and a research and manufacture pharmaceutical company. Therefore, incentives remain high, and later entrants into the market are sufficiently delayed that their losses from failing to win the patent race are not borne by the winner or originator. With a little complication evergreening can be modelled into patent race theory. Rather than considering that an innovation in a patent race corresponds to the acquisition of a single patent – the originator patent –

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[394] The degree to which the patent remains important depends on the technology sector. For a historic flavour of the variance see Mansfield, E., 'Patents and Innovation: An Empirical Study,' (1986)

[395] Harrison, C., 'Patent Watch' (2009) 8 *Nature Reviews Drug Discovery* 350-351

we can use wave theory and model subsequent market rent domination events (evergreening events) as crests.

At this point it may be useful to our understanding to consider a very simple application of patent race theory as the uses we have suggested go beyond the standard conceptions of its use. Let us consider a simplified example based on the statin market. The market is divided amongst six products. However, some competitors own more than one of these products. For the moment we will aggregate the product variables for each competitor. Which means the market is divided amongst four competitors. Let them be *a*, *b*, *c*, and *d*.

a's cumulative share of the market since it began is 45 per cent. *b*, *c* and *d*'s cumulative market shares are 25, 20, and 10 per cent respectively. Let us consider that the cumulative value of the market over its lifetime has been 100. Thus, total revenues from the market are 45, 25, 20, and 10 for *a*, *b*, *c* and *d* respectively. *a* has two products on the market that have cost it *u1* and *u2*. *b* also has two products that have cost it *u3* and *u4*. Therefore the total profit from the market for *a* is 45-(*u1*+*u2*). For *b* the total profit is 25-(*u3*+*u4*). Therefore, if *u1*+*u2* is greater than *u3*+*u4*+20, then *a*'s participation in the market has been more effective than *b*'s. By increasing the number of variables within this set of relations we are able to generate observations concerning different facets of the competitors' behaviour. Such indicators can be useful to investors wishing to place

their capital in a lucrative market, or for innovators to determine which strategies are most effective.

First mover advantages including establishment of production and distribution networks have generally been identified as more important than patents.[396] The chemical and pharmaceutical technology sectors however, are considered to be primarily patent dependent.[397] This may be because within the chemical and pharmaceutical technology sectors market access tends to have a high resource requirement threshold. Moreover, within the context of pharmaceuticals there are options for extending lead-time that are only available to competitors who have a patent[398] and pharmaceutical patents have a longer term than any other patent. Furthermore, the standard of sufficiency for pharmaceutical patents is low, which facilitates patent line extensions. Patent race theory within the context of pharmaceuticals, then is best considered as a particular distortion from market theory. Moreover, because of the resource threshold required for competition, the patent as an innovation

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[396] See Levin, R. C., 'Technical Change, Barriers to Entry and Market Structure,' (1978); and Levin, R. C.; Klevorick, A. K.; Nelson, R. R.; Winter, S. G., 'Appropriating the Returns from Industrial R&D,' (1987), but also see Taylor, C.; Silberston, Z. A., *The Economic Impact of the Patent System* (1973); and Schwartzmann, D., *Innovation in the Pharmaceutical Industry* (1976).

[397] Edwin Mansfield's 1986 survey of one-thousand US manufacturing firms between 1981 and 1983 is most often cited to show industry R&D dependence on patents. It was suggested that for automobiles, metal refining, electrical equipment, and office equipment *inter alios* that less than ten per cent of R&D was dependent on the patent. For pharmaceuticals and the chemical industry the patent was suggested to be necessary for about sixty and forty per cent respectively of new inventive steps. See Mansfield, E., 'Patents and Innovation: An Empirical Study,' (1986)

[398] For example Supplementary Protection Certificates.

incentive and primary source of reward is only addressed to a very small number of economically powerful actors.

We see a closer reflection of reality in substituting patent race theory and therefore rivalrous behaviour into the invention incentive function statement than if we simply retained (φ^B) the premise that inventors perform research leading to non-rivalrous inventive steps. However, there remains a difficulty. Both patent race theory and the premise (φ^B) that inventors perform research leading to non-rivalrous inventive steps, fail take account of innovation retarding effects of the patent system, for example the high costs involved in maintaining a patent.[399] Indeed the cost of policing a patent and prolonging the life of a patent line is extremely difficult to foresee. Retrospectively such costs can be incorporated into patent race theory, but they are problematic because patent race theory in its simplest form considers a patent race to end when a single patent is obtained. These problems are understandable, because the invention incentive function statement ends once the innovation has been achieved

[399] Currently the patent filing at the UK Intellectual Property Office (UK IPO) costs £200 GBP; it is comprised of a preliminary examination at £30 GBP, a search at £100 GBP and a substantive examination at £70 GBP. UK IPO renewal fees commence after the fourth anniversary from the filling date; they are currently £50 GBP for the fifth year augmenting by £20 GBP increments each year to £400 GBP for the twentieth year. Costs are taken from the UK IPO schedules as at December 30, 2008. See:
<http://www.ipo.gov.uk/types/patent.htm> (Last Accessed: 1st July 2009)
The most important expense of a patent arises if it needs policing. During interview (March 2004), a European Patent Attorney specialising in chemical and pharmaceutical patents admitted that contention over a patent could typically cost each party several million GBP, not taking account of settlements, awards and the unbillable costs a party's agents may sustain.

and has no consideration for the aftermath. That is the principle reason for it to assume non-rivalrous invention (φ^B): through this premise the invention incentive function statement can ignore costs arising from other patents and patent actions.

Indeed, within our simplified substitution trying to account for the cost of competitive behaviour adds a complex qualification to the appealing simplicity of the incentive invention function statement. That is, even if a competitor innovates and is an originator, there is no guarantee that they will realise any reward from their invention.

Furthermore, although patent race theory might provide a more sophisticated illustration of innovation incentive than simply assuming (φ^B) that there is no rivalry, it needs to take account of a large number of negative innovation incentives that arise from rivalrous behaviour. Although we have mentioned some of these, such as the high cost of patent policing, others include the risk of infringing a patent through the embodiment of even minor technological changes to a product, and the disincentive of competing with others for the reward, where the winner takes all. Within a system where market share is permissible winner takes all is of less significance. However, for pharmaceuticals it should be remembered that patents and data exclusivity can pose absolute bars to market entry. Moreover, in a rivalrous environment the patent system constitutes an important strategic tool, even where a patent is not in fact

existent, and may permit dominance of both market and innovation sectors in the absence of actors of comparable resources.

2.2.3. **Premise 3: No Money, No Invention**

The third major assumption (φ^C) of the innovation incentive function of patents is as equally important as the first two premiss (φ^A and φ^B). It assumes that an economic return is the most important incentive for inventive activity to occur. The patent for inventions' invention incentive is derived from its correlation of 'usefulness to society' and 'economic value' through scarcity[400] that allows the patent holder to assign or license use of the inventive step at a price. If there were no scarcity, then the most efficient producer of the product employing the inventive step would, all other parameters remaining the same, dominate the market to the extent the respective economy of scale permitted.

As this premise is closely related to the fourth premise, it is expedient to treat them both at the same time. Let us introduce premise four.

2.2.4. **Premise 4: Inventor Owner**

By granting scarcity to the patent holder in order to encourage inventive activity the patent system adopts the natural allocation principle of copyright[401] and makes the fourth important assumption (φ^D) of the

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[400] Penrose, E. T., *The Economics of the International Patent System* (1951) 27

[401] For an early example see: *Millar* v. *Taylor* (1769) 98 E.R. 201: "...it is just, that an author should reap the pecuniary profits of his own ingenuity and labour..." per Lord

innovation incentive function statement - that the inventor and patent holder are the same natural person, or group of natural persons. The function of the patent system by permitting the inventor to control scarcity makes it easier for the inventor to derive an income from their inventive step.[402] Thus, if the second premise (φ^B) is retained, and the costs of the patent are ignored, then the patent system according to the invention incentive function statement encourages perfect allocation.
However, since the patent has a cost and is necessary (φ^A) necessary then, even theoretically, the patent system cannot encourage perfect allocation.

2.2.5 **Allocation, Incentive and Inventors**

Indeed perfect allocation is unlikely to be the objective of a system that relies on artificial scarcity unilaterally controlled by the person seeking reward for the invention. The mechanism by which this artificial scarcity provides the inventor with an incentive is simple, but requires the objective of the patent holder or inventor to be pecuniary, in particular a period of maximisation. Thus, technological knowledge is sought only for the above normal profit that its respective patent may allow the inventor to reap. This

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Mansfield CJ at 252 and further Aston J. at 220-221, and Willes J at 212. Note three arguably different strands of reasoning.

[402] Plant, A., 'Economic theory concerning patents,' (1934) 32. On the patents part in reducing the licensing cost of technologies see Arrow, K. J., 'Economic Welfare and the Allocation of Resources for Invention,' (1962); Merges, R. P., 'Expanding Boundaries of the Law: Intellectual Property and the Costs of Commercial Exchange: A Review Essay,' (1995); Arora, A.; Gambardella, A., 'The changing technology of technological change: general and abstract knowledge and the division of innovative labour,' (1994)

is a problem shared by patent race theory; there has to be a prize for either to work.

Without the patent for inventions, and assuming the resources of the inventor and competitors to be alike, then the inventor is unable to assert an entry barrier to the market against their competitors. In the case of hypothetical perfect competition, supply will equal demand and above normal profit will not be available for the inventor. However, with a patent for inventions the inventor can prevent additional productive resources entering the market and in consequence will earn above normal profits for the duration of the patent. The invention incentive would conceptually function in the absence of patents, providing that another reward or 'prize' was available.

The utilitarian justification of the patent system as the means of preference to supply community demand for innovation, at this point, becomes difficult. Essentially under perfect competition when supply equates to demand then equilibrium will occur. According to market theory the equilibrium point of perfect competition will yield lower prices and higher output than under monopoly.

2.2.6. **My Labour**

Though utilitarianism has difficulties in justifying the community's award of above normal profits to the inventor, because of the reduced accessibility of the invention and the lower research productivity, there are other

justifications for the invention incentive function to be organised in this way. Primarily, amongst these are labour specialism theory[403] and labour theory. Labour specialism theory concerning patentable inventions holds that only a small portion of a community is capable of creating technological inventions. Since this small proportion of the community can earn sufficient reward from the community through means other than inventive activity there is no natural advantage for this minority to innovate rather than follow non-inventive behaviour. Furthermore, because not all innovations will be successful the risk involved in devoting resources to innovative activity makes innovative behaviour less favourable than non-inventive behaviour. Thus, the potential inventor must be offered an incentive to carry out inventive activity in preference to other opportunities for reward. As a result the opportunity to receive above normal profits creates a preference amongst the inventive portion of the community to innovate.

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[403] Not all elements of a workforce are capable of fulfilling all roles. The more complex the task the less the likelihood that a given element will be able to successfully complete every other role. See Plato, *The Republic*, trans. H. D. Lee [Penguin Books Ltd, 2003, 1st Ed., London] 103. "...let us see how our city will be able to supply this great demand: We may suppose that one man is a husbandman, another a builder, some one else a weaver–shall we add to them a shoemaker, or perhaps some other purveyor to our bodily wants? Quite right. The barest notion of a State must include four or five men..."; consider further brief mention by Xenophon on the Education of Cyrus in M. Finley, *The Ancient Economy* [Penguin books Ltd, 1992, 1st Ed., London] 135; developing contemporary treatment is found in Hume (*A Treatise of Human Nature*) and Smith (*An Inquiry into the Nature and Causes of the Wealth of Nations*); Other mention can be found amongst the discussion of the 'Division of Labour' by Eugen von Böhm-Bawerk, Émile Durkheim, Friedrich Hayek, Karl Marx, Carl Menger, Ludwig von Mises, and Henry David Thoreau.

The labour theory, sometimes labelled Lockean labour theory,[404] assumes that a person's labour is their own. It then holds that because a person's labour is their own the product of that labour is also theirs as opposed to the community's.[405] An insurmountable difficulty is resolving the transformation of resources belonging to a community as a whole into a product that belongs only to the transformer or the labourer. The difficulty in accepting the transformation is proportional to the use competitiveness of the initial resource and the accessibility of competing uses.[406] In the Two Treaties of Government[407] 1690 Locke was only concerned with real property and not intellectual property. Physical property, the main subject of Locke's writing, lends itself more readily to individual attribution than intellectual property. Physical property can only be utilised by a limited number of people, thus a distributive mechanism is needed to determine who will be able to consume resources and for which purpose.[408] The atomalistic approach to ownership, as opposed to group ownership of physical property, is the historic product of European community structures.[409] A progressive history of individualistic acquisition of property commons has a significant impact on Western legal mentality.[410] As a

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[404] Hughes, J., 'The Philosophy of Intellectual Property' (1988) 77 *Georgetown Law Journal* 287;

[405] Idea of the patent as an instrument of justice is still pertinent and can be seen in §40 Patent Act 1977 concerning compensation for employees.

[406] Thus, the problem is essential one of resource allocation and not one of post-transformation possession.

[407] Locke, J. P., *Two Treatises on Government* Laslett, P. (ed.) (1988)

[408] i.e. the appropriation function of property law or an *argumentum ad baculum*

[409] Macpherson, C. B., *The Political Theory of Possessive Individualism* (1979) 221

[410] Cohen, M. R., 'Property and Sovereignty,' in *Law and the Social Order. Essays in Legal Philosophy* (1982) 41-44

result of the property experience the Lockean labour theory was readily adopted into intellectual property theory in order to provide natural right justification for the intellectual commons' closure movement. It will be remembered that the patent does not prevent use of the knowledge of the patented inventive step, rather it restricts physical embodiment of the patented inventive step. Whilst it was true that a natural right trope for intellectual commons' closure was not applicable by virtue of allocation necessity, it was also arguable that the enclosed knowledge was an addition to knowledge and because no one had previously thought of it, thus it was not yet part of the property in common to the community. Hence, property in the inventive step was the natural right of the inventor, because the inventor was the *sine qua non* of the community knowing the inventive step.[411]

2.2.7. **All Together**

Thus, we arrive at a point where the patent system's innovation incentive function, according to its assumptions[412] (φ^A, φ^B, φ^C and φ^D) will generate more rapid innovation by giving the inventor sufficient economic incentive to innovate rather than pursue non-inventive behaviour. In addition it will give the inventor their just entitlement. For without the inventor's initiative and work, the community's knowledge commons could never be

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[411] Becker, L. C., 'Deserving to Own Intellectual Property,' (1993) 609-629, but is serendipitous innovation different?

[412] There are most important assumptions of the innovation incentive function statement. They are that the patent holder is the inventor, inventors pursue research that leads to non-rivalrous inventive steps and that without patents there would be insufficient incentive to innovate to meet community demand for innovation.

expanded. Unfortunately, we are also aware that according to market theory, which utilises the same techniques of economic analysis, but does not assume inventive incentive to be weaker in the absence of the patent, that innovation will be more expensive and slower for the community in the presence of monopoly.[413]

An examination of patent practice suggests an inherent dependence of the patent as an economic stimulus of inventive activity to be more effective when coexistent with a thriving competitive market. A wealth of empirical anecdotes exist that are unfalsifying of the convention[414] that where a market is occupied by relatively few uncompetitive firms there is a likelihood of languid technological progress.[415] Professor Cornish suggests that the pharmaceutical and software industries with markets dominated by relatively few firms are, by virtue of their 'determination to innovate,' falsifying of a general convention suggesting proportionality between market dominance and inventive indolence encompassing all

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[413] Market theory also makes assumptions which are in some cases impractical.

[414] This refers to falsifiability and as short hand states that the meaningful statement ('where a market is occupied by relatively few uncompetitive firms there is a likelihood of languid technological progress') is conclusively decideable and had not yet been falsifified by experience. See Popper, K., *The Logic of Scientific Discovery* [Routledge Classics, 2004, 7th Ed., London] 17

[415] Jewkes, J.; Sawers, D.; Stillerman, R., *The Sources of Invention* (1969)166-168; Merges, R. P.; Nelson, R. R., 'On the Complex Economics of Patent Scope,' (1990) 884; "There is abundant evidence from case studies to support the view that actual and potential new entrants play a crucial role in stimulating technical progress, both as direct sources of innovation and as spurs to existing industry members... new entrants contribute a disproportionately high share of all really revolutionary and new industrial products and processes." Scherer, F. M., *Industrial market structure and economic performance* [Rand McNally College Publishing Company, 1980, Chicago] 437-438

technological sectors capable of being patented subjects.[416] There is certainly reason for caution in proposing general descriptive relations encompassing all patent types.[417] However, the products of both software and pharmaceutical markets are by nature extremely rivalrous, thus promoting competition with regard to certain products in spite of market dominance. For software, rivalry stems from a short market longevity of each product incorporating the inventive step. With pharmaceuticals the high profitability of a blockbuster invention inspires competitive me-toos. In both cases, although relatively few firms may dominate a given market, at the *loci* where the pharmaceutical or software industry example presents falsifying elements, a thriving competitive market is seen to exist.[418] Since longevity thresholds and profit thresholds have a high correspondence with exception to an unqualified convention regarding the proportionality of market dominance and inventive indolence it is sensible to incorporate both into the epistemological construction of the convention. Thus, it may be clearer to suggest a convention that where a firm dominates a given market in the absence of rivalrous potential there is a tendency towards inventive indolence[419] (ρ^A), and where competitive

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[416] Cornish, W., *Intellectual Property: Patents, Copyright, Trade Marks and Allied Rights* (1999) 132

[417] Burk, D. L.; Lemley, M. A., 'Is Patent Law Technology-specific,' (2002) consider the courts reactions to different types of technologies and how different patent subjects do not receive homogeneous treatment across technology sectors. It should be questioned whether the entities of different technology sectors are capable of equivalent treatment?

[418] With software the Windows and Linux Operating Systems are demonstrative. Amongst pharmaceutical patents Viagra is a well known example, though Prozac is a better example.

[419] Soete, L., 'Firm size and inventive activity' (1979) 12 *European Economic Review* 319-40

potential exists regardless of the small number of rivalrous firms there is still incentive to innovate more rapidly than if there were no potential competitive provider to that given market (ρ^B).[420]

To consolidate the premises of the innovation incentive function statement are that: without the patent system, the incentive for innovation will be insufficient to meet minimal community requirements (φ^A); that inventors perform research leading to non-rivalrous inventive steps (φ^B); that economic return is the most important incentive for inventive activity to occur (φ^C); and that the inventor and patent holder are the same natural person, or group of natural persons (φ^D).

2.2.8. **Beyond the Prize**

For research to generate non-rivalrous inventive steps (φ^B), then there must be an absence of competition, which suggests there will be a reduced incentive to undertake further inventive activity (ρ^A). Thus, the extent of the inventive activity, which will be undertaken under the invention incentive function statement, is not as extensive as would be undertaken if inventive activity was rivalrous ($\sim\varphi^B$).[421]

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[420] For example rail fastening systems. The market is dominated by Pandrol, but there are other firms with competitive potential, thus Pandrol has an incentive to invent to maintain its market leading position.

[421] Let inventive activity be λ, and inventive activity as a result of the invention incentive function statement be λ^I. Therefore,

$$\varphi^A \bullet \varphi^B \bullet \varphi^C \bullet \varphi^D \supset \lambda^I$$

$$\because \varphi^B \supset \rho^A \supset \sim\lambda$$

$$\therefore \lambda^I \supset \sim\lambda$$

The invention incentive function statement lacks coherence with regard to empirically supported inventive indolence. That is to say that if patents were a sufficiently strong monopoly to be non-rivalrous,[422] then there would be no further innovation in the presence of a patent – i.e. once a patent was awarded there would be no incentive for further innovation until the patent expired or neared expiry.

Remember that another premise of the invention incentive function statement is that the longer the duration of a patent the greater the magnitude of the incentive and thus, the greater the number of potential inventors persuaded to innovate (φ^{B1}). However, this premise now has a corollary. That is, each inventor creates inventions that do not compete for resources. The greater the incentive the more people stimulated to inventive activity. However, during the period of the patent indolence replaces the incentive to invent. Thus, the labour of those actors, by definition capable of inventive activity, is wasted during the period of the patent. Thus, increasing patent times, i.e. increasing the incentive to invent, proportionally increases waste.

[422] Remember our discussion of software and pharmaceutical patents above, the monopoly would have to be large enough to encompass the particular market and of sufficient duration that the patentee felt no urge to expend resources in further innovation. For there to be a retardative effect it would only be necessary that a moment of inventive indolence occurred. Longer instances would of course yield greater retardation in invention.

As a justification then, the invention incentive function statement is problematic. It suggests that in the absence of competition inventions will be realised efficiently, but then during the period that the incentive is received there will be a waste of resources. As a tool for justifying practice, it is also undesirable as long as there is sufficient incentive to direct activity into invention and no system of distributing that inventive activity, down to the individual actor, there will be duplicated and therefore wasteful research activity. This will particularly be the case if some inventions have more desirable incentives than others.

2.2.9. **Motivation**

There are other empirical behaviours that appear anomalous with respect to invention incentive models, but conceptually should be part of the invention incentive. Consider the polio vaccines devised by Jonas Salk and Albert Sabin. Neither inventor filed a patent or sought economic reward from their inventions. Their rewards appear to be derived from their satisfaction in preventing Poliomyelitis and perhaps the knowledge that the renown that followed their invention would lead to career progression. To attribute the incentive of all innovation to the patent is historically falsifiable and presumptuous of an understanding of the human being *in toto* and the diversity of environmental factors that might influence choice. However, considering the conditions in which innovation does occur there are several, not mutually exclusive, incentive reasons for

inventive research: these are the ability to perform new tasks,[423] more effective performance, lower production cost, renown, the natural creativity of humankind,[424] a rent in the innovation, patent circumvention, and altruism. Some of these reasons for invention empirically conflict with (φ^C) the premise that a financial return is the most important incentive for inventive activity to occur. Given the empirical example of the Polio vaccines a financial return is not a necessary condition of pharmaceutical innovation incentive. Furthermore, considering the utilisation of herbs, herbal extracts, and minerals by both ancient peoples and modern cultural-community-collective herborists - the wielders of the unsatisfactorily so-called 'traditional knowledge' – substantial discovery of the medicinal properties of compositions and extracts, i.e. invention, occurred in the absence of a financial reward. That other factors than financial reward have played an important role in the devising of medicinal agents is very difficult to falsify. In a similar measure, if the nature of pharmaceutical innovation has changed fundamentally from patentless regimes of medicinal innovation, it is difficult to falsify the premise (φ^C) that an economic return is the most important incentive for inventive activity to occur. In consequence, the ability to perform new tasks, more effective performance, lower production cost, renown, the natural creativity of humankind, a rent in the innovation, patent circumvention, and altruism

[423] The ability to solve problems or improve environmental conditions is historically an important source of innovation. For example, the stirrup was devised to increase the stability of a rider.

[424] Invention for the pleasure of devising a new manner of doing something or accomplishing something hitherto not possible.

(which we label φ^{C1}) could be substituted in place of the premise to the invention incentive function statement in place of the for the premise (φ^{C}) that an economic return is the most important incentive for inventive activity to occur. This is a qualified substitution: In the advent that it can be shown that the nature of pharmaceutical innovation has changed from that of non-patent granting pharmaceutical innovation regimes - not merely in terms the evolved channels of pharmaceutical production based on legal artifice, rather as a response to changed physical factors[425] - and that a financial reward is the determinant condition for the success of the majority of innovation then our substitution (φ^{C1}) reverts to (φ^{C}) simply an economic return. On the other hand, if the nature of pharmaceutical innovation is not different by virtue of the physical characteristics of patent granting communities then (φ^{C1}) our substitution remains unfalsified and can be retained.

The ability to perform new tasks, or to solve problems has been an observable trait of humankind since the Neolithic period at the very least.[426] There were certainly no patents to incentive innovative activity for a very long period where considerable innovation took place. The most plausible explanation for the incentive for the practices of domesticating animals and fashioning tools by splitting and grinding stone are the ability

[425] For example discontinuous change in human or virus serotype physiology with the medicine genesis techniques of the past

[426] Helbaek, H., 'First Impressions of the Çatal Hüyük Plant Husbandry' (1964) 14 *Anatolian Studies* 121-123

to perform new tasks and more effective performance.[427] The practice of domesticating animals is likely the result, *inter alia*, of an incentive to perform a new task, i.e. the improvement of environmental conditions through the augmentation of resources readily available to a community. By creating tools of polished stone Neolithic humans would not only have gained the ability to perform new tasks, they also improved their ability to perform a given task. For example, Neolithic man used their stone tools to improve, *inter alia*, their ability to prepare shelters, to cure skins and to create their art. Gradual improvements to the domestication of animals and the manufacture of stone tools, through experimentation would either be for the reason of reducing the resources necessary for tool creation or to improve the efficiency of a tool.

Other reasons for the domestication of animals or the manufacture of stone tools might include the natural creativity of humankind and altruism. Whilst the natural creativity of humankind can never be discounted it is also very difficult to assert, and might constitute a necessary condition of inventive activity.[428] Altruism can only be asserted in those cases where a detailed account of motive is available.[429]

2.2.10 **Inescapable Waste**

As there are incentives to invent new and more efficient ways of performing tasks, there are also incentives to invent alternative or less

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[427] Edwards, M., *Stone Tools and Society* [Routledge, 2002, 2nd Ed., London] 9-12

[428] This is a problem of cognitive theory and one that is an industry in the subject.

[429] For example in the cases of Florey, Salk and Sabin

efficient methods. Patent circumvention was unnecessary for Neolithic humans, but other beliefs or customs might have demanded that alternative methods of performing some tasks were devised.[430]

Another problem of the invention incentive function statement is that it assumes that an incentive is a necessary condition for invention to occur, and thus, neglects the importance of serendipity in the invention process. Serendipity (φ^{E}) is not a necessary condition for invention incentive, but it is a sufficient condition.[431]

It might be argued that though an invention is conceived it will not be developed further without an incentive. The invention incentive function statement is not concerned with consequent development of an invention so its premiss were not assumed with any justificatory intent towards post patenting, or rather post reward, activity.[432] The invention incentive function statement is simply not concerned with what comes after acquisition of the patent. Therefore, problems such as inventive indolence (ρ^{A}) do not feature within its justification.

If the invention incentive function statement is to be considered part of a coherent model of patent justification alongside the other posited justifications then the consequences of its premiss after the award of a

[430] Edwards, M., *Stone Tools and Society* [Routledge, 2002, 2nd Ed., London] 12-14

[431] Where the disjunctive is exclusive invention will occur, according to the invention incentive function statement, when φ^{E} v $(\varphi^{A} \bullet \varphi^{B} \bullet \varphi^{C1} \bullet \varphi^{D})$. Thus, $\sim (\varphi^{A} \bullet \varphi^{B} \bullet \varphi^{C1} \bullet \varphi^{D})$, $\therefore \varphi^{E}$ and $\sim \varphi^{E}$, $\therefore (\varphi^{A} \bullet \varphi^{B} \bullet \varphi^{C1} \bullet \varphi^{D})$.

[432] However, the organised derivative invention function statement is. See 2.5. below.

patent need to be considered. Having done this we are well are of the statement's limitations as well as the realism of its premiss. Thus, we are well placed to consider how its premiss cohere with the premiss of other function statements. Moreover, when it arises in patent literature we will be immediately aware of its limitations and therefore the validity of syllogisms that utilise it or its elements.

2.3. **Disclosure Incentive Function Statement**

Whilst the invention incentive function statement assumes (φ^{A}) that without the patent system the incentive for innovation will be insufficient to meet minimal community requirements, the disclosure incentive function statement has a very different premise.

2.3.1. **Premise 1: No Patent, No Disclosure**

It assumes that inventions will occur without patents and that the existence of patents, through their requirement of specification, widens the use of an otherwise undisclosed inventive step by making the respective knowledge available to the community. Indeed the disclosure incentive function statement considers (φ^{B1}) the assumption that longer patent terms provide a larger incentive inconsequential. Since it assumes that the same degree of innovation will occur in the absence of the patent as in its presence. The only difference is that without the patent the essential knowledge of the inventive step will not be distributed to the community.

The premise (φ^{B2}) that the larger the breadth of entities capable of being patented then greater the domain of inventors to which the patent system provides incentive, is also irrelevant as such. However, this premise is relevant to the disclosure incentive function statement in that if a technology area is not eligible for patents then knowledge about invention in that area will not be disclosed. Therefore premise (φ^{B2}) would be understood in the context of the disclosure incentive function statement to be: The larger the breadth of entities capable of being patented then greater the domain of disclosure to which the patent system provides incentive.

The first premise (φ^{A}) of the invention incentive function statement and the first premise of the disclosure incentive function statement do not cohere. Therefore, the invention incentive function statement and the disclosure incentive function statement conflict.

As there remain many interesting points to raise concerning the interplay of these two function statements, and to avoid complication, we shall distort the two premiss. We will replace both conflicting premiss with a new premise (φ^{A1}). Which is as much as possible a compound of important elements from the two premiss. This is then, that without the patent there would be too little invention and disclosure of that innovation, to meet minimal community requirements (φ^{A1}).

The disclosure incentive function statement needs to be considered as two components: a principle and an auxiliary. The principal statement for the disclosure performed by the patent system is that without the patent there would be no disclosure: i.e. the *modus tollendo tollens* relation, only if there is a patent system will disclosure take place. If there is no patent system, then no disclosure takes place.[433] Substituting for the distorted premise (φ^{A1}) this would be: if there is no patent system, then too little disclosure will take place to satisfy minimal community requirements. The auxiliary statement is that disclosure through the patent system is desirable. The statement concerning the desirability of disclosure through the patent system is auxiliary because it is only necessary when the principal, that the patent system is the only manner of disclosure that has incentive, is falsified. Usually within a scientific discipline scientific papers are a more fertile source of knowledge than patent specifications. However, there is a growing trend for scientific information that may have practical applications to be withheld from publications in the hope that a patent might be obtained: Thus, the patent acquires more validity as an

[433] This is an interesting position to consider in the context of the appropriation of cultural-community-collective herbalist knowledge through the patent system, where such knowledge was obtained outside of the patent system, and the defensive effect that this appropriation through the patent has on creating defensive practices regarding the disclosure of cultural-community-collective herbalist knowledge. See Magaisa, A. T. *Knowledge and Power: Legal, Political and Socio-Historical Perspectives on the Protection of Traditional Medical and Knowledge Systems in Zimbabwe*, Warwick University thesis collection.

important form of disclosure, but at the same time loses its strength as a desirable incentive for scientific research.[434]

Falsification of the principal, that the patent system is the only manner of disclosure, through empirical example is straightforward.[435] Furthermore, given the rapid advances in reverse engineering facilities and the increasing availability of technical information through media and technical publications, including the document subjects of mosaicing, then the community's ability to discover the knowledge of a given inventive step is highly probable: A chemical's structure can be analysed and its constituents identified. From there the source from which the chemical was extracted can be prospected or the chemical itself can be synthesised.[436] A mechanical embodiment of an inventive step can be taken to pieces the function of each piece and the incidence of each piece's properties on the comportment of the system can be identified. Thus, although disclosure by the patent system may facilitate the acquisition of knowledge by a community it is not a necessary condition for knowledge concerning an inventive step to become available to a community.

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[434] Lei, Z., Juneja, K., Wright, B., 'Patents versus patenting: implications of intellectual property protection for biological research' (2009) 27 *Nature Biotechnology* 36-40

[435] Invention occurred before a patent system existed and continues outside of the patent system. Moreover, invention should always occur before patent registration and therefore invention should always precede patenting. We state should as the invention sometimes occurs after the application. For a contemporary example, consider the unamended specification of US patent 6,410,516.

[436] A good example is the anti-malarial artemisinin, produced from sweet wormwood, that in spite of the limited availability of information concerning its source or manufacture was successfully reengineered adding enormously to community knowledge.

2.3.2. **Inadequate Disclosure**

There is another reservation on the effectiveness of the patent specification as an adequate disclosure of knowledge concerning an inventive step.[437] The organisation of patent grants in the UK is such that the responsibility for policing insufficient specifications falls on private parties either by opposition proceedings or more likely as a counterclaim in infringement litigation following the patent grant.[438] As a result the quality of information concerning the inventive step in the specification of some granted patents is exceedingly poor. Considering that patent technical information is addressed to the notional person skilled in the art and the diversity of patentable technology fields it is unrealistic to assume that the patent office has access to sufficient expertise in all technology fields to judge that a specification is sufficient.[439] This is the main justification for the inclination of the patent system towards granting rather than refusing patents and the post implementation theoretical justification of the current

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[437] For an understanding of the framework of a well drafted claim see Mickelthwaite, E. W. E., "Brushing up our drafting," [2003] CIPA, 320-324, 379-386; and Mickelthwaite, E. W. E., "Effective specification drafting," [2003] CIPA, 482

[438] For example insufficiency as a ground of revocation §72(1)(c) UK Patent Act 1977 grants the comptroller the ability to revoke a patent, but this is almost always as a consequence of successful defence litigation by a rival manufacturer of the embodiment of the inventive step, by showing that the patent specification was insufficient to instruct someone skilled in the art to perform the inventive step.

[439] Grubb, P. W. *Patents for chemicals, pharmaceuticals, and biotechnology: Fundamentals of global law, practice and strategy* (2004) 365; see Barton, J. H., 'Patenting Life,' (1991) 254(3) *Scientific American* 40-46; Eisenberg, R. S., 'Proprietary Rights and the Norms of Science in Biotechnology Research,' (1987) 97 *Yale Law Review* 177-231; Merges, R. P.; Nelson, R. R., 'On the Complex Economics of Patent Scope,'(1990) 90(4) *Columbia Law Review* 839-916.

system whereby private parties can bring actions that may or may not result in the revocation of grants. In economic efficiency the present system of private party policing is, *prima facie*, cost effective to the state. In reality the situation is more complex and the uncertainty of the value of some patents as determinant actors in litigation proceedings is likely to increase the overall cost of inventions especially during the lengthy reconstruction of the notional addressee.

A clearer instance of the difficulty of relying on patent specifications for disclosing technical information to the community is the case of technology transfer. There has been much revile of the patent system especially over the last two decades as a source of information transfer.[440] The Indian generic pharmaceutical experience was that breakthrough medicines were more readily understood through analysis of the chemical composition of the drug rather than reference to patent specification data.[441] Another difficulty of patent specification data is that often what the non-patent specialist would consider to be part of the same inventive step is broken down into many more patent claims for inventive steps,[442] a process

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[440] This discontent concerning academic research has arisen because of the changes in government attitudes to research. See, Eisenberg, R., 'Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research' (1996) 82(8) *Virginia Law Review* 1663-1727; On the discontent see, Bozemanr, B., 'Technology transfer and public policy: a review of research and theory' *Research Policy* 29 (2000) 627–655 at 644,646

[441] Lanjouw, J., 'The Introduction of Pharmaceutical Product Patents in India: "Heartless Exploitation of the Poor and Suffering"?' (1998) NBER Working Paper No. W6366. 6-7

[442] In the UK this practice is a product of the 'partial validity' allowance first instituted by the Patent Act 1919

occasionally known as insurance enclosure.[443] This insurance enclosure can frequently yield as many as forty or fifty patents.[444] In this case not only is it difficult to join information together concerning the overall functioning of an invention, but the clever draftsman can draft the multiple patents in such a way that the entirety of the inventive step is anticipated whilst an essential part of the information necessary for a community to understand the inventive step is absent from the specifications taken as an ensemble.

2.3.3. **Premise 2: More Than It Seemed**

This is the point at which the auxiliary disclosure incentive function statements become important. It is clear that a community will undertake discovery of information regarding an inventive step if the application of the inventive step is considered useful and there is no disclosure or insufficient disclosure, formally or informally declared. Thus, why is the patent system as a source of disclosure important? The answer lies within

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[443] This informal term is likely the product of the reasoning that if a claim is divided into many claims then these many claims can push the boundaries of the patent claim providing some of the claims are stable enough to exclude rivals from the overall invention with some certainty. If the expansive patent claims are revoked then the stable claims and the multiplicity of them provide a comfortable fall back to exclude rivals from the flagged domain. There is also for the larger repeat players a form of insurance available in the complexity of proceedings for rivals when there are numerous patents rather than a single patent.

[444] In several jurisdictions, though not the UK, excessive multiple claims are discouraged by an increase in fees when an application has claims in excess of a set number. For example, the EPO has a substantial fee increment for applications with claims in excess of ten. The Amend Rule 29(2) has, since January 2002, permitted the EPO to adopt a strong position against multiple independent claims within a patent application. See EPO Guidelines C III 4.

the enmeshment of three other reasons for the importance of the disclosure accomplished by the patent system. As with the principal, these reasons are posited as advantages for the community rather than generation of individual incentive. The individual incentive for the information holder to disclosure arises from the benefits that the patent system bestows on the inventor, i.e. a rent, and not the formalities of patent acquisition.

The first auxiliary disclosure incentive function statement is that a patented inventive step might have more applications than the first patentee anticipated (φ^F) and that through increasing the fraction of the community exposed to knowledge of the inventive step other useful embodiments of the inventive step will be discovered (ρ^C). An inventive step might have more applications than the inventor realises and disclosure permits others the opportunity to discover those other applications.[445]

2.3.4. **Incompatible Again**

The first auxiliary disclosure incentive function statement is, *prima facie*, incompatible with the invention incentive function statement in another way. The invention incentive function statement makes available a reward to the inventor by granting the inventor the ability to enforce scarcity in the embodiment of the inventive step. In effect, once the inventive step has been discovered the patent, in the invention incentive function statement,

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[445] $(\varphi^F \bullet x) \supset \rho^C$, $(\varphi^F \bullet x)$, $\therefore \rho^C$, where x is, in this equation, representative of a disclosure method; e.g. reverse engineering, mandatory publication, or patent specification: $(\varphi^F \bullet \varphi^{A1}) \supset \rho^C$, $(\varphi^F \bullet \varphi^{A1})$, $\therefore \rho^C$. Clearly, $(\varphi^F \bullet x) \supset \rho^C$, $\sim x$, $\therefore \sim \rho^C$

reduces the use of the inventive step that would, in the absence of a patent system, be made.

The first auxiliary disclosure incentive function statement takes a very different stance when it holds that:

A patented inventive step might have more applications than the first patentee anticipated (φ^F) and that with the patent system (where the incentive for innovation will be sufficient to meet minimal community requirements of innovation and disclosure (φ^{A1})) then increasing the fraction of the community exposed to knowledge of the inventive step other useful embodiments of the inventive step will be discovered (ρC).[446]

2.3.5 **Already Owned**

Given (φ^F) that a patented inventive step might have more applications than the first patentee anticipated, what incentive does the patent provide for Y to disclose their knowledge when inventor Z is awarded a patent that anticipates the unforeseen new application invented by Y? Neither, the invention incentive function statement, nor the disclosure incentive function statement provides Y with an interest to make the knowledge of the new 'invention' available to the community. The clearest example of patent claim anticipation of unforeseen uses of an inventive step is the product *per se* patent for chemical inventions. If a patent is granted for the chemical compound itself, a compound *per se* patent, then all process

[446] $(\varphi^F \bullet \varphi^{A1}) \supset \rho^C$

involving the respective compound have been anticipated.[447] If the case of the compound *per se* patent is considered anomalous and temporarily excluded from consideration then concordance of the assumption by the invention incentive function statement, concerning the patent as a means to obtain scarcity, and the first auxiliary disclosure incentive function, regarding the patent as a means of stimulation new applications, is possible. The conditions for concordance are that the new application is not anticipated, hence capable of being patented, and that the specification of the first patent is sufficient to stimulate the second inventor to make the cognitive connections for the new application. However, the first condition will no longer be a necessary condition where the possession of a patent and the expertise of another may convey sufficient incentive to a patent holder to create contractual agreements, usually cross licensing, with non-rivalrous inventors to pluralise embodiment of the inventive step.

2.3.6. **Sanctioned Cartel**

If there are two patents in a common pool for example, i.e. one from each party, and the two firms are engaged in non-rivalrous markets then for both parties there are advantages of finding new applications.[448] This patent pooling relation is concordant with the invention incentive function statement in the case where inventors would otherwise have insufficient means to develop and or exploit an invention themselves. Moreover, were

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[447] See Grubb, P. W. *Patents for chemicals, pharmaceuticals, and biotechnology: Fundamentals of global law, practice and strategy* (2004) 345-348

[448] An empirical example of this benefit chain is Bell Labs transistor.

they to begin rivalrous behaviour each would receive lower returns than the share they would receive from splitting revenues arising from the patent pool. In the context of patent pooling then the compound *per se* patent is no longer anomalous and the invention incentive function statement and first auxiliary disclosure incentive are compatible with regard to first auxiliary disclosure incentive function statement,[449] and the incentive for the discoverer of the new application to share their discovery amongst the patent pool contributors.

2.3.7. **Patent Advertising**

The second auxiliary disclosure incentive function statement is that the patent advertises the availability of an inventive step thereby facilitating licensing of that inventive step. By facilitating licensing the patent reduces transaction costs and makes embodiment of the inventive step more accessible to a community than if higher transaction costs were involved. However, considering that the marginal cost of increasing the utilisation of information is zero[450] and that the patent system is expensive for parties wishing to exclude competitors[451] to hold that the patent system as a form of advertising reduces transaction costs is an unsatisfactory statement. It

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[449] $(\varphi^{F} \bullet \varphi^{A1}) \supset \rho^{C}$

[450] See Arrow, K. J., "Economic Welfare and the Allocation of Resources for Invention," R. R. Nelson (eds.) *The Rate and Direction of Inventive Activity: Economic and Social Factors* [Princeton University Press, 1st Ed., 1962, New York] 616-617

[451] Blanco White, T. A., *Patents for Inventions* (1974) 9-10

fails to consider all the extra transaction costs a patent system creates.[452] Considering particular industries, For example agriculture, it is seen that specialist markets advertise their products through a number of forums, particularly specialist magazines and shows. The pharmaceutical industry advertises in journals, both by actual advertisements and articles. Other than the journals the key marketing tool of the pharmaceutical industry is the pharmaceutical representative, on whom the task to educate the health practitioner falls. These methods of distributing specialist products to a professional audience have been highly successful and continue to work well. Applying the same market economics, used to show that the patent specification facilitates licensing of the inventive step's embodiment thereby making the invention more accessible to a community, does not yield empirically the expected outcome. If the patent system through the advertising capability of disclosure were able to reduce transaction costs and increase marginal revenue then a comparable institution to the patent system for the purpose of advertising would have evolved within the trade industries. That has not been the case, nor is the evolution of the patent system a suitable example. As we have noted the patent system did not evolve from the nature and characteristics of the inventive steps themselves, but rather as a result of the technocratic power wielded by patent practitioners[453] in the aftermath of a technology migratory policy.

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[452] For example in the presence of a patent system it is necessary for inventors to conduct infringement searches to determine whether their activity infringes anyone else's patent rights.

[453] Drahos, P; Braithwaite, J., Information Feudalism: Who Owns the Knowledge Economy? [Earthscan Publications Ltd, 1st Ed., 2002, London] 43-48

The second auxiliary disclosure incentive function statement is a very weak patent function statement.

2.3.8. **Technology Transfer**

The third auxiliary disclosure incentive function statement is that the patent system serves as a method of technology transfer by requiring that complex technical information be expressed with sufficient clarity that a person skilled in the art be able to replicate the embodiment of the inventive step.[454] The patent system's specification requirement is however, as already indicated, a frequently insufficient tool for insuring disclosure of information capable of permitting a community to replicate the inventive step. The tension between technical complexity and non-obviousness in a patent application is inevitably biased in favour of technical complexity that would make an invention seem as non-intuitive as possible. Thus, even an obvious and anticipated invention can seem inventive. Consider for example the meaning of 'a physiologically acceptable substance stabilized in an acidic medium.'[455] Whilst it does refer to a pharmaceutical compound that is non-toxic and can be stabilised in tablet form by an organic acid it also refers to many foodstuffs that are pickled, i.e. a jar of pickled onions. The institution in Western Europe of

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[454] This is exemplified by §14(3) UK Patent Act 1977 which states that "[t]he specification of an application shall disclose the invention in a manner which is clear enough and complete enough for the invention to be performed by a person skilled in the art." Failure to comply with this requirement provides a ground of revocation for insufficiency under §72(1)(c) UK Patent Act 1977.

[455] This is actually taken from a claim rather than a specification, but although on a more complex level for a specification the same spirit of mystification can pervade the patent drafter's style. See UK 45,6671 CELLTRIX H/AO 441

competing patent offices has not had a desirable effect on the grant of patents with clear scope. In fact the competition between patent offices and the applicant friendly approach has resulted in many patents being granted for unclear and poorly drafted patent applications.[456]

2.3.9. **Together Again**

So far according to the assumptions of the invention incentive and disclosure incentive function statements, that if there is a patent system then there will be sufficient invention and disclosure of that innovation to meet minimal community requirements (φ^{A1}). Moreover, when there is disclosure through a patent then the increased fraction of the community exposed to knowledge of the inventive step will permit other embodiments of the inventive step will be discovered (ρ^{C}).[457]

To be a viable justification, the disclosure incentive function statement requires[458] that the invention arising from the patent system and its method of disclosure is greater than the invention and disclosure which would occur in the absence of the patent system. This returns us to our methodological problem, that available data is insufficiently comparable to generate statistical inferences: There is either a patent system or there is not; In the circumstances that there is not then cross migration of ideas

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[456] See Cornish, W., *Intellectual Property: Patents, Copyright, Trade Marks and Allied Rights* (1999) 133

[457] $\varphi^{A1} \bullet \varphi^{F} \supset \rho^{C} \supset \lambda([\varphi^{A1}]$

[458] $\lambda([\varphi^{A1}]>[\sim\varphi^{A1}])$

between that system and systems where there is a patent system will contaminate data.

However, we are aware that the patent system is not an adequate form of conveying technological information to the community and we can use this as an indicator of the truth of the first premise (φ^{A1}) of the disclosure incentive function statement. Thus, if disclosure of knowledge about the invention is greater in the absence of the patent system then the disclosure incentive function statement is falsified.

The disclosure incentive function statement of the patent system, even when the principal is leant assistance by the auxiliaries, is unpersuasive except in one circumstance: Where patent pooling, or the contracting of external resources is necessary or preferable to the patent holder. In this scenario possession of a patent, by virtue of the bargaining power the patent bestows, is likely to make the patent holder contract with others who possess the required resources, including expertise, to increase the patent holder's marginal revenue. This incentive model can also be extended further by substituting the desire for an increased marginal revenue for the ability to perform new tasks, more effective performance, renown, the natural creativity of humankind, or altruism. This cooperative development of a patent and new embodiments of an inventive step is closely related to the prospect theory and commercialisation theory of the organised derivative innovation function statement. It is also an important description for the trend described in Chapter II for current pharmaceutical

research and patenting. The small biotechnology company, in Schumpeterian terms a competence-destroying industry,[459] through a closer linkage with the breakthrough knowledge of the old science bases, immunology and molecular biology,[460] and the availability of resources through the university and government institutions of which its key researchers are part, has created an environment more favourable to pharmaceutical innovation then the pharmaceutical manufacturing and research firms. The small biotechnology company, however, lacks access to finances, regulatory approval expertise and marketing savvy that the pharmaceutical manufacturing and research firms possess. For the sustained economic viability of either organism both knowledge sets are necessary conditions. Taken together the knowledge sets are also a sufficient condition for the economic success of the small biotechnology company and the pharmaceutical company. The biotechnology company supplies new applications or new inventions and the pharmaceutical company passes these through the hurdles of regulatory approval and then delivers them to the market. When the biotech company fails to find a viable drug candidate then it will go into liquidation and the pharmaceutical manufacturing company, which would formerly have been conducting such research, will be insulated from the loss.

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[459] Creative destruction according to Schumpeter is responsible for long term economic growth. This is a process by which innovative entrepreneurs enter established markets or created new ones thereby destroying the value and market dominance of companies that exerted some monopoly power. See Schumpeter, J. A. Capitalism, Socialism and Democracy [Harper & Row Publishers, 1942, Reprint 1975, New York] 82-85

[460] Abernathy, W.; Clark, K., 'Innovation: Mapping the Winds of Creative Destruction,' (1985) 14 *Research Policy* 3-22; Powell, W., 'Collaboration in the Biotechnology Industry,' (1996) Journal of Institutional and Theoretical Economics 152(1) 197-215, 202-203

2.4. Investment Incentive Function Statement

The co-operative relation between the inventor and external resources necessary to the commercialisation of an invention can be described in terms of the investment relations of the investment incentive function statement. Although in this expression there is no longer a sense of parity in status between the inventor and the investor.[461]

2.4.1. **Premise 1: Investor Not Inventor**

The origin of the inventor's subordinate relation begins during the first phase of the Age of Reform. When increasing the flow of capital to industry and encouraging the participation of investors in research were economically desirable.[462] The patent system was designed to serve as the bridge between industrial research and investment, with the value of the inventive step being the risk and the prize. The inventor themselves, became irrelevant except as a mechanical component in the invention process. Inventors become interchangeable and the contract of service

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[461] The motivation to innovate is directed at the inventor in the invention incentive function statement. (φ^{C}, φ^{C1}, φ^{D})

[462] Holdsworth, W., *A History of English Law* Volume XV Goodhart, A. L.; Hanbury, H. G. (eds.) (1965) 4. However, 'development' of the patent system during this period is attributable to substantially more than encouraging investors. See Select Committee reports BPP 1829 (332) III and BPP 1851 (486) XVIII; Royal Commission BPP 1864 (3419) XXIX; Select Committee BPP 1871 (368) X, 1872 (193) XI. For a very brief account of reasons for reform see Cornish , W., *Intellectual Property: Patents, Copyright, Trade Marks and Allied Rights* [Sweet and Maxwell, 4th Ed., 1999, London]113-115

became the standard engagement for 'workers' in invention.[463] In this fashion the investment incentive function of patents for inventions conflicts with the patent indigenisation of the copyright natural allocation principle necessary to the invention incentive function. In the invention incentive function the investor or institution is irrelevant to the process of innovation except as mechanical part that can be changed with impunity with regard to the success of the innovation itself. In the investment incentive function the investor or institution is determinant of research resulting in an invention.

2.4.2. **Conflicting Statements**

The apparent conflict of the innovation and investment function statements arises not from an incompatibility of the innovation and investment incentives themselves, but rather from an epistemological error in the construction of the two function statements. To both the innovation and investment incentive for the acquisition of a patent both the invention of the 'worker' and the resources of the investor are necessary conditions. The epistemological difficulty arises from the lack of consequence the invention and incentive function statements place on the participation of a certain actor. It is easy to visualise the origin of this inconsistency of perspectives in the two function statements when it is seen that the perspectives are a result of maximising the appeal of the patent system to the addressed actor. Thus, the inconsistency is a deliberate politic and not an academic error. For the investor the greater the degree of certainty,

[463] An ethos that is embodied in all current patent regimes. See §39(1) UK Patent Act 1977.

that where there is a patent the return on the patent will be a return that they receive the better and the more they will invest in innovation activity. If a particular inventor is recognised as being a necessary actor in discovering the inventive step, the *corpus* of the patent claim, the inventor may acquire some equity in the patent: the so-called Lockean labour theory of reward.[464]

2.4.3. **Capital But No Genius**

On the other hand the investor cannot be important to the incentive function statement because it is assumed that the incentive is addressed to the inventor (φ^c). If the investor was as important, as they are empirically and legally[465] then (φ^c) that the incentive is addressed to the inventor cannot be assumed as the patent does not grant the inventor a greater incentive to undertake inventive activity than other activities. The labour specialism theory, an important descriptive element in the construction of the invention incentive function statement, holds that only a small portion of a community is capable of creating technological inventions. Since this small proportion of the community can earn sufficient reward from the community through means other than inventive activity there is no natural advantage for this minority to innovate rather than follow non-inventive behaviour. Indeed as these gifted inventive

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[464] Idea of the patent as an instrument of justice is still pertinent and can be seen in §40 Patent Act 1977 concerning compensation for employees. In fact compensation for employees under this section is relatively unknown and very unsuccessful as a ground of litigation.

[465] §39(1) Patent Act 1977 is the manacle on the patent at the end of the chain owned by the totality of investors.

individuals may reap less reward acquiring incentives for investors, than they might acquire elsewhere for themselves, they may be lost from the investor controlled technology area. As they are irreplaceable according to the invention incentive function statement, any inventions they might have realised will be lost from the system.

2.4.4. **Combining Incentives**

This is where substitution of 'inventive activity occurs for the ability to perform new tasks, more effective performance, lower production cost, renown, the natural creativity of humankind, a rent in the innovation, patent circumvention, and altruism' (φ^{c1}) for 'economic return is the most important incentive for inventive activity to occur' (φ^{c}), is important, because although inventing is no longer as financially enticing, because the ownership of the patent vests in another, other incentives still make invention a more favourable activity for the potentially inventive portion of the community. At least this is the only method of reconciling the invention incentive function statement and the investment incentive function statement.

Then, let us consider the invention that the inventor produces as a result of other incentives than the patent system.[466] This invention would be compatible with the investor incentive function statement, provided that the investor's use of artificial scarcity does not conflict with the inventor's desired reward (φ^{c1}). However this relation is incomplete as the investor's

[466] $\varphi^{c1} \supset \lambda$

choice, exercised by their agents in the case of shareholders, is dependent on the shareholders perceiving a profit.

Therefore, invention will only occur under the combined auspices of the invention and investment incentive function statements, *iff* the inventor perceives they can receive their desired incentive, and the investor perceives they can receive an attractive economic return.[467]

In this form only can the investment incentive function statement be considered compatible with the invention incentive function statement. Interestingly at the point when the patent has been acquired there may have already been investment, indeed the capital provided by prior investment might have been a necessary condition. However, where development of the invention is necessary then the patent may capture further investment, providing that there is a likelihood of (φ^{C}) an economic return for the investor.

2.4.5. **Patent Attracts Investment**

Acquisition of a patent may constitute an approbation that the invention is a viable commodity, indeed the patent as a property right and monopoly enables the patent holder to seek funding from capital markets. In the case of pharmaceuticals the acquisition of a patent may stimulate some interest but of greatest concern is the likelihood that clinical trials and market approval will proceed favourably. However, the pharmaceutical

[467] $\varphi^{c1} \bullet \varphi^{C} \supset \lambda$

patent presents the confidence of enclosure, that may attract the funds necessary for the development phase necessary for market approval. With the growing presence of biotech firms as innovators in the pharmaceutical technology sector, large pharmaceutical research and manufacturing companies are repositioned as investors or buyers.[468] For the purposes of the investment incentive function statement it is sufficient to consider investment up to the moment that the invention is patented. When we consider the practicalities of pharmaceutical innovation and safety approval then post-patenting costs will be considered.

In the stark form that we have presented the investment incentive function statement, it is clear that innovators will only be encouraged to innovate when the investors perceive that they will receive a return on their invested capital. This is especially significant in pharmaceuticals where the invested capital is great. If it is necessary for an invention to be developed before it can be used and the only established channels for that development are perceived to be secondary investors then the initial investors must be equipped with some vehicle to ensure that they will recoup their investment when the secondary investors develop the

[468] This is not a new phenomena, it had been DuPont's policy in the interwar period. See Mueller, W. F., 'The Origins of the Basic Inventions Underlying DuPont's Major Product and Process Innovations, 1920 to 1950' in *The rate and direction of inventive activity: Economic and social factors* [National Bureau of Economic Research, Princeton University Press, 1962, Princeton] 323-346

product. For better or worse, at the moment the patent serves this purpose.[469]

2.4.6. **Pharmaceutical Incentive**

Within the context of pharmaceuticals this poses an interesting situation. With the fierce competition by pharmaceutical companies to develop generic, copycat or me-too drugs and the separate regulatory requirements each entails, there seems little likelihood that pharmaceutical innovation resulting from public funding would not serve an economic purpose and result in a commercial product. Thus, what is interesting is to track down where (φ^C) the economic return must occur in the investment chain for the investment incentive function statement to function. Regulatory approval will be very important to the return of investment.

We will show later that the research institution benefits, but the secondary investors receive the greatest economic return. The primary investors, however receive nothing,[470] and are responsible for meeting (φ^C) the

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[469] The University and Small Business Patent Procedures Act 1980 (USA), better known as the Bayh-Dole Act, provided universities, small businesses and non-profit organisations in the USA with the ability to obtain intellectual property rights on innovations and creations achieved with public funding. The principal argument for this act was the investment incentive function. statement. See 35 U.S.C. § 200: "It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities..."

[470] See 35 U.S.C. § 212. Of course the invention will become available, if not necessarily accessible to the primary investor.

economic return expected by the secondary investors. To make this clearer, it is useful to consider the primary investor as being the general public and who underwrite the research. The secondary investor only becomes involved once there is a product to be developed and a return seems viable.

The dispositive issue is whether there would be greater development of the invention where the inventing institution was able to offer an exclusive licence for the invention, or where non-exclusive licences were available to all potential developers of the invention.

2.4.7. **If It Pays Best**

If the magnitude of (φ^C) the economic return is the determinate factor, then in the absence of an exclusive license developing the invention is *prima facie* less favourable, as it will not permit monopolistic rewards.[471] However, other factors may affect the magnitude of (φ^C) the economic return, such as subsequent development sharing clauses[472] or the cost of initially acquiring the information.

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[471] There may be instances where it will be advantageous to develop an invention in the absence of monopolistic rewards. This might be the case with computers, where compatibility issues may be determinative of development prospects.

[472] These are conditions to the patent license contract that require the contractee to share all their developments with other contractees. They sometimes include compensation clauses or lead time stipulations to ensure the fairness of the arrangement for the more innovative contractee.

Where the investment incentive function statement is especially successful in the context of publicly funded research, is that it prompts the funded research institution, that is the inventor, to promote their invention, thus ensuring that the invention is developed and commercialised. Unfortunately, since the license may be exclusive the assignee may have purchased the patent title in order to suppress the invention. In which case the intentions of the Bayh-Dole Act are undermined.[473] A further problem is that research with the greater economic returns will be favoured over research leading to economically less or unprofitable applications. The economic return from the invention and the invention's usefulness to society may not coincide, other than in economic terms.

2.5. Organised Derivative Innovation Function Statement

This is potentially a clever post patent operational function statement. However, couched beneath a very superficial veneer is its self-vitiation.

2.5.1. **Premise 1: I Know Best**

The organised derivative innovation function statement provides, as per the prospect theory of Edmund Kitch,[474] that the utility of a patent occurs after an initial invention is made: In that the patent holder, through

[473] Working requirements in the case of pharmaceutical patents can be offset for a greater delay through use of market approval application. Since bioequivalence is an important factor in medicines this either very rarely necessary or is performed extremely cleverly.

[474] Kitch, E. W., 'The Nature and Function of the Patent System' (1977) 20(2) J. Law & Econ. 265-290

selective and conditional patent licensing is able to control future improvements and developments in the technology area and thereby ensure that resources are not squandered on developing rivalrous derivative technologies. As did Kitch, it implicitly assumes that a single patent can control an entire technology area allowing the holder of the patent to determine which products are developed. We can with little difficulty extend the theory to a patent pool or cross licensing agreement providing that one actor can control subsequent product development within the technology area.

As such the organised derivative innovation function statement is pessimistic about the ability of competitive forces to develop useful rivalrous derivative inventions which may in themselves produce divergent strands of useful derivative invention. Thus, for this theory it is extremely important that the standard of the patent is perfectly balanced. That is, that the patent standard does not permit a patent holder to bar too large an area from subsequent development, but at the same time the barrier is a enough that the patent holder can retain control over their prospect.

2.5.2. **Contrariness Again**

This function statement is then, extremely optimistic of the foresight of the prospect patent holder. As a result it is an important consideration in determining how long patent monopolies should endure. For different technology areas technology uptake varies, and in some cases the availability of different development paths is preferable for the users, e.g.

consumers. This is the case with pharmaceuticals where variations can have enormous therapeutic benefits for particular patients, but drug tailoring is extremely expensive and then further limited by organised development through patent restrictions.

Thus, organised derivative invention presumes that the invention which will occur as a result of non-rivalrous development of a technology area will be greater than if there were competition.[475] To be more clear, the function statement states that there would be less wasteful invention and that subsequent development in the directed non-rivalrous environment would be greater than the wasteful developments during competition.

Which is incompatible with the disclosure incentive function statement. Remember the disclosure incentive function statement holds that more invention will result from disclosure through the patent system than if there was no disclosure, since there may be more applications of the invention that the inventor realises (φ^F) and that revealing the invention to a larger section of the community will permit those other applications to be identified (ρ^C).[476]

2.5.3. **Better, Not More**

In particular the organised derivative invention function statement disagrees with the presumption that more innovation is necessarily a

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[475] $\lambda([\varphi^B]>[\sim\varphi^B])$

[476] $\lambda([\varphi^F \bullet \rho^C]>[\sim \varphi^F \bullet \rho^C])$

preferable channelling of resources. Providing that technological advancement is the objective and that resources saved through the limitation of research to systematic non-rivalrous research are reinvested in further systematic development of the prospect, then (φ^{B}) non-rivalrous research produces more effective invention.

Let us consider the reinvestment of resources gained from an earlier invention (φ^{G}).[477] Providing that exterior investment is momentarily eschewed then it is expected that invention as a result of reinvestment will be greater than where there is no reinvestment.[478] This would be a valid conclusion if investment is proportional to invention for a given technology sector. Serendipity (φ^{E}) must also be ignored, or considered to be sufficiently infrequent that it has no statistical significance.[479]

2.5.4. **Externalities and Market Behaviour**

However, the organised derivative innovation function statement relies on the prospect patent to regulate the behaviour of externalities, thus exterior investment cannot be ignored. There is therefore a potential conflict with the investment incentive function statement which holds that there will be more innovation if other than the economic incentive that the investor requires, there is also an incentive for the inventor, than in the same conditions except there is no incentive for the inventor.[480]

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[477] Let these be φ^{G}

[478] $\lambda([\varphi^{G}]>[\sim\varphi^{G}])$

[479] $\lambda([\varphi^{G}\bullet\sim\varphi^{E}]>[\sim\varphi^{G}\bullet\sim\varphi^{E}])$

[480] $\lambda([\varphi^{c1}\bullet\varphi^{C}]>[\sim\varphi^{c1}\bullet\varphi^{C}])$

Whilst for the prospect patent holder the economic return (φ^C) may be greater if subsequent technology is controlled, gross economic return within the technology market may be reduced. Moreover, we are aware from the invention incentive function statement that where competitive potential exists, regardless of the limited number of rivalrous firms, there is still incentive to innovate more rapidly than if there were no potential competitive providers to that given market (ρ^B).

If the market is non-rivalrous, as required by the invention incentive function statement and the organised derivative innovation function statement, then the total innovation will be the result of the initial investment and the result of innovation funded by reinvestment.[481] Because, invention is non-rivalrous and the prospect is controlled there will be no development of applications that the prospect patent holder does not perceive. Moreover, there will be inventive indolence because there are no potential competitive entrants to the market.[482] Therefore let us consider if innovation of the technology area would be preferable in the control conditions of organised derivative innovation or where there was rivalry and no total control over a prospect.[483]

Thus, the dispositive issue is whether the innovation which arises out of reinvestment is greater than the innovation which would result from

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[481] $\varphi^B \supset \lambda^I + \lambda(\varphi^G)$

[482] $\therefore \varphi^B \supset \rho^A + \sim\varphi^F + \sim \rho^B + \sim \rho^C \supset \sim\lambda$

[483] $\therefore (\lambda^I + \lambda[\varphi^G]) \vee (\lambda^I + \lambda[\varphi^F + \rho^B + \rho^C]) \cdot \sim(\lambda^I + \lambda[\varphi^G + \varphi^F + \rho^B + \rho^C])$

inventors other than the prospect patent holder being able to participate in subsequent development paths of the prospect, the new uses that they might discover and the increase in development due to competition.[484]

Particular market behaviours may also undermine or reinforce the importance of the organised derivative innovation function statement. For example, evergreening vitiates the necessary perception of the organised derivative innovation function statement that the prospect patent holder is a technologically foresighted and benevolent guide for subsequent technology development. The cost of monopolies and (φ^G) the low reinvestment of resources gained from an earlier inventions provide further important considerations.

Licensing or exploitation of a patent must be profitable to the patent holder. Thus, if another party improves on the patent holder's invention, but utilises the patent holder's inventive step, the patent holder may have an interest in refusing a license permitting the other party to exploit the refined invention. This will occur in many instances, though primarily, where the patent holder has incurred expenditures that outweigh assignment or foreseeable licensing returns.

2.5.5. **Further Failings**

Organised derivative innovation is contrary to (φ^F), the notion that there may be other useful embodiments of the invention that the inventor does

[484] $\lambda([\varphi^G]>[\varphi^F+\rho^B+\rho^C])$.

not perceive, in its assumptions. This is because it holds that the first patentee's control over the 'prospect' is desirable because it establishes a standard and reduces the wastefulness of rivalry. Thus, the organised derivative innovation function statement is an antithesis of the conventional view that scientific progress is a series of increments building on the knowledge of others. In this function statement the progressive development of the inventor's own ideas are preferable. Where it is preferable to have a larger population consider information as they may possess different expertise and skills. Thus the larger population will be better equipped to propose more increments in the progress of science. In the realisation of a technology this might result in a greater number of applications. Thus, an increase in use value that might be curtailed if subsequent development is limited to a strict agenda perceived by an individual or very restricted group who may not perceive possible applications. This contradiction is rendered clearer if the Popperian notion of falsification is considered.[485] Moreover an orderly and systematised progression of development is unnatural, especially considering φ^E as a sufficient term for innovation to occur, and may cause some useful applications to be neglected. Thus organised derivative innovation is likely to be more costly than an organic uncontrolled development outside of an institutionalised prospect.

[485] See Popper, K., *The Logic of Scientific Discovery* [Routledge, 12th Ed., 2002, London] p. 9

Empirically there is not one example where the utilisation of control over a 'prospect' has lead to the most desirable standardisation for a future technology tree.[486] The notion of control over a prospect and improvement of a patent outside of the patent holder's technological paradigm is incompatible lest the improver have the cooperation of their rival. In the case of partnerships and low prior investment in establishing a prospect there may be a degree of freedom in developing other standards, but equally there may be a greater cost that is not realised until much later. A particularly poignant and well documented example of this is the development Steam engine.[487]

2.5.6. **Bad Choice**

Knowledge that is gained earlier provides a basis for future advance. Where an actor can dictate the initial channels of development from an invention then that actor is empowered to create greater opportunity for themselves. Depending on perspective this may or may not be positive. Consider for example the computer industry. At present almost all computers, especially those available to the public, are binary machines based on electrical signals. Far superior, light has three states and is therefore a ternary system. Thus instead of bits, information is conveyed in

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[486] Also see Merges, R., and Nelson, R. R., 'On the complex economics of patent scope' (1990) 90 *Columbia Law Review* 839-916

[487] For a well presented account of the steam engine development in the context of the organised derivative innovation function statement see: Boldrin, M. and Levine, D. K., *Economic and Game Theory: Against Intellectual Monopoly* [e-publication 2008] Chapter 1: 1-5. Available at: <http://levine.sscnet.ucla.edu/general/intellectual/againstnew.htm> (Last Accessed: 1st July 2009)

trits. Where one trit is the equivalent of 1.58596 ($\log_2{}^3$) bits. Moreover, light travels faster than electricity, has less attenuation than electrical current, and therefore produces less heat and has lower power consumption. Yet with the mass-produced binary components for computers, binary machines quickly established their place in society. With the result that now the start up costs in implementing a superior light based machine are unviable. Inevitably if our demand for processing power, bandwidth and ecological interest continues those costs will have to be met[488], and moreover when the switch finally occurs we will have less of a knowledge base than if the superior platform had been initially adopted. This is the danger of Kitch's proposed prospect theory of development for the societal benefits of patents. Empirically the paradigm adopted and maintained through economic and market advantage in the context of organised derivative invention will not be the most effective technology for purpose.

Another consideration is the attractiveness of some patents compared to others. Patents that have potentially much greater (φ^C) economic return than others, are likely to be more contested in patent races, and as such be over sought leading to the very wasteful and duplicate activity the organised derivative invention function statement purports to alleviate. Moreover, if the prospect patent is sufficiently broad to be determinative of

[488] Knuth, D.E., The Art of Computer Programming - Volume 2: Seminumerical Algorithms [Addison-Wesley, 2nd Ed., 1980] 190-192

subsequent development and monopolistic enough to permit that control then it becomes even more of a prize for patent races.

2.5.7 **More Disfavour**

Furthermore, as broad patents unless they are licensed easily and widely, i.e. have low transaction costs, then the broad patent is counterproductive as it limits the size of the population whom can access the technology and contribute to its development. Moreover, as we will see in conjunction with stable cartels, a broad patent shared only amongst a very limited population may create a situation where derivative inventions within the cartel are less competitive than rival inventions. Thus, this invention function statement undermines itself once again. In consequence it is difficult to perceive how the organised derivative innovation function statement might not render technological advance more difficult and costly.

Transaction costs are inarguably increased by the presence of a patent. As patent transactions require both the contractual agreement and completion of patent formalities. It may also be necessary to demonstrate the robustness of the patent enclosure. Thus, in addition to restricting the population which can work on derivative invention, a broad patent also adds extra dead weight costs to transactions.

Even in the absence of a broad prospect patent the patent may still constitute an effective prospect patent. If the technology is realised

through additions to the prospect invention it is possible that the more advanced product requires access to several prior inventions, and thus the prospect patent may be determinative of whether the advanced improvement is a viable product for commercialisation.

CHAPTER 3

MISALLOCATION AND ASSEMBLY OF PHARMACEUTICAL KNOWLEDGE

"The suitability of the expenditure is relative therefore to the spender himself, and to the occasion or object." [489]

As a vehicle of ownership and control the aptitude of patent rights goes beyond control simply over the invention. Indeed patents serve two significant policy control objectives. These are the property sovereignty function and the knowledge feudalism function. As they are not overtly used in statements to justify intellectual property and are directly related to misallocation and the assembly of pharmaceutical knowledge they were considered more correctly to be part of this chapter despite their theoretical nature.

3.1. **Property Sovereignty Function**

This function statement concerns controlling the property of others, particularly countries which are poorer technologically, but rich in resources. Base goods trade for far less on markets than manufactured goods. This seems self evident as the manufactured good, even if we eschew other factors, requires the base material and labour. Therefore, if a country can impose barriers that prevent countries rich in resources converting its base goods into manufactured goods, then a wealth gap can be maintained. The way in which this is done is through controlling

[489] Aristotle, Nicomachean Ethics, IV. ii. 3.

knowledge. Preferably, through preventing use or acquisition of knowledge of technological applications that are currently in demand.

3.1.1 **Knowledge As Control**

Knowledge has an irrepressible power, it cannot be contained and eventually it will escape. The only real reason for a knowledge economy is that those in a position to dictate the national law of property and to force multilateral agreements have no desire for competitive markets in real goods where they may have a disadvantage in access to base materials and cheap labour. With intellectual property you can manufacture your goods where the labour is cheap with resources from the cheapest suppliers and prevent access to markets by anyone who lacks expertise in obtaining intellectual property rights.

Knowledge is synonymously a public good, a social product, or a merit good. To qualify as such knowledge satisfies two essential criteria. Firstly, knowledge is non-rivalrous. Which means that one individual can use knowledge without concern that their use will consume the knowledge and thereby prevent the use of the same knowledge by other people. Secondly, knowledge is non-excludable. Which means that it is extremely difficult or impossible to prevent people who have not paid for the good from accessing it. Thus, when we consider knowledge it is necessary to distinguish knowledge from skills whose acquisition is dependent on training or experience. Since knowledge is difficult to exclude others from, trying to do so is both unnatural and expensive.

Thus, for the holders of the reins of power there has to be an advantage in trying to control knowledge. Preventing access to knowledge, has historically failed. Thus, more clever tools are needed and this is the role of intellectual property, specifically patents.[490]

> "...a note of realism about what intellectual property represents: 'intellectual property is really an issue of survival within the world system'... It is the price that countries have to pay, largely to US companies, to enter the world trading system."[491]

The standard of living[492] that a nation can afford its citizens is dependent on a number of factors, that are particularly reflected in the gross domestic product per capita. Gross domestic product (GDP) is the 'total money value of all final goods and services produced within an economy over a one-year period.'[493] The backbone of GDP calculations is constituted by addition (and subtraction) of private consumption, investment, government

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[490] Copyright plays a significant role in reducing access to educational materials and participation in research publications in almost all disciplines.

[491] Drahos, P. and Braithwaite, J. *Information Feudalism: Who Owns the Knowledge Economy?* [Earthscan publications Ltd, 2002, London] 104

[492] 'Standard of living' although a nebulous concept and difficult to quantify in real terms, is a good general guide to relative quality of life in different localities. In this instance the UN Human Development Index was the primary measure employed. Its factors are: the Life Expectancy Index, Education Index, Adult Literacy Index, Gross Enrolment Index, GDP Index. However, it was later noted that a comparison of 'gross domestic product per capita' provided a less complicated and almost as informative tool.

[493] Pass, C., Lowes, B., and Davies, L. Dictionary of Economics [HarperCollins, 3rd Ed., 2000, Glasgow] 228

expenditure, and the value of gross exports and gross imports. Many factors of GDP calculations, such as private consumption and government expenditure directly overlap with consideration of standards of living. For some countries, especially those with large populations, such as India and China, where population wealth is disparate GDP is a poor indicator. Instead it was found that there is a better correlation between gross domestic product per capita and standards of living, rather than GDP and standards of living. It is therefore in the interest of a nation's populace for their country to have a high gross domestic product per capita relative to other nations.[494]

3.1.2. **Over Natural Resources**

However, the natural resources available within a nation's territories do not necessarily reflect the wealth of that nation. If the distributions of minerals, plants, and animals were determinative of population wealth then a relative index of national standards of living would remarkably differ from those presently existent. Instead as most minerals, plants and animals are not consumable in their natural form they must be transformed in order that society can consume them. Thus, if control were exerted over the transformed form or the method of obtaining the transformed form, then some control would also be exerted over the natural form. Where there are competing possible transformations from the natural form many factors

[494] This work although intermeshed with a naturalistic positivism is biased towards utilitarianism and efficiency, where they are coincident, rather than elitism. Otherwise GDP might serve as an acceptable measure of comparison, as is the case in many development reports.

will affect the choice of transformation, including economics and technical facilities. The ability of the acquirer of the natural form resource to continue to supply a market is dependent on the demand of the transformed form, and therefore on the transformer of the natural form. Since the supplier of a natural resource can be interchanged with another supplier of that natural resource each supplier must remain competitive and therefore has a reduced choice as to the final transformed form that their natural resource will realise. The transformer of the resource, most notably at the level of final transformations, is economically subject to the whims and tastes of society, but to a degree can also dictate whim and taste. Where the whims and tastes of society closely correlate with objects of intellectual property such as a patents, then employment of natural resources can be determined through ownership of transformed forms and the methods of transformation. Thus, intellectual property, particularly patents can exert indirect control over natural resources by influencing both the economics and the technical choices available to transformers and therefore to the economy of natural resource supply.

For a nation with a scarcity of natural resources in comparison to other nations, the ability to control the value that the natural resources of the other nations can realise is extremely important and determinative of relative standards of living. Moreover, between competitive nations the economic value of knowledge that cannot be kept secret or be controlled is low. Were there not bars to other nations undertaking the transformations that would make their natural resources favourable to consumers then an

index of standards of living and GDP would correlate with the originators of natural resources. For example consider the economic growth of the USA from 1915 to 1940 and China in the 1980-2000 when recognition of other nations' intellectual property was limited or inexistent.

Where knowledge, which is determinative of product superiority or improved production and can only be exploited by disclosure of the knowledge, then that knowledge has a very high value. This high value is realised by the positive effect that the knowledge has on a nation's GDP through the indirect control over natural resources both national and foreign. Simplistically this can be visualised as the difference in imports and exports where the knowledge is restricted, compared to the sum of imports and exports if that knowledge were freely disseminated and employable.

3.1.3. **Over Labour Resources**

Thus, for a nation where the cost of labour is higher and the access to base resources is lower than its competitors, the employment of knowledge to gain product superiority or improved production is the only method of achieving sustained productivity growth. Patents, through providing a means of limiting knowledge exploitation, serve to accommodate control over the natural resources of other nations. Thereby exerting a property sovereignty function. Historically patents

have long served this purpose. Even with greater acuity before the Statute of Monopolies.[495]

Nations with high labour costs and low natural resources, providing they can secure enough patents and have these respected by other nations, can economically dominate countries rich in resources and labour. However, where the other nations, rich in resources and labour are able to channel their energies into securing patents or attracting patent holders to economic activity within their nations then the rich originator of transformations, both poorer in labour and resources will dwindle in importance. Thus,

> "In 1980, less than one-tenth of manufacturing exports came from the developing world. Today it is almost one-third and in 20 years' time it is likely to be one-half."[496]

As transformation choices permutate and ownership of the transformation or transformed form is only temporary then the ability of property vehicles, such as patents, to control natural resources is also transient. Their effect

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[495] Consider, the use of saltpeter licenses, whereby deputies of the patentee used their authority to dig in the lands of others, including their houses, cellars, and barns. See Clode, C. M., *The early history of the Guild of Merchant Taylors of the Fraternity of St. John the Baptist, London, with notices of the lives of some of its eminent members.* [Harrison Printers, 1889, London] 87

[496] Sainsbury Review. The Race to the Top: A Review of Government's Science and Innovation Policies. [HMSO October 2007] 4

is visible as retardative of the economic development of nations with greater natural resources but less patent acquiring expertise.

> "In fact, patentability always came after the industry had already emerged and matured on its own terms."[497]

However, the exploitive ability of patents is not limited to control over resources in other countries, an effective scheme can be run nationally or globally regardless of the wealth of a particular nation. Outside of intellectual property this organised control of a market would be penalised as cartelisation.[498]

3.1.4. **Maintaining Cartels**

Technology cartels were and are formed in two essentially distinct patterns, both of which are based on the late Nineteenth Century German company strategy of using patents to enclose a technology area. For lack of a better term in the literature I classify these as unstable and stable technology cartels. In the unstable cartel the company holding the dominant patent portfolio conditionally licences their portfolio to others to manufacture dependent products. In return the licensor demands a return from the licensees, thereby effectively fixing prices, limiting total industry

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[497] Boldrin, M. & Levine, D. K., Economic and Game Theory: Against Intellectual Monopoly [e-publication 2008] Ch.3 p. 4. Available at: <http://levine.sscnet.ucla.edu/general/intellectual/againstnew.htm> (Last Accessed: 1st July 2009)

[498] Drahos, P. and Braithwaite, J. *Information Feudalism: Who Owns the Knowledge Economy?* [Earthscan publications Ltd, 2002, London] 151

output, partitioning the market, and allocating categories of consumer and territories. I refer to this as an unstable technology cartel because it is dependent on the licensor retaining control over technologies essential to the industry.

This first form of cartel is fairly weak and contemporaneously is usually only attempted by University spin-out companies attempting to enter the pharmaceutical market and retain niche control.[499] Cartels of this kind are usually largely ineffective at controlling prices and distribution. There are however notable exceptions such as the protease inhibitor market, where Abbott has utilised Norvir pricing to effect prices and market share from December 2003 onwards.[500]

The second form of technology cartel is stable because it functions on the basis of on cross-licensing agreements for technologies. In the formation

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[499] For liability reasons, I am unwilling to name companies, but as search of news about pharmaceuticals including the terms 'university spin-out companies' and 'consortium' in conjunction with an appraisal of the territorial distribution of the spin-out product and its pricing structure will provide several examples.

[500] Norvir's remaining patent expiration dates are: January 30, 2014; March 13, 2014, December 3, 2014; January 15, 2015; and December 26, 2016. (Data checked with USPTO online database.) It is expected that Norvir will continue to be used to control the market prices of protease inhibitor therapies that require Norvir to improve their efficacy until patent and exclusivity expiry. However, following a settlement payment on August 18, 2008 to an antitrust class action regarding its pricing of Norvir, Abbott's long term pricing policy is not yet clear. Abbott purportedly will pay $10 million to $27.5 million USD in settlement (http://www.healthcare-digital.com/Judge-approves-Abbott-Settlement-in-Norvir-Lawsuit_7222.aspx), in 2008 Norvir sales were $311,245,000 USD (DrugPatentWatch.com. Available at: <http://www.drugpatentwatch.com/premium/preview/detail/index.php?searchtype=alpha&category=Tradename&searchstring=NORVIR> (Last Accessed: 1st July 2009)

of the stable cartel, rival companies nucleate around a common technology, this may be initiated by a patent holder of the common technology who instead of an attempt at overarching control through the licensing of their patent, will instead license their patent for a small or token buy-in and a strong agreement that technological derivations and improvements will be shared amongst the cartel members. This has the consequence that multiple companies can benefit from each other's innovation, thus rejuvenating the existence of the cartel, whilst excluding outsiders. Formation of price setting agreements and division of markets and territories can be effected through the terms of cross-licensing thereby eschewing the vigilance of competition laws and providing an effective basis for legal enforcement of the cartel, which ironically can take place within the qualified court or intellectual property office. Compensation clauses within the cross-licensing agreements provide for an *indemnitas* for the more innovative cartel members.

Ernest Solvay instituted the alkali cartel as a stable cartel. In return for a licence to use his ammonia-soda process, Solvay required that the licensees share all improvements with him, which he in turn reserved the right to share with other licensees. In consequence not only did Solvay retain control of the industry, but his process was kept competitive with respect to rival processes.[501] The dispositive for the categorisation on the

[501] Krause, W., and Puffert, D. J. 'Chemicals, strategy, and tariffs: Tariff policy and the soda industry in Imperial Germany' (2000) 4 *European Review of Economic History* 285-309; Haber, L.F., *The Chemical Industry During the Nineteenth Century* [Clarendon Press, 1958, Oxford] 89

alkali cartel as a stable cartel is the presence of cross-licensing, of which Solvay acted as a broker.

ICI and DuPont, supposed rivals, present an interesting history of possible cartelisation.[502] Their enduring cross-licensing of technologies encompassed both the sharing of information and expertise. This was to the extent that even when one company had control over the core patents for a technology area the other firm had the incentive to innovate in order to retain a viable membership of the partnership and access to the core inventions.[503] To further ensure a balance in their sharing compensation clauses existed to value the weight of each firm's contributions to the patent pool.

Early purchase of technologies is essential in the maintenance of a cartel. Non-manufacturing innovators have a trend of licensing their inventions to anyone able to afford the royalties, thus promoting the largest market entry of competitive firms.

Arora puts explicitly reported cross-licensing agreements amongst pharmaceutical licenses for the period 1980 to 1990 at around fifteen per cent, whilst for the chemical industry explicitly reported cross-licensing

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[502] Drahos, P. and Braithwaite, J. *Information Feudalism: Who Owns the Knowledge Economy?* [Earthscan publications Ltd, 2002, London] 53

[503] Spitz, P.H., *Petrochemicals: The Rise of an Industry* [John Wiley, 1988, New York]

forms about sixty per cent of all licensing.[504] This difference is explained through the lack of competing technologies within the pharmaceutical sector. Where there is the possibility of rival technologies then the payoff strategy has to be changed; it is more advantageous to license early and for a lower margin to ensure uptake of the technology and some return. Whereas in the pharmaceutical sector, with the difficulty for rivals to create bioequivalents, there is generally no necessity to pre-empt the uptake of rival technologies.

In 1923, Hermann Isay,[505] remarked of the manufacturing industries that "...no other industries have at their disposal for cartellizing purposes as effective a device as the... patent."[506]

Because of its focus on control, the property sovereignty function statement is closely linked to the knowledge feudalism function statement. However whilst the property sovereignty function statement is concerned with control over resources, price setting and market sharing, the knowledge feudalism function statement is concerned with the control of knowledge itself and the retardation of expertise.

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[504] Arora, A., 'Patents, licensing and market structure in the chemical industry' (1997) 26(4-5) *Research Policy* 391-403, at 397

[505] Author of the *Patentgesetz Und Betreffend Den Schutz Von Gebrauchsmustern*, published in a 6th edition in 1932.

[506] Drahos, P; Braithwaite, J., *Information Feudalism: Who Owns the Knowledge Economy?* [Earthscan Publications Ltd, 1st Ed., 2002, London] 44

3.2. **Knowledge Feudalism Function**

Pursuit of knowledge might be considered to have two underlying motivations: The valuing of knowledge for its own sake and the acquisition of power through the benefits that knowledge conveys.[507] In the research of pharmaceuticals there exists a notion that the purpose of research is for the benefit to health and lives that knowledge acquisition will grant, and though in some instances this may be the case, the economics of knowledge acquisition predominate.

3.2.1. **Knowledge As Power**

In the present patent driven pharmaceutical innovation regime pharmaceutical research is about empowerment. It is about the economic value of the product and the pecuniary benefit that can be obtained. Intellectual property can be used or exploited, depending on one's conception of intellectual property's purpose, to act as a buffer between the 'haves' and the 'have-nots'.

> "Developing countries are poorer not only because they...[control] fewer resources, but because there is a gap in knowledge... But by strengthening the developed world's stranglehold over intellectual property,... TRIPS reduced access to knowledge for developing countries."[508]

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[507] Kingston, W., The political economy of innovation [Nijhoff Publishers, 1984, The Hague] 21

[508] Stiglitz, J. 'Give prizes not patents' (2006) 2569 *New Scientist* 21

Growing an empire where there is not always a new product is difficult if the playing field remains unchanging. However, if the legal rules can be altered, then boundaries of the map can be changed. One way to ensure this is to retard the uptake of information and the development of expertise. If the expertise of rivals is prevented from attaining the same level, then superiority of products can be ensured and markets can be dominated. The purpose of the knowledge feudalism function statement is to ensure lead-time in knowledge creation by retarding knowledge uptake and development of expertise by rivals.

3.2.2. **Paying the Piper**

Government granted monopolies create a special relation between the monopolist and the Government. Providing that the monopolist can emphasise the necessity of their activity to influence popular opinion then the monopolist can distort the political system by sharing the benefits of their monopoly with the government, thereby acquiring preference at the expense of those paying the rent on the monopoly. Between 1998 and 2004 the USA pharmaceutical industry has spent has spent $758 million USD in lobbying,[509] which is more than any other industry in the USA or elsewhere.

The expenditure on lobbying may have paid dividends, as pharmaceuticals have the longest potential patent term of all technology areas. Of course

[509] USA Today Looks at Prescription Drug Industry's Lobbying Efforts (28 Apr 2005)

the reasoning for this is that they have the longest market approval delay. In 1984 the USA Drug Price Competition and Patent Term Restoration Act, known as the Hatch-Waxman Act, provided for an extension of patent protection for pharmaceutical patent holders to compensate for delays caused by FDA approval requirements. This extension was limited to five years. [510] The UK followed with the Patent (Supplementary Protection Certificates for Medicinal Products) Regulations 1992[511]. Where extension of the patent term to 25 years is possible subject to the period of delay between the grant of the patent and authorisation of the drug to enter the market. Every year of delay beyond five years entitles the patent holder to an additional year of patent protection up to a maximum of five years following a ten-year delay.

In a study of the knowledge transfer effects of patents for invention in a developed nation, Bascavusoglu and Zuniga[512] applied a reduced-form econometric equation relating French cross-border receipts in technology services to an index of patent strength, real GDP per capita, openness, and the technological characteristics of knowledge-recipient countries.

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[510] The patent term in the USA for pharmaceuticals was 17 years prior to TRIPs compliance in 1995, which extended the patent term in the USA to 20 years. US Code Title 35 Section 154(2). As a result of the 1999 amanedment the five year extension period for delays as a result of the market approval for pharmaceuticals was annulled thus there is no limitation to this extension period in the USA, see Subsec. (b). Pub. L. 106–113, § 1000(a)(9) [title IV, § 4402(a)].

[511] S.I. 1992 No. 3091

[512] Bascavusoglu, E; Zuniga, M. P., 'Foreign Patent Rights, Technology & Disembodied Knowledge Transfer Cross Borders: An Empirical Application' (2002) Working paper Université de Paris I Panthéon Sorbonne.

They concluded that once countries reached a certain market size and level of income then the implementation of stronger intellectual property rights could improve technology markets. They state that this is true only when conditions are favourable for knowledge transfer. [513] There are two factors which are essential to the transfer of knowledge these are that the country possesses the capacity to innovate, and thereby benefit from the knowledge of others and secondly that commercialisation of technologies has a guaranteed profitability.[514]

3.2.3. **Exclusive Melody**

As patents increase the cost of technology transactions they require higher prices for technologies. As a result knowledge transfer may be affected as patent rights are strengthened.[515] For example implementing product patents where there had only previously been process patents, may prevent firms that had previously competed to supply a market from being able to continue. As a result the local prices for the affected technologies

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[513] Bascavusoglu, E; Zuniga, M. P., 'Foreign Patent Rights, Technology & Disembodied Knowledge Transfer Cross Borders: An Empirical Application' (2002) Working paper Université de Paris I Panthéon Sorbonne.

[514] See Benchekroun, H., and Vishwasrao, S., 'On welfare reducing technological change in a North-South framework' (2009) 61(3) *Oxford Economic Papers* 603-622; Vishwasrao, S., and Bosshardt, W., 'Foreign ownership and technology adoption: evidence from Indian firms' (2001) 65(2) *Journal of Development Economics* 367-387; Smith, P., 'Are weak patent rights a barrier to U. S. Exports?' (1999) 48 *Journal of International Economics* 151-177; Vishwasrao, S., 'Intellectual Property Rights and the mode of technological Transfer' (1994) 44(2) *Journal of Development Economics* 381-402

[515] For a discussion couched as an econometric investigation on the effects different degrees of intellectual property rights have on decisions to license technologies see Yang, G, and Maskus, K. E., 'Intellectual property rights and licensing: An econometric investigation' (2001) 137(1) *Review of World Economics* 58-79

may rise. With a reduction in the competition between firms and in the number of experts working in the speciality there will be an overall decline in expertise. Moreover, if the stages of research and manufacture are undertaken elsewhere, for example in another country, then there is no forum for specialists to be trained, gain experience or contribute to local competition.

On the other hand in the absence of local expertise to produce products from local knowledge, the entry of outside expertise may be able to commercialise knowledge previously existent and provide new commodities. Within the context of pharmaceutical development this can require greater capital than is available locally and thus the patent permits the firm with capital to acquire and suppress the commercialisation potential of a local product. This is a very favourable position for firms from wealthy nations and any strengthening of patent rights should be accompanied by an increase in the complexity and costs of patent law. Which in turn will increase the dead weight of transaction costs and further insulate patent right holders from the germination of competitive expertise.

3.2.4 **Missing Picture**

Viswasrhao,[516] Yang and Maskus,[517] suggest that stronger IPRs have a tendency to increase licensing activity. For Korea, Mexico, Brazil, and

[516] Vishwasrao, S. Intellectual Property Rights and the mode of technological Transfer. (1994) 44(2) *Journal of Development Economics* 381-402

[517] Yang, G, and Maskus, K. E., 'Intellectual property rights and licensing: An econometric investigation' (2001) 137(1) *Review of World Economics* 58-79

Indonesia large responses have been identified.[518] However, although patents may acts as catalysts for technology market growth, the potential increase in licensing fees that emerge with increased patent protection[519] have not been taken into account: it is not reported if increases in licensing flow is a product of a greater frequency of licensing or a result of the higher royalty rates paid. Most importantly, is the distribution of technical knowledge masked by the centralization of licensing and production catalysed by patent monopoly? In 1997 Lanjouw[520] reported that imitation by Indian firms of pharmaceuticals newly marketed in Europe or the USA takes less than 2 years and that production and distribution was undertaken competitively by over

> "250 large pharmaceutical firms,... about 9,000 registered small-scale units, [and] another 7,000 unregistered small-scale units."[521]

This is a completely different infrastructure compared to the pharmaceutical industry in the USA, UK or the European Union, where

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[518] Maskus, K. 'Parallel Imports' (2000) 23(9), *World Economy* 1269-1284

[519] Shapiro, C., 'Navigating the patent thicket: cross licenses, patent pools, and standard-setting' (2000) Working Paper No. CPC00-11. at 12. Available from: <http://www.escholarship.org/uc/item/4hs5s9wk#page-1> (Last Accessed: 1st July 2009)

[520] Lanjouw, J. O., 'The Introduction of Pharmaceutical Product Patents in India: "Heartless Exploitation of the Poor and Suffering"?' (1998) NBER Working Paper No. W6366

[521] Lanjouw, J. O., 'The Introduction of Pharmaceutical Product Patents in India: "Heartless Exploitation of the Poor and Suffering?"' (1998) NBER Working Paper No. W6366: at 9. Lanjouw attributes this data to clippings: "Pharmaceuticals" from major Indian Newspapers from various years on file at the Institute for Studies in Industrial Development, New Delhi.

relatively few very large pharmaceutical companies comprise the pharmaceutical market, including bulk supply and generics.

3.3. Cost and Resource Allocation

By virtue of the private profit driven system of innovation that the patent system, business and lawyers engender, the high increment on the cost of patented medicines is to permit companies researching new pharmaceutical patents to recoup the cost of *research and development* and *clinical testing.*[522]

The factors determinative of whether a chemical compound is developed or therapeutic investigation takes place were described by Maclayton, Smith *et al.*[523] Whom inferred these factors from an empirical study of 150 USA companies, specialised in the provision of health products, and their decision to enter foreign markets. The factors proposed were: the market and marketing opportunity, legal barriers, the company's economic objectives, cultural unity and physiographic barriers, political stability,

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[522] PhRMA, Tough Questions, Straight Answers: A Discussion of Today's Pharmaceutical Issues [PhRMA, Summer 2004, Washington]; PhRMA, Why Do Prescription Drugs Cost So Much and Other Questions About Your Medicines [PhRMA, June 2000 Washington]

[523] Maclayton, D., Smith, M. and Hair, J., Determinants of Foreign Market Entry: A Multivariate Analysis of Corporate Behavior (1980) 20(3) Management International Review 40-52

economic development and performance.[524] The WHO Global Atlas of Infectious Diseases, or the size of which populations in which diseases occurred were not important enough to mention where the economic development in which the afflicted populations occurred did not meet the company's threshold for its economic objectives. Considering that the purpose of pharmaceutical companies, usually profit for its shareholders,[525] then it should not be anticipated that they undertake altruistic work or combat disease without profit.

Risk is present in most forms of economic life, and if one party is insulated from it then another will bear the extent of that insulation. There are two fashions of displacing risk, to reduce the elements which may cause it, i.e. not developing drugs that will have poor markets, and to be compensated for bearing the risk.

3.3.1. **Avoidance and Compensation**

As this subchapter highlights the mechanisms in place certainly present both characteristics; risk reduction and compensation for risk taking. An alternative view of Plant's notion that patent rights can direct activities to more useful purpose might correlatively be viewed in the context of pharmaceuticals that patent rights partially shift the innovation risks to the public. This is not a total shift of risk in an economic sense as the turning of profits significant to a company the size of most large research and

[524] Albaum, G., and Peterson, R. A., 'Empirical Research in International Marketing: 1976-1982' (1984) 15(1) *Journal of International Business Studies* 161-173

[525] Companies House, DVD Rom Directory, March 2009

manufacturing companies requires marketing savvy and consummate commercial skills, as well as a product pipeline. There are no complete indemnities for failing pharmaceutical giants, but then they have not seemed to need any more than they already possess, even with the market entry of generics.

From 1982 to 2001, the pharmaceutical industry was the most profitable industry in the USA every year.[526] In 2002, however the pharmaceutical industry suffered a significant profit crisis. In that year, although seventy-eight medicines were approved by the USA Food and Drug Administration (FDA),[527] only seventeen contained new active ingredients. Moreover, of the seventeen containing new active ingredients, only seven were FDA classified as improvements over older medicines. Which means that seventy-one of the approved drugs (91 per cent) were variations of old drugs or deemed no better than drugs already on the market. None of the improved medicines came from major USA based pharmaceutical companies. This lead to a general restructuring amongst large pharmaceutical companies, which has the effect that research has been increasingly out-sourced. Thus, the risk of conducting research has been increasingly borne by other companies.

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[526] 'Rx R&D Myths: The Case Against The Drug Industry's R&D "Scare Card"' Public Citizen, July 2001. <http://www.citizen.org/documents/ACFDC.PDF> (Last Accessed: 1st July 2009); Fortune Magazine data

[527] FDA, CDER NDAs Approved in Calendar Years 1990-2004 by Therapeutic Potential and Chemical Type. Available at: <http://www.fda.gov/cder/rdmt/pstable.htm> (Last Accessed: 1st July 2009)

It has thereafter remained one of the most profitable industry in the USA.[528]

> "Some two billion people around the globe cannot get the medications they need because they are too poor, or drugs for their diseases are not in production. Big pharmaceutical companies... cannot fix the problem unless it is profitable."[529]

There are insufficient finances available to make it profitable for 'Big Pharmaceutical companies' to undertake research on all the diseases that afflict human beings. Moreover, because of their inefficiency and their need for profitability 'Big Pharmaceutical companies,' are not best qualified to try.[530] Monopolies use inefficient and extremely costly methods of production. The objective of a monopoly is to obtain remuneration far greater than opportunity cost. Even if opportunity cost were met, in the absence of the pharmaceutical patent and substantial reliance on monopoly industry to innovate, there is little likelihood that cures to all diseases and remedies for all conditions could be found. Resources

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[528] In 2006 the mining and crude-oil production sector surpassed the pharmaceutical sector in terms of profits as a per cent of revenues. Fortune 500 data.

[529] MacKenzie, D., 'GSK tops new ethical ranking for investors' (16 June 2008) *NewScientist.com*. Available at: <http://www.newscientist.com/channel/health/dn14141-gsk-tops-new-ethical-ranking-for-investors.html> (Last Accessed: 1st July 2009)

[530] Resources are always going to be channelled into the most profitable product, even if that product is a 'me-to' with no therapeutic improvement. Considering products on the market, research by large pharmaceutical companies into symptom suppressants and prophylactics has been far more successful than at finding cures. Of course finding useful active ingredients is a complex and difficult activity and it may only be coincidence that the more economically valuable treatment is obtained more often than a cure.

available for research are finite, just as they are for the manufacture and distribution of medicines. However, channelling these finite resources into a system that is inefficient and requires large forecast profit before it will consider investigating a condition or chemical, is not a desirable method of improving the availability of medicines or the accessibility of medicines to everyone; that is not just to the poor, but to the wealthy as well.[531]

3.3.2. **Cost Of Innovation**

In 1991, Di Masi *et al.*, building on the work of Hansen's 1979 report,[532] estimated that for a sample group of 93 NCEs developed by twelve pharmaceutical companies through the late 1970s and 1980s the average expenditure per approved product was $114 million USD (1987 USD value).[533] Which lead Di Masi *et al.* to conclude fully capitalised costs of $231 million USD (1987 USD value). Hannah Kettler, updating Di Masi's figure to 1997 values on the basis of the GDP implicit price deflator suggests that the fully capitalised costs are $321 million USD (1997 USD

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[531] Conditions such as diabetes, hypertension, heart disease, high cholesterol, and arthritis are presently chronic illnesses and therefore require ongoing therapies. Treatment of these conditions outside of insurance schemes can be expensive even for people within economies with a high per capita income. For the super wealthy the prices of pharmaceuticals is not a problem, however expensive they are. However, availability is. See, i.4. at 32, 3.3. at 246.

[532] Hansen, R. W., 'The pharmaceutical development process: Estimates of development costs and times and the effects of proposed regulatory changes,' in Chien, R. (eds.) Issues in Pharmaceutical Economics [Lexington Books, 1979, 1st Ed., Boston] 151-187

[533] Di Masi, J. A., Hansen, R. W., Grabowski, H. G., Lasagna, L., 'Cost of Innovation in the Pharmaceutical Industry' (1991) 10 *Journal of Health Economics* 107-142

value) per approved pharmaceutical product.[534] In 2003, Di Masi *et al.* produced another estimate of $802 million USD (2000 USD value) fully capitalised costs for the research and development of a new pharmaceutical product.[535]

A further report by Di Masi, *et al.*, suggests $1.318 billion USD (2006 USD value).[536] Utilising the published methodologies of Kettler in conjunction with the discount rate and increased capitalised costs of Di Masi *et al.* this suggests that in 2009 figures, that the fully capitalised cost of a new industry innovated and developed pharmaceutical product is about $1.525 billion USD (2009 USD value). Of course this figure comprises full re-imbursement for all projects that failed to generate approved pharmaceutical products[537] and does not take account of only pharmaceuticals that were candidates for therapeutic improvement. As a result the figure is an extremely poor indicator of the cost of new drugs.

3.3.3. **Mansfield Questionnaire**

Edwin Mansfield conducted a survey by questionnaire amongst the research and development directors of one hundred corporations in the USA. In response to the question of what fraction of inventions would not

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[534] Kettler, H. 'Updating the cost of a new chemical entity' [Office of Health Economics, 1999, London] 14-15

[535] Di Masi, J., Hansen, R., Grabowski, H., 'The Price of Innovation: New Estimates of Drug Development Costs' (2003) 22 *Journal of Health Economics* 151-185

[536] DiMasi, J. A., and Grabowski, H. G., 'The Cost of Biopharmaceutical R&D: Is Biotech Different?' (2007) 28 *Managerial and Decision Economics* 469–479

[537] Kettler, H. 'Updating the cost of a new chemical entity' [Office of Health Economics, 1999, London] 26

have been developed between 1981and 1983 in the absence of a patent protection, found that for pharmaceuticals this was 60 per cent, whilst the average across all industries was only 14 per cent.[538]

Mansfield's survey is supportive of the hypothesis that the development decisions of pharmaceutical research and manufacture companies are directed towards perceived profit-making opportunities and that the patent is an important factor in the realisation of profits. As the goal of industrial research policy is to evaluate research and development project costs with respect to expected returns so as to secure the achieve the most profitable allocation of resources practically possible, this is not an unexpected result.[539] Moreover, Mansfield's survey does not suggest that the inventions that the twelve pharmaceutical companies would not have developed in the absence of patent protection would not have been developed by another company. Nor does it reveal how many pharmaceuticals were not developed as a result of patent protection.

3.3.4. **From Whence**

There should be little doubt in the mind of most economists that monopolies use inefficient and costly methods of production. Pharmaceutical research requires substantial funding and this money has to come from somewhere. Almost all pharmaceutical innovations can be

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[538] Mansfield, E., 'Patents and Innovation: An Empirical Study' (1986) 32(2) *Management Science* 173-181

[539] Mansfield, E., Rapoport, J., Schnee, J., Wagner, S., *et al. Research and Innovation in the Modern Corporation* [Newton, 1971, 1st Ed., New York] 48-49

designated as originating from one of two sources: these being publicly funded research institutions and pharmaceutical research companies. In the USA, pharmaceutical industry research and development accounts for only 43 per cent of pharmaceutical research and development. 29 per cent of pharmaceutical research and development is generated by the NIH.[540] Jeffrey Robinson has suggested that forty-five out of fifty best selling drugs were in fact substantially developed with taxpayer's money.[541]

If the research produced through public funding is for the moment ignored, then out of the money society spends on pharmaceuticals only about thirteen per cent is allocated to research, development and clinical trials. It is desirable that pharmaceutical innovation takes place, however that only thirteen per cent of spending on pharmaceuticals is directed into research, development and clinical trials, where innovation is the justification for the monopoly, is clearly suggestive of an inefficient and costly method of

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[540] Chang, H-J., *Kicking away the ladder: Development strategy in historical perspective.* [Anthem Press, 2004, 1st Ed., 2nd Reprint, London] 31; see <http://www.pharma.org/publications> (Last Accessed: 1st July 2009). Whilst this figure corresponds with data provided in news articles, a definitive and attributed break down of source data is desirable.

[541] Robinson, J., *Prescription Games* [Simon and Schuster, 1st Ed., 2001, London] 121; Also see, Dembner, A., 'Public handouts enrich drug makers, scientists' (April 5, 1998) *The Boston Globe* A1 – "The Globe looked at 50 top-selling drugs approved by the Food and Drug Administration over the past five years: 35 new drugs, which are bestsellers among those the FDA deemed most important or most unique, and 15 "orphan" drugs targeting rare diseases. Thirty-three of the 35 new drugs and 12 of the 15 orphans received money from the National Institutes of Health or the FDA to help in discovery, development, or testing... 45 of 50 top-selling drugs got government subsidies total[l]ing nearly $175 million [USD]."

innovating. Moreover, the magnitude of the deadweight grows in proportion to patent rents.

Consider Ritonavir (Norvir), which was developed by Abbott, through substantial NIH assistance including grants. As a result Abbott's investment in developing Ritonavir was approximately fifteen million USD of its own funds,[542] which was mostly spent on pre-approval clinical trials and studies to obtain market approval for Ritonavir. By 2002, Abbott had in cumulative sales of Ritonavir received over one billion USD, which is more than sixty times the estimated cost of Ritonavir pre-approval expenditure. Thus, Abbott's expected income from Ritonavir over the next decade would have been around two billion USD for Abbott over the next 10 years.[543] However, Abbott increased Ritonavir's price by 500 per cent in December 2003,[544] thereby increasing the expected income on Ritonavir to around twelve billion USD by 2010.

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[542] "NIH didn't ask for any financial return and Abbott didn't offer..." Dembner, A., 'Public handouts enrich drug makers, scientists' (April 5, 1998) *The Boston Globe* A1

[543] Cafferty, P., Families USA, Big PhRMA Behaving Badly: A Survey of Selected Class Action Lawsuits Against Drug Companies [Families USA, January 2005, Washington] 2

[544] Alcorn, K., '*Ritonavir price increase: what are the consequences in 2004? Consequences for competitors*,'18 December 2003. Available at: <http://www.aidsmap.com/en/news/1E63C821-275E-45C2-95BC-6F6B99F38D54.asp> (Last Accessed: 1st July 2009); Cafferty, P., Families USA, Big PhRMA Behaving Badly: A Survey of Selected Class Action Lawsuits Against Drug Companies [Families USA, January 2005, Washington] 2;
'*Price of AIDS Drug Soars Fivefold*' Seattle Times, 5 January 2004.

3.3.5. **Your Money Or Your Life**

What is clear is that individual pursuit of self-interest to a pharmaceutical research manufacturer (whose articles of association and memorandum are not conceived on the basis of a trust and altruism, but rather shareholders' wants) is not compatible with the close correlation of cost and price of a pharmaceutical, or with society's interest in accessing medicines.[545] In fact the rent seeking behaviour of pharmaceutical companies suggests that in the majority of cases, if not all, the price of patented pharmaceuticals has little if no correlation to the actual cost of supply, but is entirely determined on the strength of a strong monopoly.[546] On the basis of the strong monopoly the patent holder can charge almost any price they desire for products incorporating the technology of their patent. This situation presents a large distortion to the expected balancing of classical supply and demand. Moreover, the high prices that the monopoly permits are not in society's economic interest, even though they may be in the interest of the company's shareholders and the lobbied political entities. The financial health of society is improved by the less spending on wasteful or deadweight activities.

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[545] In the present context there are three components to 'society's interest.' These are (i) the availability of a drug, (ii) the accessibility of a drug, and (iii) transparency about the performance of a drug (i.e. the side effects and effectiveness).

[546] Robinson, J., Prescription Games: Life, Death and Money Inside the Global Pharmaceutical Industry [Simon & Schuster Ltd, 1st Ed., 2001, London] 85

Baker and Chatani, 2002,[547] identified six areas of rent seeking behaviour in the pharmaceutical industry that result in wasteful, and or harmful activity. These are:

1) Research and development of copycat medicines
2) Large financial expenditure on marketing
3) Restrictions on the dissemination of research and falsification of data
4) Legal costs and bribes to generic manufacturers
5) Lobbying and grass root campaigns
6) Incentive for grey markets

Whilst all of these points are responsible for the introduction of deadweight into the innovation, development and distribution of pharmaceuticals points 3 and 6 are treated in the subsequent subchapters. Point 3 (Restrictions on the dissemination of research and falsification of data) is considered as two separate issues; as a burden on innovators and as a safety concern. Thus, the different issues of Point 3 are treated in subchapters 3.4 and 3.6. Point 6 (Incentive for grey markets) is considered within subchapter 3.6.5 with regard to safety concerns.

[547] Baker, D., and Chatani, N., Promoting Good Ideas on Drugs: Are Patents the Best Way? The Relative Efficiency of Patent and Public Support for Bio-Medical Research (2002) CEPR Briefing Paper [Centre for Economic and Policy Research, Washington] 2-3

3.3.6 **Circumvention And Copying**

Remember, copycat medicines do little more than copy existing medicines, unlike generic drugs they do not present therapeutic improvement over the copied drug. Moreover in the instance that they follow a pharmaceutical still in patent, then they need to employ different active agents, have a different composition and process of manufacture. When these differences constitute sufficient novelty in their own right then the copycat medicine is patented and termed a me-too, but does not necessarily present any therapeutic improvement over the copied medicine. Nevertheless, since a me-too needs to accomplish similar effects to the originator, but with a different active ingredient, amongst other things, it will have different side effects and therefore may be suitable for some people the originator drug is not. As such a me-too may pose a positive contribution to the medicine chest, even if it is a small one.

The presence of copycat drugs on a market may reduce the price of the copied medicine. However it is deemed a substantial dead weight expenditure because of the lack of therapeutic improvement and the expense required to innovate the chemical, to develop it, and put it through regulatory approval. Moreover, other costs will also arise. These will invariably include a marketing initiative, but may also require legal costs. Such costs would be entirely unnecessary but for the patent system which requires inventing around to occur and the attractive rewards of the engendered monopoly. PhRMA profiling of industry members suggests

that over seventy per cent of members research spending is directed towards copycat medicines.[548]

3.3.7. **Good Sell**

Pharmaceutical company sales teams adopt several strategies. These include: advertising to health care professionals, direct consumer advertising, provision of samples, promotional gifts for prescribers, and the employment of pharmaceutical sales representatives. Pharmaceutical marketing activities comprise about twenty-eight per cent of a pharmaceutical company's total spending.[549]

In the UK, pharmaceutical advertising is specifically controlled by the Medicines Act 1968,[550] the Medicines (Advertising and Monitoring of Advertising) Amendment Regulations 1999 and the Control of Misleading

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[548] Pharmaceutical Research and Manufacturers of America,. Pharmaceutical Industry Profile 2001. [Pharmaceutical Research and Manufacturers of America, 2001, Washington, D.C]. The 2001 profile is no longer available online, but the 2008 and 2009 profiles may be accessed from: <http://www.phrma.org/publications/publications/> (Last Accessed: 1st July 2009); see Baker, D., and Chatani, N., Promoting Good Ideas on Drugs: Are Patents the Best Way? The Relative Efficiency of Patent and Public Support for Bio-Medical Research (2002) CEPR Briefing Paper [Centre for Economic and Policy Research, Washington] 2

[549] Data derived from the USA Securities and Exchange Commission (SEC) filings for the companies: Pfizer Inc, Johnson & Johnson, Merck & Co. Inc., Abbott Laboratories, Bristol-Myers Squibb Company, Wyeth, and Eli Lilly and Company. Sectors represent the mean expenditures by these companies over a four year period.

[550] In particular Part IV, which implements EU Directive 2001/83/EC which seeks to harmonise the advertising of medical products for human use within the European Union.

Advertisements (Amendment) Regulations 2000.[551] In addition there are several voluntary practice guides to which companies can adhere. These include: The British Code of Advertising Practice, Association of the British Pharmaceutical Industry (ABPI) Code of Practice for the Pharmaceutical Industry, the Proprietary Association of Great Britain Code of Standards of Advertising for Over-the-Counter Medicines (Known as the 'PAGB standard'), the Radio Authority Codes, and the Practice Guide of the Independent Television Commission.

As a result of amendments to the Medicines Act 1968 only a limited class of medicines can be marketed directly to consumers. However, the creation of patient groups to supply pharmaceutical manufacturer's information to consumers has been recognised as a valid method of circumventing direct-to-consumer restrictions in the UK. The ABPI Code of Practice has been updated to reflect this trend.

In addition to the domestic practice guides there are two further guides which are potentially applicable to pharmaceutical advertisers in the UK market. These are the European Federation of Pharmaceutical Industries' Associations and the International Federation of Pharmaceutical Manufacturer's Associations. Both of these bodies have their own codes. The European Federation of Pharmaceutical Industries' Associations' code closely follows the regulations of Articles 86-100 of EU Directive 2001/83/EC including a failure to identify 'essential information.' Each

[551] The Trade Descriptions Act 1968, will be relevant where companies make false claims about the products or services.

association, including the ABPI, which is a member of the European Federation of Pharmaceutical Industries' Associations, must adhere to the associations. Since EU Directive 2001/83/EC has either been implemented into the law of member states or is now directly applicable the benefits of the European Association is debatable. The European Federation of Pharmaceutical Industries' Associations does however in very restricted circumstances permit complaints against members. Otherwise complaints against breeches of advertising good practices presented in the guides of national associations must be made to those associations. The bottom line is that association standards are not well policed and appear more as an argument that the UK pharmaceutical industry has an ethical code of conduct and that further government regulation is not required.

A survey by the Institute for Evidence-Based Medicine, in Germany, evaluated the information presented on 520 pharmaceutical products contained in 175 brochures that were distributed amongst forty-three General Practitioners. It found that ninety-four per cent of the information had no basis in scientific evidence, whilst fifteen per cent of the brochures contained no citations. A further twenty-two per cent had citations which could not be found. Amongst the remaining sixty-three per cent the citation information was for a relevant research article, but the results in the research article and the brochure did not correspond. A mere six per

cent of entries comprised statements citing relevant supportive scientific evidence.[552]

The Medicines Act makes it an offence to issue false or misleading advertisements, or to make representations about an unauthorised indication. This includes promoting products prior to obtaining a license authorising sales of the pharmaceutical. It also requires retailers to make the special product characteristics of their medicines to be supplied every time they promote a product to any person qualified to prescribe or supply the medicine. The ABPI publishes the ABPI Data Sheet Compendium every fifteen months, which it distributes to all practicing doctors and pharmacies thereby creating constructive notice of the special product characteristics or their member's medicines.

The Medicines (Advertising and Monitoring of Advertising) Amendment Regulations 1999 restricts the supply of free samples, the provision of training by medical representatives and the distribution of gifts and other such incentives.

Enforcement of these restrictions is through the Control of Misleading Advertisements (Amendment) Regulations 2000, which empower the MHRA to undertake civil actions against breaches of the regulations, including injunctions and damages. Offences under the Medicines Act 1968 are subject to criminal proceedings, but where the Act and

[552] Tuffs, A., 'Only 6% of drug advertising material is supported by evidence' (2004) 328 BMJ 485

Regulations overlap health care practitioners may appeal to the MHRA to undertake civil action. The presence of the criminal proceedings in addition to the qualification of the MHRA to bring civil actions may constitute a potent deterrent against misleading advertising, but the extent to which policing is undertaken is a point of some controversy. Technically the promotion of Seroxat and Vioxx in the UK constituted misleading information, however no action was taken.

Moreover, the pharmaceutical industry comprises some of the brightest and most creative people of any industry. Even with the threat of onerous enforcement there are many potential avenues available to stimulate sales. For example, creating the perception of a cure for an illness that does not exist[553] or exaggerating and transforming normal sexual difficulty into the symptoms of treatable affliction.[554] Whilst patient groups with their websites, news letters and meetings present excellent forums to 'inadvertently' circumvent promotional restrictions.

Charities also present a suitable target for the engines of mass marketing. By establishing a charity a pharmaceutical company benefits from tax deductions from its marketing costs, a target audience who are placed into a relationship of trust, and impunity from advertising and promotion

[553] Vedantam, S., 'Drug Ads Hyping Anxiety Make Some Uneasy' (July 16, 2001) *Washington Post* A1

[554] Loe, M., The Rise of Viagra: How the Little Blue Pill Changed Sex in America [New York University Press, 2004, New York]

regulations. Moreover, the charity might even receive donations to subsidise its surreptitious marketing campaign.

> "Object of the Charity is to promote the study and advancement of knowledge about [condition]... and to improve the health and welfare of [condition sufferers]..."[555]

Another method of employing the positive image of charities is to utilise their name in conjunction with medicines, thus inspiring greater confidence in the product.[556]

Other groups not readily perceived as creatures of the pharmaceutical industry, are think tanks and patient advocacy groups. Pharmaceutical companies regularly fund these and, although such groups bear no affiliation other than their source of funding with pharmaceurical companies, they regularly adopt the pharmaceutical companies' cause.[557] One such example is the National Patient Advocate Foundation, whose sources of funding include Pfizer, Merck and GlaxoSmithKline.[558]

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[555] This is the form of several Charitable Organisations' charitable purpose statements. Of the four registered charities considered most dubious and contacted for information, three provided information on different products all of which were produced by the same company or its subsidiaries. Moreover, one provided detailed information about the performance of a USA drug not yet approved in the UK.

[556] Abelson, R., 'Sales Pitches Tied To Charities Draw States' Scrutiny' (May 3, 1999) *New York Times*, A1

[557] Anonymous, 'USA Today Looks at Prescription Drug Industry's Lobbying Efforts' (28 April 2005).*Medical News Today*. Available at: <http://www.medicalnewstoday.com/articles/23518.php> (Last Accessed: 1st July 2009)

[558] Drinkard, J. 'Drugmakers go furthest to sway Congress' (April 26, 2005) USA Today

According to PhRMA a 2008 KRC Research survey[559] they commissioned, found that sixty-nine per cent of doctors described free drug samples as either "always useful" (fifty-two per cent) or "often useful" (seventeen per cent).[560] The report goes on to state that ninety-five per cent of doctors agreed that the provision of samples permitted patients to begin immediate treatment.

Samples constitute an extremely effective method of attaching a patient to a therapy that they might not otherwise select. Changing drug therapies can have harmful repercussions; in addition to negating improvements in the patient's condition, it can aggravate adverse effects. For patients who cannot afford the medicine starting them on a sample is a cruel and possibly health detrimental course of action. Of course the availability of samples may permit a doctor to effectively subsidise a patient's therapy. However, in terms of contributing to therapeutic improvements and their deadweight incidence on funds available for reinvestment in research and development samples present negative indications.

Another deadweight is promotional gifts: a pad of paper bearing the company's trade mark, a pen, umbrella, or weekend in Paris. Gifts can

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[559] Source is cited as: "KRC Research, 'Physicians' Opinions About Pharmaceutical and Biotech Research Company Activities and Information' n=501, 2008, sponsored by Pharmaceutical Research and Manufacturers of America."

[560] PhRMA 'Pharmaceutical marketing in PersPective' (2008) at 6 Available at: <http://www.phrma.org/files/Marketing and Promotion Facts_071108_FINAL.pdf> (Last Accessed: 1st July 2009)

take a number of forms from promotional merchandise to outright payments.[561] None of which contribute positively to the vitality of drug development, or reduce the barriers to access that high prices create.

3.3.8 **Well Represented**

Pharmaceutical sales representatives provide doctors with company information about new treatment options that is designed to influence prescribing habits. In 2000 PhRMA's own data indicated that the USA pharmaceutical industry employed nearly twice as many people in sales as it did in research; with 87,810 people in sales compared to 48,527 people in research.[562] In contrast, and also according to PhRMA, only about fourteen per cent of doctors said pharmaceutical representatives have a "major impact" on prescribing habits.[563] Which suggests that even the limited effectiveness of pharmaceutical sales representatives generate substantial income. During the period 2003 to 2005 where job

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[561] Dyer, G., and Williamson, H., "German Doctors Accused of Taking Bribes," (March 12, 2002) *London Financial Times* B3

[562] Pharmaceutical Research and Manufacturers of America,. Pharmaceutical Industry Profile 2001. [Pharmaceutical Research and Manufacturers of America, 2001, Washington, D.C]. The 2001 profile is no longer available online, but the 2008 and 2009 profiles may be accessed from: <http://www.phrma.org/publications/publications/> (Last Accessed: 1st July 2009); see Baker, D., and Chatani, N., Promoting Good Ideas on Drugs: Are Patents the Best Way? The Relative Efficiency of Patent and Public Support for Bio-Medical Research (2002) CEPR Briefing Paper [Centre for Economic and Policy Research, Washington] 9

[563] The following report is cited as the source data, but it was unavailable: Boston Consulting Group, 2002 BCG Proprietary Physician Survey, n=399, 2002; See PhRMA 'Pharmaceutical marketing in PersPective' (2008) at 4 Available at: <http://www.phrma.org/files/Marketing and Promotion Facts_071108_FINAL.pdf> (Last Accessed: 1st July 2009)

advertisements for pharmaceutical sales representatives were placed in the UK, listed salaries ranged from £24,000 GBP to £68,000 GBP with a median of £41,000 GBP. In terms of salaries alone, the employment of so many pharmaceutical representatives constitutes a large expenditure. Moreover, the methodology of pharmaceutical representatives requires further capital.

Pharmaceutical Sales Representatives build relationships with doctors through a number of strategies, which include calling on doctors at their workplaces and the organisation of Speaker Meetings. Speaker meetings might include one or several doctors and will usually involve a presentation by an invited doctor or by the pharmaceutical sales representative. In some cases these may involve seminars at resorts, with additional incentives for those who attend.[564]

During an informal discussion (2003) a pharmaceutical representative explained

> "We're instructed to keep profiles on our doctors so that we can report what data interests them the most. It makes meetings more productive for both of us... I don't go on about stuff that doesn't interest them and they get to hear about cool new introductions that they need to prescribe."

[564] Zuger, A., 'Fever Pitch: Getting Doctors To Prescribe Is Big Business' (January 11, 1999) *New York Times* A1

She also revealed that it was useful to find out as early as possible what the doctor's hobbies and interests were, so that relevant promotional items could be left at the meeting. Or so she could take them to a restaurant that they liked, which "could be a great ice-breaker."[565]

3.3.9. **Keeping Abnormal Profits**

> "...it has become too obvious to most writers that the size of the monopoly profits earned under the protection of patents is not at all correlated with the efforts, capital funds, or sacrifices invested in the innovative work."[566]

Any profit greater than that which is just sufficient to ensure that a supplier will continue to supply its existing product is conventionally labelled excess profit or abnormal profit. The pricing of a patented pharmaceutical that satisfies a strong demand for a therapy will always generate higher than normal profit. However, the high pricing will not always result in a sufficient imbalance between market supply and demand that other suppliers enter the market, because of the technical burdens the presence of a patent places on would be market entrants.[567] In wealthy

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[565] Pharmaceutical Sales Representative interview, London (December 2003)

[566] Machlup, F., An Economic Review of the Patent System: Study of the Subcommittee on Patents, Trademarks, and Copyrights of the Committee of the judiciary (1958) US Senate, 85th Congress, 2nd Session, Study Number 15, Washington: United States Government Printing Office, at 29-30

[567] However for patented pharmaceuticals in very poor therapeutic markets, having a pharmaceutical patent may not result in more than normal profit. This is a particular

economies, such as the USA, the majority of in-patent pharmaceuticals earn abnormal profits, but not all do.[568]

Since in the USA the parameters set by insurers distort the prescribing habits of doctors, it is unsurprising that companies go further and collect data on the individual prescribing habits of doctors.[569] Not only would this data reveal the conditions which receive the most prescriptions, but it would also reveal the income bracket of a doctor's patients and the degree of influence company promotional behaviour had on the doctor. Thereby permitting more targeted pricing and adoption of more effective marketing policies. Moreover, where a doctor is intractable efforts can be devoted to prescribers on whom efforts and expenditure will present the most return.

Moreover, as monopolists expect far greater returns, i.e. substantially above marginal costs they engage in rent seeking behaviour. In the context of pharmaceuticals where the alternatives to taking a therapy are either serious reduction in quality of life or death, the monopolists and their shareholders have for the last four decades expected abnormal profits. Which results in their monopoly increasing the deadweight in the product

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problem of the pharmaceutical patent in directing research efforts into less lucrative but important therapeutic areas such as neglected diseases.

[568] From a sampling of 4914 patented pharmaceutical products in the USA, Roberts identified that more than 95 percent of those products returned abnormal profits from sales in any year that they were marketed and in patent. Roberts, P., 'Product Innovation, Product-Market Competition, and persistent profitability in the US Pharmaceutical Industry' (1999) 20 *Strategic Management Journal* 655-670, 660

[569] Stolberg, S., Gerth, J., 'High-Tech Stealth Being Used To Sway Doctor' (November 16, 2000) *New York Times* A1

or method of production, that they monopolise, to a greater extent than other awards of privilege that permit competition. Although patents are the most important tool for controlling a pharmaceutical market, there are other instruments to be exploited in synergy.

Evidently, once a monopoly is established and if it is a successful monopoly, i.e. the profits are above normal, then there is reason to maintain the monopoly at all costs. Thus, resources are channelled into strengthening the existent monopoly, and preventing potential competitors from entering the market. This includes preventing the introduction of new technologies before the monopoly of the old technology is extinguished. In Pharmaceutical Patent Life Cycles,[570] some of the methods of extending the patent monopoly, For example Orphan Status, and erecting other barriers to market entry, such as data exclusivity, were described. So far though the most politically significant factor in the expenditure that ought to be destined for improving availability and access of medicines and vaccines has been ignored.

Through lobbying and support of political entities the political system is distorted, as the donor may withhold the future promise of assistance if their desires are not approached. When a powerful industry collective is making the donations, during the elections is just one point of opportunity, the donated funds can have significant impact for the receiving party. In the 2004 USA presidential election the Bush campaign received a

[570] Section 1.5. Pharmaceutical Patent Life Cycles

$516,000 USD[571] boost to their campaign funds from Big Pharma.[572] With the USA congress firmly in Democratic hands in the present election funding has favoured the Democratic candidates. Whilst the Republican candidate McCain received $44,000 USD from Big Pharma, the Democratic candidates Obama and Clinton received $181,000 USD and $174,000 USD respectively from Big Pharma.[573] Although only a small fraction of squandered resources it is enough money to equip, train and pay many well educated researches. Moreover, considering that in 2003 there were 1,274[574] registered lobbyists hired by pharmaceutical

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[571] Although there seems to be great discrepancy in what was contributed. Mathiason, N., Big Pharma puts block on cheap drug imports (3 August 2003) *Guardian.co.uk / The Observer.* Available at: <http://www.guardian.co.uk/business/2003/aug/03/aids.theobserver> (Last Accessed: 1st July 2009)
Suggests *Big Pharma* contributed $14 million USD to Bush's Presidential election campaign; Anonymous, 'USA Today Looks at Prescription Drug Industry's Lobbying Efforts' (28 April 2005). *Medical News Today.* Available at: <http://www.medicalnewstoday.com/articles/23518.php> (Last Accessed: 1st July 2009)
USA Today, courtesy of Medical News Today suggest that during the 2004 USA presidential elections the pharmaceutical industry donated "at least $17 million [USD] to federal candidates, including $1 million [USD] to President Bush.

[572] Smith, A., Big Pharma opens wallet to Dems (7 March 2008) CNNMoney.com. Available at: <http://money.cnn.com/2008/03/04/news/companies/pharma_votes/index.htm> (Last Accessed: 1st July 2009)

[573] Smith, A., 'Big Pharma opens wallet to Dems' (7 March 2008) *CNNMoney.com.* Available at: <http://money.cnn.com/2008/03/04/news/companies/pharma_votes/index.htm> (Last Accessed: 1st July 2009)

[574] Anonymous, 'USA Today Looks at Prescription Drug Industry's Lobbying Efforts' (28 April 2005). *Medical News Today.* Available at: <http://www.medicalnewstoday.com/articles/23518.php> (Last Accessed: 1st July 2009)
But see Mathiason, N., 'Big Pharma puts block on cheap drug imports' (3 August 2003) *Guardian.co.uk / The Observer.* Available at:

companies on Capitol Hill, redirection of funds from distortion of the political system could pay for substantially more researchers. Pharmaceutical lobbyist salaries vary, but the most prominent usually have annual salaries in millions of USD. In 2010 Billy Tauzin earned 11.6 million USD as the head of PhRMA.[575]

Lobbying has yielded favourable outcomes for the pharmaceutical industry in the USA. These have recently included expansion of Medicare coverage to prescription pharmaceuticals, the blocking of government price discount negotiations, quickened FDA drug approval, and maintenance of the barriers against exhaustion through the ban on the import of low price prescription medicines from Canada.[576]

3.3.10 **Great Hole**

As of the January 1, 2006, Medicare Prescription Drug, Improvement, and Modernization Act of 2003 expanded the very restrictive funding options for prescription medicines available in the original Medicare. A Part D, the prescription drug benefit, was introduced, which for a monthly premium

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<http://www.guardian.co.uk/business/2003/aug/03/aids.theobserver> (Last Accessed: 1st July 2009) Claims 625 pharmaceutical lobbyists using the present tense, *id est* 2002 or 2003.

[575] Wayne, A., and Armstrong, D., 'Tauzin's $11.6 Million Made Him Highest-Paid Health-Law Lobbyist,' 29th September 2011. Bloomberg. Available from: <http://www.bloomberg.com/news/2011-11-29/tauzin-s-11-6-million-made-him-highest-paid-health-law-lobbyist.html> (Last Accessed: 5th December 2011)

[576] Drinkard, J. 'Drugmakers go furthest to sway Congress' (April 26, 2005) USA Today; Medical News Today – unattributed text 'USA Today Looks at Prescription Drug Industry's Lobbying Efforts' (28 April 2005) *Medical News Today*. Available at: <http://www.medicalnewstoday.com/articles/23518.php> (Last Accessed: 1st July 2009)

provides fairly comprehensive pharmaceutical coverage. The positive benefits to subscribers of receiving assistance to some prescription drugs is also of financial benefit to pharmaceutical companies who have thereby gained customers. However, when Part D was passed through congress there was apparently a failure to estimate how much the plan would really cost, although price inflation by pharmaceutical companies supplying medicare drugs,[577] and the presence of pharmacy benefit managers might also a significant factor in the estimation flaws. As a result there is a large deficit in the available finances, which has resulted in a phenomenon known as the 'doughnut hole'. Medicare subscribers are able to gain assistance with seventy-five per cent of prescription medicine costs up to $2,700 USD in yearly prescription costs. However, once they pass this amount they are responsible for all their costs until they exceed $6,100 USD. Over $6,100 USD they receive assistance once again with ninety-five per cent of the cost of prescription medicines.[578] Part D premiums vary with the plan[579] and are based on regional medical costs and range from $1.87 USD to $17.91 USD per month.[580]

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[577] Families USA, 'Medicare Legislation Will Be A Deep Disappointment for America's Seniors' (Nov. 25, 2003). Available at: <http://www.familiesusa.org/resources/newsroom/statements/2003-statements/press-statement-medicare-legislation-will-be-a-deep-disappointment.html>; see 'overcharging' at 1095, Austin, G. E., and Burnett, R. 'An Innovative Proposal for the Health Care Financing System of the United States' (2003) 11(5) *Pediatrics* 1093-1097

[578] Medicare - Official U.S. Government Site for People with Medicare. Available at: <http://www.medicare.gov/pdp-things-to-consider.asp> (Last Accessed: 1st July 2009)

[579] Medicare - Official U.S. Government Site for People with Medicare. Available at: <http://www.medicare.gov/pdp-things-to-consider.asp> (Last Accessed: 1st July 2009)

[580] http://www.seniorark.com/medicare/Medicare Part D 2009 Guidelines.htm. However, case comments on the internet suggest that some people's premiums are much higher.

In 2007, Federal Centers for Medicare & Medicaid Services estimated that over eight million, thirty-two per cent of the twenty-six million, Part D subscribers reached the coverage gap.[581]

However, the positive effect of the Medicare Part D fro pharmaceutical companies is the new pool of buyers that has been created. Many of those utilising medicare would have purchased some medicines without the scheme, but there are also users who would have not. Moreover, users crossing the coverage gap are more likely to purchase all of the drugs under the coverage plan that their doctor has suggested to treat their conditions, which too has increased sales.[582]

> "The ten largest pharmaceutical companies enjoyed substantial profit increases in the first six months of the new Medicare drug

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As a result these figures need verification from an authorative source. Unfortunately Medicare do not provide data directly

[581] Medicare Coverage Database. Available at: <http://www.cms.hhs.gov/MCD/overview.asp> (Last Accessed: 1st July 2009)

[582] "Three factors account for the Medicare drug program's impact on profits: increased demand for popular drugs; the inability of the drug plans to obtain discounts from drug manufacturers; and the ability of the drug manufacturers to increase prices significantly for drugs used by over six million dual-eligible beneficiaries." Committee on Government Reform, House of Representatives, 'Analysis Pharmaceutical Industry Profits Increase by Over $8 Billion After Medicare Drug Plan Goes Into Effect' (September 2006) at 4. Available at: <http://oversight.house.gov/documents/20060919115623-70677.pdf> (Last Accessed: 1st July 2009)

program. In the first half of 2006, profits for these companies increased by over $8 billion, a 27% increase."[583]

3.3.11. **Hired Help Or Insiders**

One of the reasons for the success of pharmaceutical lobbying and the reluctance in the USA to implement price control schemes might result from the frequency with which the highest echelons of USA government have personal interests in the pharmaceutical industry.[584]

Consider Gilead Sciences, in November 2005 government notables with an interest in Gilead included USA Secretary of Defense Donald Rumsfeld (board member and former chairman of Gilead Sciences), former USA Secretary of State and Bush campaign advisor George Schultz (board member), Vice-Chairman of Suez-Tractebel and Honorary Chairman of Bilderberg Etienne Davignon, and Defense Business Board and corporate advisory council to the USA Department of Defence John W Madigan.[585] Gilead Sciences is notable in 2005, and indeed still is, because of the

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[583] Committee on Government Reform, House of Representatives, 'Analysis Pharmaceutical Industry Profits Increase by Over $8 Billion After Medicare Drug Plan Goes Into Effect' (September 2006) at 2. Available at: <http://oversight.house.gov/documents/20060919115623-70677.pdf> (Last Accessed: 1st July 2009)

[584] Although the distinction between lobbyist and congressman is not particularly clear. Bykowicz, J., 'Gingrich Firm Top Clients Got to Attend Signing of Favored Bill,' (26th January 2012) Bloomberg. Available at: <http://www.bloomberg.com/news/2012-01-26/gingrich-company-helped-clients-attend-bill-signing-of-favored-legislation.html> (Last Accessed: 29th February 2012)

[585] GRAIN, 'Fowl play: The poultry industry's central role in the bird flu crisis' Briefing Document (2006) at 15. Available at: <http://www.grain.org/briefings_files/birdflu2006-en.pdf> (Last Accessed: 1st July 2009)

potential for an influenza pandemic and Gilead's ownership of the patent for Tamiflu.[586] As an antiviral useful in the prophylaxis of both influenzavirus type A and B infections, Tamiflu is one of several drugs that may be useful in reducing the loss of life in an influenza pandemic. Prior to 2005 the market for Tamiflu was small however following the wake of concerns over a flu pandemic by the WHO, USA President Bush announced measures to counter incursions of the pandemic into the USA. These included a fund of $1.4 billion USD to purchase Tamiflu.[587]

In 2005 sales of Tamiflu rose by four hundred per cent and Gilead's royalty earnings from the patent grew by 166 per cent. Rumsfeld in that period owned $5 million USD to $25 million USD of Gilead equity.[588]

In the UK the situation is startlingly similar with many instances of donations that are shortly followed by government contracts or government investment initiatives. The pharmaceutical company PowderJect founded by Paul Drayson - later to became Lord Drayson (six weeks before donating £500,000 to Labour) - received a £32 million

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[586] Oseltamivir phosphate

[587] GRAIN, 'Fowl play: The poultry industry's central role in the bird flu crisis' Briefing Document (2006) at 15. Available at: <http://www.grain.org/briefings_files/birdflu2006-en.pdf> (Last Accessed: 1st July 2009)

[588] GRAIN, 'Fowl play: The poultry industry's central role in the bird flu crisis' Briefing Document (2006) at 15. Available at: <http://www.grain.org/briefings_files/birdflu2006-en.pdf> (Last Accessed: 1st July 2009)

government contract to supply smallpox vaccine, shortly after Mr. Drayson donated £50,000 to Labour.[589]

3.4. Burden on Innovators

Pharmaceutical research and the bundled industry costs of developing and retailing medicines are substantial. Funding can come from a diversity of sources, but for private pharmaceutical companies there is a shareholder expectation that the company will strive to enhance shareholder value (3.4.1 - 3.4.2). With the pharmaceutical giants adopting the 1990's investigation paradigm of big mining companies - by letting entrepreneurial small companies handle early stage exploration and the risk of not making a valuable find - investment losses in identifying important molecules to develop should have been reduced (3.4.3). Nevertheless, the cost of medicines has continued to rise.[590] With the large pharmaceutical companies, demonstrating growth to shareholders is a problem. The only pharmaceuticals that are capable of generating noticeable revenue increases are blockbusters. Investing in anything less, regardless of the therapeutic advance it conveys, is economically unviable, or requires

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[589] Sparrow, A., Tycoon gave £0.5m to Labour after receiving peerage (24 August 2004) Telegraph.co.uk. Available at: <http://www.telegraph.co.uk/news/uknews/1470152/Tycoon-gave-andpound0.5m-to-Labour-after-receiving-peerage.html> (Last Accessed: 1st July 2009)

[590] "[usual and customary] price index for our first basket of 100 commonly used prescription drugs increased at an average annual rate of 6.6 percent from 2006 through the first quarter of 2010" GAO-11-306R Prescription Drug Price Trends Available at: <http://www.gao.gov/assets/100/97284.pdf> (Last Accessed: 1st November 2011)

investment in a subsidiary. With the development and market regulation expertise firmly in the hands of large pharmaceutical companies, smaller biotech firms without affiliation are unlikely to successfully bring a product to market and maintain an exclusive market presence through their patent.

3.4.1. **Must Profit**

Consider Pfizer. Pfizer is an enormous company, with revenue of $52 billion USD. To make a positive difference to its revenue a drug needs to annually generate revenues in the range of $1 billion to $2 billion USD. For most companies the addition to the company's base line of a $400 million USD per annum product, at an 80 percent profit margin, is very welcome indeed. For Pfizer, it does not even touch the performance indicators.

In 2005 Pfizer had very good revenues, but overall its earnings fell by 28.8%. In 2006, through layoffs and the sale of its consumer-products division to Johnson & Johnson, Pfizer managed to post a 139% increase in earnings. Whilst layoffs and sale of its consumer-products division provided a one off regeneration of Pfizer, this was simply a stopgap and streamlining measure. In the long run Pfizer needs new blockbusters to restore its vitality.

A paucity of major drugs in a company's property portfolio, or viable NCEs in its development pipeline, is a serious problem to a big pharmaceutical company's health. By the end of 2008, Pfizer will have weathered four

years of patent protection losses on medicines[591] that have major revenue significance: that is an annual sales loss of $14 billion USD. The independent market analysts Datamonitor estimate that by 2016 the annual sales loss for pharmaceutical companies as a result of expiring patents will be $140 billion USD.[592]

Considering the significance of blockbuster drugs to the pharmaceutical giants' earnings, and the difficulty of realising a blockbuster medicine, it is unsurprising that so many companies have so much riding on a handful of potential pharmaceuticals.[593] The attitude that blockbusters are to be sought or created in priority has several detrimental effects, as will be highlighted. For the research scientist, generation of a future product line that has blockbuster potential is an important requisite of good career and financial prospects. Thus, as innovation is seen to dwindle and shareholders become furious at pharmaceutical giants for not making the dramatic gains in earnings that the shareholders have come to expect,[594] a new trend has emerged in shareholder soothing. Pharmaceutical companies have started to reveal their future hand, by detailing the revenue potential of pharmaceuticals in their development pipeline.

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[591] Expired patents include the anti-depressant Zoloft; the blood pressure pill, Norvasc; and the antibiotic Zithromax.

[592] Patents Shine, but Don't Be Blinded by Them. May 18, 2007. Available from: <http://www.fool.com/investing/high-growth/2007/05/18/patents-shine-but-dont-be-blinded-by-them.aspx> (Last Accessed: 1st July 2009)

[593] Simons, J., CNN Money.com Dec 2006. Available from: <4http://money.cnn.com/2006/12/04/news/companies/pluggedin_simons_pfizer.fortune/index.htm?source=yahoo_quote> (Last Accessed: 1st July 2009)

[594] Fortune 500 Snapshots. Available from: <http://money.cnn.com/magazines/fortune/fortune500/snapshots/>

For example in December 2006, simply the disclosure by the Swiss pharmaceutical company Actelion Ltd of its potential new tissue-targeting dual endothelin receptor antagonist, Actelion-1,[595] raised Actelion's shares by 1.4% in a much lower Swiss market.[596] At the time Actelion-1 was only in Phase II trials[597] and thus hardly a strong indicator that it would reach the market, let alone realise the performance of Actelion's flagship drug Tracleer. Nevertheless, investors will often count preclinical compounds as "in the pipeline." Unfortunately, when the blockbusters do not appear share futures can suffer, that is unless they receive further soothing.

The impact of this situation on the scientist is significant. The scientist must ensure, that future blockbuster drugs reach the market by passing smoothly through regulatory approval. To an industry outsider this might be considered unethical, however the pharmaceutical industry is self-regulating and the pressure to maintain sales and product lines is immense. The 'ought' does not cost the company billions, whereas the shareholders and market might. The pressure that the pharmaceutical

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[595] The Actelion Annual Report 2006. Available from: <http://annualreport06.actelion.com/home/cornerstones/clinical-developement.html>

[596] Drug Pipeline and Pharmaceutical Market Data, Sunday, December 10, 2006. Available from: <http://chartsbank.blogspot.com/2006/12/actelion-about-to-disclose-new.html> (Last Accessed: 1st July 2009)

[597] Pre-clinical compounds are considered to be in the pipeline by some pharmaceutical investors. Patents Shine, but Don't Be Blinded by Them. May 18, 2007. Available from: <http://www.fool.com/investing/high-growth/2007/05/18/patents-shine-but-dont-be-blinded-by-them.aspx> (Last Accessed: 1st July 2009)

company experiences is translated to the patent specialists, technology consultancy firms and the research scientists.

3.4.2. **Must Delay**

With the decline of the pharmaceutical industry from its position as the most profitable industry and the move of investment portfolios to mining and crude-oil production, the research scientist is under greater pressure than ever before to produce a portfolio of drugs that are potentially strong earners and are clearly seen to be so. Already research spending had been focused on products which carried blockbuster potential regardless of their added therapeutic value[598], *ceteris paribus* this trend will be strengthened in the coming years.

> "Patent laws..., in effect,.. do not... appreciably stimulate inventive activity,... but they do direct it into channels of general usefulness."[599]

As far as therapeutic value is neglected where it does not coincide with blockbuster creation, or the market for a pharmaceutical is discounted because it does not meet profitability criteria, then the pharmaceutical patent cannot be considered as channelling inventive activity into general usefulness, where usefulness is therapeutic advance.

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[598] Hollis A. An Efficient Reward System for Pharmaceutical Innovation. 2005, 1. Available at: <http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf> (Last Accessed: 1st July 2009)

[599] Pigou, A. *The Economics of Welfare* [Macmillan, 1924, 2nd Ed., London]; Menell (1999) p.132

Other than the difficulty in identifying a chemical with blockbuster potential, is the difficulty in finding one that it is safe to market. One way to achieve profit from an invention monopoly is to ensure that there is little or no product competition, thus by obstructing or stifling the innovation of medicines targeting the same or similar conditions, or by delaying disclosure of the monopolist's own improvements. Pharmaceutical companies spend considerable amounts of money and employ large teams of patent specialists and technology consultancy firms in order to close all access to their monopoly, plan for its life cycle maximisation, and if possible to prevent any market entry. For example more than twenty per cent of human genes are already patented and some of these genes are patented more than twenty times.[600] As a result other pharmaceutical firms, particularly if they are producing 'me-too' medicines, also employ large teams of patent specialists and technology consultancy firms.

The patenting of chemicals of the same family, similar transport vehicles, the methods or administration and preparation creates a strong barrier to market entry and a formidable obstacle to potential competitors seeking to invent around the patent. Such a barrier is sometimes referred to as a 'patent thicket.'

> "These 'patent thickets'... basically inflate the transactions costs of developing a new innovation, and are, therefore, likely to inhibit the

[600] Jensen, K., and Murray, F., 'Intellectual property. Enhanced: intellectual property landscape of the human genome' (2005) 310 *Science* 239-40

rate of development of new ideas or the good[601] and services that come from them."[602]

They can be a bar to research because of the unavailability of a licences or because acquisition of a licence is prohibitively expensive.[603] In some cases patent thickets have also discouraged researches and slowed research and development because of the complexities of dealing with large numbers of patents.[604] Constant review of immense and rapidly growing patent databases also requires resources.[605] This type of work is often out sourced to patent agents and technology consultancy firms. The technology consultancy firms produce a report, usually containing copies of prior art documents or claims that they consider the most relevent. These are then studied and reported on by the patent agent. Thoroughness in this type of work is extremely important and displacing

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[601] Typically the phrase is 'goods and services,' although in this instance 'good' would also make sense in a welfare, quantative inovation sense; *id est* more inovation is better, that extra innovation conveys added benefit. However, we question whether a typographical error was made here.

[602] Geroski, P. A., Intellectual Property Rights, Competition Policy and Innovation: Is There a Problem? (2005) 2:4 *SCRIPT-ed* 422-428 at 424-425. Available at: <http://www.law.ed.ac.uk/ahrc/script-ed/vol2-4/geroski.pdf> (Last Accessed: 1st July 2009)

[603] Wadman, M., 'Licensing fees slow advance of stem cells' (18 May 2005) *Nature*. E-pub. Available: <http://www.nature.com/news/2005/050516/pf/435272a_pf.html> (Last Accessed: 1st July 2009)

[604] Eisenberg, R., 'Expanding the boundaries of intellectual property: Innovation policy for the knowledge society.' In Dreyfuss, R. C. (eds.) *Bargaining over the transfer of proprietary research tools: Is this market failing or emerging?* [Oxford University Press; 2001, 1st Ed., Oxford] 223–250

[605] Simmons, E., S. 'Prior art searching in the preparation of pharmaceutical patent applications' (1998) 3 (2) DRUG DISCOV TODAY 52-60

the liability for searchers is an important factor in the outsourcing. A patent thicket can create considerable difficulties for would be competitors searching for unenclosed avenues and it can require considerable time and effort by specialist searchers and scientists to identify if all approaches have been sealed off.

3.4.3. **Outsourcing Invention**

It has been claimed that the pharmaceutical patent favours small firms against the economic strength of larger companies. Such a statement if it holds any validity is based on a theoretical model whereby the small company is perfectly placed, i.e. financially,[606] technically, and legally. In practice, small firms (which are not subsidiaries of larger pharmaceutical companies) innovating in the area of pharmaceuticals are usually spin-off companies from university and public research institutions and are very dependent on the university for the provision of expertise and resources in obtaining a patent.[607] Therefore, the university's Technology Transfer Office is significant in assisting the spin-off company obtaining a patent, and is also key in determining strategy, such as licensing a product at as

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[606] "...what the inventor receives from our patent system is not so much a monopoly in the working of his invention as a licence to compel his competitors to join him in spending large sums in litigation." Blanco White (1974, 9-10). 'Low cost' patent infringement cases can cost millions in litigation, whilst 'high cost' patent infringement cases can cost substantially more. *See,* CJA Consultants Ltd, Patent Litigation Insurance - A Study for the European Commission on the feasibility of possible insurance schemes against patent litigation risks [CJA Consultants Ltd, 2006, London] 13, 36.

[607] Macho-Stadlera, I.,Pérez-Castrilloa, D., Veugelers, R., 'Licensing of university inventions: The role of a technology transfer office,' (2007) 25(3) *International Journal of Industrial Organization* 483–510

early a stage as possible.[608] The principal reasons for early licensing of patents on potential pharmaceuticals are connected with resources either for in vitro testing models, development, or simply because if the invention has good remunerative prospects the patent will be circumvented, revoked, or infringed by a company with deeper pockets and greater legal expertise. Where pharmaceutical patents are obtained by spin-off companies the patents with potential tend either to be assigned or become the subject of a cooperative agreement with a large pharmaceutical company or a large pharmaceutical companies subsidiary. It is estimated that there are 3,000 biotechnology companies worldwide, but that only 100 of them have products with market approval.

Up until 2008 patent assignments from spin-off companies and small biotechs were usually with larger pharmaceutical companies, who would then conduct clinical trials, secure further patents, and if viable bring a product to market. Despite the increasing visibility of small biotechs, there are no new pharmaceutical companies on the scale of the old research and manufacturing giants such as Pfizer, Johnson & Johnson, Merck, Abbott Laboratories, Eli Lilly, Bristol-Myers Squibb, and Amgen. Small companies such as the university spin-off biotech companies, lack the resources, legal knowledge and regulatory savvy of the large

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[608] Concerning university intellectual property commercialisation see Siegel, D., Veugelers, R., Wright, M., 'Technology transfer offices and commercialization of university intellectual property: performance and policy implications,' (2007) 23(4) Oxf Rev Econ Policy 640-660; For an outline of the important factors in University Technology Transfer Office licensing of patents see Haour, G., Mieville, L., From Science to Business [Palgrave Macmillan, 2010, 1st Ed., New York] 62-65, 68-69, 95-97.

pharmaceutical companies. In order for them to grow they either have form partnerships with experienced pharmaceutical developers or to aggregate[609] and aggregation requires partners who can strengthen and complement a company's expertise. Such partners because of those very properties are likely to have been acquired or even set up as subsidiaries of larger companies. For example the Belgium biotech company Galapagos was registered in 1999 from a joining of the Dutch biotechnology company Crucell N.V., which is a subsidiary of Johnson & Johnson, and Tibotec, which is a spin-off company from the Rega Institute for Medical Research, Leuven University.

Since 2008 there has been a growth of pharmaceutical companies who specialise in developing products for markets or, in the USA since 1998, in providing manufacturing facilities for biotechs.[610] Other companies have speculated in buying patents from biotech research companies and trying to license them to larger research and manufacturing companies, but this has not been successful and only the subsidiaries of Hoffmann–La Roche, Johnson and Johnson or Eli Lilly endured into 2010. In terms of future trends there is a balance between profit and risk that will in some areas of

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[609] Champsi, F.H., 'Biotechnology mergers and acquisitions,' (2003) Bioentrepreneur. Available at: < http://www.nature.com/bioent/2003/030101/full/nbt0598supp_61.html> (Last Accessed August 2011)

[610] The Food and Drug Administration Modernization Act, enacted in November 1997, amended the Federal Food, Drug, and Cosmetic Act relating to the regulation of food, drugs, devices, and biological products. The legislation replaced establishment licenses and product licenses with a biological license. Which made manufacturing outsourcing possible, as manufacturing premises no longer had to be a participant in the ownership of the product.

pharmaceutical development inhibit the patent acquisition by middleman patent trading companies. Indeed, private equity investors are increasingly concentrating on divesting the research functions of large pharmaceutical companies, so the companies can be run "more efficiently."[611] The early signs of which are already visible.[612] Where research institutions and affiliated companies produce multiple patents with market potential, the larger market dominant pharmaceutical companies reposition themselves to have closer ties to that new generation pharmaceutical innovator.[613] This relationship may be in the form of sponsorship, research expertise, or equipment. Eli Lilly who are the current market leaders in establishing close connections with university biotech research facilities offer two principle advantages in return for patent rights: These are use of their in vitro model systems and their sophisticated phenotypic screening systems. Since Eli Lilly conducts assays of molecules submitted by members of its research network[614] for free it provides researches to more readily identify the in vitro traits of their molecules an Eli Lilly to assay a much larger variety of molecules than its

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[611] Available at: http://www.pmlive.com/pharm_market/earlier_news.cfm?showArticle=1&ArticleID=5924 (Last Accessed September 2007)

[612] Eli Lily from June 2011 has operated a research and development program, known as the Open Innovation Drug Discovery Platform, with leading pharmaceutical research universities across Europe.

[613] e.g. in September 2011 an Open Innovation Drug Discovery agreement was made between Lilly and the University of Valencia. In January 2012 the University of Cambridge agreed to an Open Innovation Drug Discovery Platform. As of February 2012 there are currently over sixty-members in Eli Lilly's Open Innovation Drug Discovery Platform.

[614] Open Innovation Drug Discovery Platform, which was formerly called PD2.

former research departments could have, as well as permitting Eli Lilly to keep constant track of the prolificity and quality of research network members. In terms of the extent of assayed molecules under this research model one is reminded of the Eighteenth Century German dye industry. Outsourced pharmaceutical innovation appears to be the paradigm for the next period of pharmaceutical innovation. With the potential for greater numbers of molecules to be assayed this had good ramifications for availability. However, as the cost of patented pharmaceuticals continues to rise there is no indication whatsoever that reducing the investment risks in finding NCEs has improved the accessibility of medicines.

3.5. Duplicated Resource Expenditure

In theory patent databases can be exploited to create and develop further inventions, thereby greatly reducing the duplication of effort. However, because of the necessity of continuous review, the patent system in effect channels funds into the policing of patent databases.

> "Critics imply that it would be better if only one company raced for each target. But if that were so, wouldn't they be likely to slow down? Even if that weren't the case, you have a big problem, which is that not all drugs clear the regulatory burden. If ten companies set out to target, say, serotonin reuptake inhibition, some of their

drugs will prove toxic or ineffective. If only one company is going for it, many categories will end up with no drug, as the candidate in that category falls out of the pipeline for one reason or another."[615]

3.5.1. **Sometimes Revealed**

One justification of the patent system is the disclosure incentive function statement, which assumes that distribution of knowledge to the community concerning the inventive step is preferable to that information remaining concealed or requiring others to invest resources in the same discovery. In contrast and existing alongside the duties imposed on everyone, but the patent holder and licensees, by the patent right are the duties bundled within data exclusivity. Data exclusivity follows the same reasoning as trade secrets. The functional characteristic of data exclusivity, that is the inability of competitors to make use of that information, is akin to the *modus-operandi* of trade-secrets. Theoretically the market power of data exclusivity is less restrictive when compared with patents. This is because data exclusivity does not legally prohibit other companies from generating registration data of their own. In practice however, the large financial resources and extended time required for gathering and generating pharmaceutical registration data for a new drug create a market barrier that is too high for many generic-based companies.[616] Moreover, it is a

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[615] More on me-toos Economist.com. Available at: <http://www.economist.com/blogs/freeexchange/2007/04/more_on_metoos.cfm> (Last Accessed April 2007)

[616] Pugatch, M.-P., Intellectual property and pharmaceutical data exclusivity in the context of innovation and market access, ICTSD-UNCTAD - Dialogue on Ensuring Policy Options for Affordable Access to Essential Medicines Bellagio (2004). Available at:

grotesque waste of resources and prevents the thorough screening and examination of clinical testing results that would occur if the data was retrievable or publicly disclosed.

Since the Jacquard loom, digital media and data retrieval systems have become increasingly capacious, more sophisticated, reliable, easier to transfer, and cheaper. Consequently, the marginal cost of digitally duplicating anything capable of being transmitted via digital media converges towards zero. If all research which was conducted was open, sharable and attributed, then reduced expenditure on duplicate research, greater rapidity in therapeutic improvements, as well as different variants of drugs in a category could be identified to suit individual optimisation more effectively are expected.

The research methodology and redaction of findings by industry and university pharmaceutical researchers demonstrates a statistically significant greater dependence on academic research publications than on patent databases. It is not suggested that patent databases are useless to the researcher. Indeed for the academic researcher they can provide a short cut. For example in the case of a description of a preparation the steps of the methodology will usually be placed in the patent claim in a nicely enumerated form, rather like a cooking recipe, that can be printed off and used in the laboratory. Whereas, in the academic literature the methodology will be presented in a form that may require a little work to

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<http://www.iprsonline.org/unctadictsd/bellagio/docs/Pugatch_Bellagio3.pdf> (Last Accessed: 1st July 2009)

produce a printed guide which can be used in the laboratory. Most often within the industrial pharmaceutical research environment the patent serves as a definition outside of which the objective product must lie, but academic publications form the backbone of starting theory and inspiration.[617]

However, as the system is presently set up, pharmaceutical research conducted for the purpose of producing a marketable innovation requires the purview of patent databases in addition to academic publications.

> 'Only if the invention is one that need never be revealed to the rest of the industry in the course of exploiting it does the patent provide a clear long-term gain in terms of publicity.'[618]

Patent law can permit greater assurance of monopoly than trade secrecy and saves the inventor the cost of keeping their invention secret. However, it can be expensive to obtain a patent[619] and to police it.[620] Depending on the properties of the invention and its technological context protecting a monopoly in an invention may be far more expensive through a patent, than through secrecy.

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[617] Discussions with industry and university pharmaceutical researchers: 2004, 2005, and 2006.

[618] Cornish, W., Intellectual Property: Patents, Copyright, and Allied Rights [Sweet and Maxwell, 4th Ed., 3rd Impession, 1999, London] 135

[619] Lemley, M. A. Rational Ignorance at the Patent Office. (2001) 95(4) *Northwestern University Law Review* 21-56

[620] Blanco White, T. A., *Patents for Inventions* (1974) 9-10

Patent data bases do not work effectively as knowledge transfer tools.

> "Historically, the information contained in patent databases has not been fully exploited, with estimates that up to 30 per cent of worldwide research and development projects are merely a duplication of existing technology."[621]

3.5.2. **Buying Access**

This is an indicia of the patent system's failure or inefficiency as a utilitarian construct. Since, theoretically, the cost of reproducing a non-rivalrous good, once that good has been discovered is zero, then the marginal cost of such a good is zero. In practical terms the cost of communicating knowledge of the discovery raises the cost. However in the case of the patent, not only is there a cost involved in the communication of the discovery, the formalities of its publication and in assertion of the owner's proprietorship, but there is also a 30 per cent further deadweight through duplication.[622]

Transfer of information might be considered a secondary function of the patent system with respect to the patent system's primary function of asserting property claims. However, in a society that considers itself

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Sainsbury Review. The Race to the Top: A Review of Government's Science and Innovation Policies. [HMSO October 2007] 6

[622] Let us label duplicated research and development project expenditure on existing technology W^P.

technologically progressive communication of existing technology is to research and development is both essential for a nations technological welfare as well as a nation's economic well being. Thus, even if the patent system was to be mistakenly considered to poses only a secondary function as setting the state of the art another forum, or training, to effectively communicate to research and development projects the state of existing technologies is required. If a replacement of the pharmaceutical patent can effectively provide a more effective forum for technology transfer, then the cost of creating an additional forum or providing the necessary training must be considered.[623]

As innovation involves the drawing out the concrete implications of new things it involves learning. The cost in both time and resources can be greatly reduced by the sharing of expertise. Global public goods can facilitate access knowledge and the transfer of technology and expertise. The Human Genome Project and other open and accessible public research projects are increasingly presenting more rapid accumulations of information than any private initiatives.

> "It is accepted that health research has been accelerated through immediate free access to the sequence of the human genome and other related genomic datasets. This success can be seen as part

[623] Let this additional cost or training be $W^{\prime P}$.

of a larger shift in public policy towards requiring research data to be openly accessible.[624]

Moreover, the full implications of an invention are not always immediately apparent.[625] Equipping a larger portion of society with the information statistically increases the likelihood that society may benefit from the discovery of other uses for the information.

3.6. Safety Concerns

"No product is 100 per cent safe, because all products have side effects. These may be very minor, but they may also be serious... Different people respond to medicines differently. Several factors can influence the chances of side effects. These include the prescribed dose, the condition being treated, the age and sex of the patient, and other treatments which the patient may be taking, including herbal / complementary medicines."[626]

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[624] Arzberger, P., Schroeder, P., Beaulieu, A., Bowker, G., *et al.* 'Science and government. An international framework to promote access to data' (2004) 303 *Science* 1777-1778

[625] Kingston, W., *The political economy of innovation* [Nijhoff Publishers, 1984, The Hague] 22

[626] MHRA, Medicines and Medical Devices Regulation: What You Need to Know (2008) 2. Available at: <http://www.mhra.gov.uk/home/groups/comms-ic/documents/websiteresources/con2031677.pdf> (Last Accessed: 1st July 2009)

3.6.1. **Profit Not Safety**

If the pharmaceutical patent system is really about protecting the investment in regulatory approval, then grant of approval is considered as the end point. It seems obvious once stated, that the purpose of regulatory approval is to ensure as far as is possible, balancing policy issues such as resource allocation, that the State is satisfied of the benefit the medicine conveys against the risks it poses. Thus, safety is, as it ought to be, the end point of the processes leading to regulatory approval. Thus, whether or not regulatory approval is obtained is immaterial to the end point, i.e. that the product is safe, even if not to the means of attaining it. However, this is not the case, as the patent is valid immaterially of its safety. Thus, it cannot be claimed that pharmaceutical patent system is really about protecting the investment in regulatory approval.[627] Lack of confidence in regulatory approval, as an indicator of safety, is statistically significantly exhibited amongst UK healthcare professionals. [628]

This is illustrated by the low UK confidence in new pharmaceutical products compared to Australia, Canada, France, Germany, Italy, Japan, the Netherlands, New Zealand, Spain, Sweden, Switzerland and the USA taken together.[629] UK spending on new medicines begins lower than in the other countries and remains lower throughout the five year period over

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[627] Nor does it seem to have ever been. See Blake, J. B. (ed.) *Safeguarding the Public: Historical Aspects of Medicinal Drug Control* [Johns Hopkins University Press, 1970, Baltimore] 112-122, 144-157

[628] PICTF, Competitiveness and Performance Indicators 2004, 10

[629] PICTF, Competitiveness and Performance Indicators 2004, 10

which data was assessed. Typically the newer a pharmaceutical product is then the lower its rate of uptake in the UK compared to the comparator countries. For example, in 2004, apart from Japan, at 16 per cent, UK medicines expenditure on products launched during the previous five years was the lowest at 17 per cent. In contrast medicines expenditure on products launched during the previous five years in the USA was 27 per cent. Moreover, 2004 median per capita use of new medicines, that is medicines in their first year after launch, in the UK was 17% of the group mean per capita use of medicines in their first year after launch in Australia, Canada, France, Germany, Italy, Japan, the Netherlands, New Zealand, Spain, Sweden, Switzerland and the US taken together.[630]

For new medicines in the UK, the rate of uptake relative to the US and other EU countries increases as a function of time form the medicines launch. However, after three years the UK median rate of uptake of new pharmaceuticals is only 39% of the mean international levels. Five years from market entry of the new medicine the UK mean uptake rises to only 54%.[631] The cautious uptake of new medicines in the UK is not indiscriminate. A minority of medicines are used above the group mean for Australia, Canada, France, Germany, Italy, Japan, the Netherlands, New Zealand, Spain, Sweden, Switzerland and the US.[632]

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[630] PICTF, Competitiveness and Performance Indicators 2004, 10

[631] PICTF, Competitiveness and Performance Indicators 2004, 10

[632] PICTF, Competitiveness and Performance Indicators 2004, 10

Lack of confidence in the safety of new medicines granted regulatory approval is reflected outside of trends in the uptake of new pharmaceuticals. Increasingly pharmaceutical companies are accused by patient groups and healthcare practitioners' representative bodies of hiding important contra-indications and data sensitive to the validity of safety information. Disclosure of negative information regarding a medicine's complete contra indications, and effectiveness is essential to achieving the most beneficial employment of those medicines and ought to publicly available.[633]

In most countries including the UK and USA, pharmaceutical companies are able to withhold unfavourable studies and trial results from the public. Surprisingly, this is the case even if a medicine is ineffective against the targeted condition. Where pharmaceuticals are inspected by regulatory authorities, providing an indication to national drug purchase schemes of a drug's cost benefit, this situation is less likely to occur unless the submitted data was inaccurate or incomplete. However, where a drug gains approval for a particular condition, but is then distributed "off-label" to treat another condition then there is a possibility that the drug may be ineffective and possibly have detrimental health ramifications.

[633] The Food and Drug Administration Modernization Act 1997 (USA), that made promotion of off-label uses to physicians legal, provides translation of the ethical ought into a should in §401.

3.6.2. **Whole Truth**

Pharmaceutical companies have often promoted pharmaceuticals to physicians for off-label conditions, where the pharmaceutical patent owner's tests revealed that the drug did not function statistically significantly better than the placebo in treating the proposed off-label condition. Recognition of this problem by physicians, whom are often at the forefront of legal reprisals for ineffective off-label treatments, and the lethargic response of the legislator has lead to some leading medical journals, including the New England Journal of Medicine[634] and the Journal of the American Medical Association,[635] refusing to publish the results of clinical trials, unless those clinical trials were registered and disclosed prior to the study taking place.

In response the Pharmaceutical Research and Manufacturers of America (PhRMA) publicised a new clinical database where pharmaceutical trials could be registered and their data recorded. It argued that the journal's

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[634] See Laine, C., Horton, R., DeAngelis, C., Drazen, J. M., Frizelle, F. A., Godlee F., *et al.* 'Clinical Trial Registration – Looking Back and Moving Ahead' (2007) 356 (26) N Engl J Med 2734-2736; De Angelis, C., Drazen, J. M., Frizelle, F. A., Haug, C., Hoey, J., Horton, R., *et al.* 'Is This Clinical Trial Fully Registered?' (2005) 352 (23) N Engl J Med 2436-2438; De Angelis, C., Drazen, J. M., Frizelle, F. A., Haug, C., Hoey, J., Horton, R., *et al.* 'Clinical Trial Registration: A Statement from the International Committee of Medical Journal Editors' (2004) 351 (12) N Engl J Med 1250-1251

[635] Current *Journal of the American Medical Association* Trial Registration policy is available at: <http://jama.ama-assn.org/misc/ifora.dtl#TrialRegistration> (Last Accessed: 1st July 2009)

stance was unnecessary as pharmaceutical companies were already voluntarily disclosing their study results. [636]

PhRMA's statement of confidence was almost simultaneously undermined as New York Attorney General Eliot Spitzer brought an action against GlaxoSmithKline plc for "repeated and persistent fraud by concealing and failing to disclose to physicians certain information about Paxil [Seroxat in the UK] a drug used to treat depression." The action was brought following the leak of a confidential GlaxoSmithKline plc memo to the press.[637] The memo documented a 1998 clinical trial that concluded Seroxat/Paxil "failed to demonstrate any separation of Seroxat/Paxil from the placebo,"[638] that is Seroxat/Paxil was only as effective as the placebo. Independent trials revealed that a statistically significant population of adolescents taking serotonin reuptake inhibitors approved by the FDA suffered induced adverse effects,[639] including a two-to three-fold increased

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[636] New bill targets drug data disclosure: Drugmakers criticized for only publicizing favorable study results. September 2004. Available from: <http://www.marketwatch.com/News/Story/Story.aspx?guid=%7B80E3167D-8965-4AC9-9FE4-1EA8D7B05EF2%7D> (Last Accessed: 1st July 2009)

[637] McGoey, L., and Jackson, E., 'Seroxat and the suppression of clinical trial data: regulatory failure and the uses of legal ambiguity' (2009) 35 (2) J. Med. Ethics 107-112; Kondro, W., 'Drug company experts advised staff to withhold data about SSRI use in children (2004) 170 (5) CMAJ 783

[638] The GlaxoSmithKline plc memo is viewable online at: <http://www.ahrp.org/risks/SSRI0204/GSKpaxil/pg1.html> (Last Accessed: 1st July 2009)

[639] Preda, A., Maclein, R., Mazure, C., Bowers, M. 'Anti-depressant associated mania and psychosis resulting in psychiatric admissions' (2001) 62 *Journal of Clinical Psychiatry* 30-33; Jain, J. 'Fluoxetine in child and adolescents with mood disorders: a chart review of efficacy and adverse reactions' (1992) 2 *Journal of Child & Adolescent Psychopharmacology* 259-265; Riddle, M. A., King, R. A., Hardin, M. T., Scahill, L., Ort,

risk of suicidal behaviour.[640] Worldwide Seroxat/Paxil sales reached just under $4.97 billion USD in revenue for GlaxoSmithKline plc and its subsidiaries in 2003.[641]

Despite the positive initiative by the New England Journal of Medicine and the Journal of the American Medical Association, which was followed in 2005 by a ruling of the International Committee of Medical Journal Editors requiring trials to be registered prior to participant enrolement as a precondition for publication in member journals, adequate pre-registration has not been particularly effective.

In 2009 a particularly damning report on the effectiveness of pre-trial registration was published.[642] It found that out of a sample of 323 trials, only 147 (45.5 per cent) were adequately registered. That is they were registered before the end of the trial, with a clear specification of the objective. However of the 147 adequately registered trials 46 (31 per cent)

S.I., Chappell, P., *et al.* 'Behavioral side effects of fluoxetine in children and adolescents' (1991) 1 *Journal of Child & Adolescent Psychopharmacology* 193-198

[640] Breggin PR. 'Suicidality, violence and mania caused by selective serotonin reuptake inhibitors (SSRIs): A review and analysis.' (2003/2004) 16 *International Journal of Risk & Safety in Medicine* 31-49; King, R. A., Riddle, M. A., Chappell, P. B., Hardin, M. T., Anderson, G. M., Lombroso, P., Scahill, L., 'Emergence of self-destructive phenomena in children and adolescents during fluoxetine treatment' 1991 30 *Journal of American Academy of Child & Adolescent Psychiatry* 179-186

[641] Kondro, W., 'Drug company experts advised staff to withhold data about SSRI use in children (2004) 170 (5) CMAJ 783; Pharmaceutical patents - Paxil sales soar despite dispute CHEM IND-LONDON (5): 6-6 MAR 3 2003

[642] Mathieu, S., Boutron, I., Moher, D., Altman, D. G., *et al.* 'Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials.' (2009) 302(9) JAMA 977-984

showed discrepancies between the outcomes registered and the outcomes that were published. Moreover, the significance of the discrepancies could only be assessed in 23 of the 46, but within those 23 discrepancy vitiated adequately registered trials 19 (82.6 per cent) favoured statistically significant results. That is they presented an exaggerated report of success from the trials.[643] As a point of major concern this suggests that less than a third (105 out of 323) of peer reviewed clinical trial findings published in medical journals that require pre-trial registration actually presented adequate pre-trial reporting. As Mathieu *et al.* only reported with respect to the registration and subsequent reporting and did not conduct a detailed analysis of experimental modelling for each trial. Therefore, as deliberate falsification may have been undertaking elsewhere, fewer of the trial reports may be dependable.

Furthermore, the effectiveness of trial pre-registration is greatly undermined by the fact that 89 published reports (27.6 per cent) had no trial registration whatsoever and 45 trials (13.9 per cent) were registered following completion of a study. All of which according to journal publication requirements of pre-trial registration should have been refused publication. A further 39 (12 per cent) were registered but lacked a description of the objective or provided an ambiguous or indecipherable description of the objective. 3 (0.9 per cent) of the sample population were

[643] Mathieu, S., Boutron, I., Moher, D., Altman, D. G., *et al.* 'Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials.' (2009) 302(9) JAMA 977-984. At 977

both registered after completion of the trial and had an unclear description of the objective. [644]

The safety issues concerning a medicine are not as straight forward as one might initially imagine. For example demonstrating drug safety in high-risk populations is not necessarily sufficient to presume safety in apparently less-risky populations.[645] Thus, the presentation of clinical results can be difficult to interpret for regulatory authorities whom are presented with a summary of the information prepared by a self-interested party and required to process it within tight time constraints.

Moreover the accuracy of the data submitted to regulatory authorities and to the public is sometimes deliberately misleading. For example, a study published in March 2000 indicated that patients taking Vioxx were five times more likely to suffer heart attacks than those using the generic medicine Naproxen. Merck's response was to claim that the difference resulted from cardioprotective properties of naproxen, rather than a defect in Vioxx. However, a Merck memo dated November 21, 1996, depicts a strategic dilemma faced by Merck.[646] The company wanted to demonstrate through clinical trials that Vioxx was less likely to cause

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[644] See Mathieu, S., Boutron, I., Moher, D., Altman, D. G., *et al.* 'Comparison of Registered and Published Primary Outcomes in Randomized Controlled Trials.' (2009) 302(9) JAMA 977-984

[645] See Chan, F. K.L., J. Y.L. Ching, L. C.T. Hung, V. W.S. Wong, V. K.S. Leung, N. N.S. Kung, *et al.* Clopidogrel versus Aspirin and Esomeprazole to Prevent Recurrent Ulcer Bleeding. (2005) N Engl J Med 352: 238-244.

[646] Mathews, A. W., and Martinez, B. 'E-mails suggest Merck knew Vioxx's dangers at early stage' (November 1, 2004) *Wall Street Journal* (Eastern edition) A1

gastrointestinal problems than older painkillers. However illustrating the difference would require Vioxx patients not to take aspirin. Aspirin reduces the risk of cardiac events, but can lead to gastrointestinal problems, such as ulceration. Thus, the memo dutifully warned that the trial would show that "there is a substantial chance that significantly higher rates" of cardiovascular problems would be exhibited by the Vioxx group.[647] That the warning in the memo was not an oracular mistake is reinforced by a Merck internal e-mail of February 25, 1997, by Briggs Morrison informing senior research staff that if patients in the Vioxx group did not also receive aspirin then "you will get more thrombotic events and kill [the] drug."[648] In an e-mail Alise Reicin, soon to become Merck vice president for clinical research, proposed that people with high cardiovascular risk be excluded from the Vioxx population for the study so that the difference in the rate of cardiovascular problems between the Vioxx sample group and the other test groups would not be evident.[649]

There is a statistically significant increase in the positive outcomes of clinical trials, when the trials are conducted by the corporation owning the rights to the pharmaceutical being trialed.[650] Independent research

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[647] Mathews, A. W., and Martinez, B. 'E-mails suggest Merck knew Vioxx's dangers at early stage' (November 1, 2004) *Wall Street Journal* (Eastern edition) A1

[648] Mathews, A. W., and Martinez, B. 'E-mails suggest Merck knew Vioxx's dangers at early stage' (November 1, 2004) *Wall Street Journal* (Eastern edition) A1

[649] Mathews, A. W., and Martinez, B. 'E-mails suggest Merck knew Vioxx's dangers at early stage' (November 1, 2004) *Wall Street Journal* (Eastern edition) A1

[650] For example see Mack, A., Examination of the evidence for off-label use of gabapentin (2003) 9(6) *Journal of Managed Care Pharmacy* 559–568; and Pande, A. C.; Crockatt, J.

findings frequently reveal a very different set of safety findings than those achieved in-house. Muraglitazar is a dual Peroxisome proliferator–activated receptor agonist that was approved, based on the drug manufacturer's trial data,[651] by the FDA advisory committee on 9 September 2005 for use in controlling blood glucose levels in patients with type 2 diabetes. A later independent evaluation of Muraglitazar lead to the conclusion,

> "Compared with placebo..., muraglitazar was associated with an excess incidence of the composite end point of death, major adverse cardiovascular events (MI, stroke, TIA), and CHF. This agent should not be approved to treat diabetes... until safety is documented in a dedicated cardiovascular events trial."[652]

The patent, or rather the notion of a monopoly ownership for pharmaceuticals, is so at odds with the reason for regulatory authority that whilst the patent exists as a determinant of long term above normal profit

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G., Janney, C. A., Werth, J. L., Tsaroucha, G., Gabapentin in bipolar disorder: a placebo-controlled trial of adjunctive therapy (2000) 2 (3 Pt 2) Bipolar Disord. 249–255

[651] On 23 December 2004, Bristol-Myers Squibb announced that it had submitted a New Drug Application to the FDA for muraglitazar, as an agent under development for the treatment of patients with type 2 diabetes. Within a New Drug Application the investigation of the compound as administered to humans and evaluated for safety and effectiveness in treating, preventing, or diagnosing a specific disease or condition comprises the single most important factor in the approval or disapproval of a new drug. See <http://www.fda.gov/cder/Regulatory/applications/> (Last Accessed: 1st July 2009)

[652] Nissen, S. E., K. Wolski, E. J. Topol. Effect of Muraglitazar on Death and Major Adverse Cardiovascular Events in Patients With Type 2 Diabetes Mellitus (2005) JAMA 294: 2581-2586.

and regulatory authorities are dependent on proprietary data undisclosed to the public the opportunity for economic benefit will trump safety considerations. Thus, rather than human beings being the end-in-itself of the pharmaceutical patent and regulatory systems the human being is merely a component on route to the end-in-itself which is above normal profit. This development is hardly surprising considering that the pharmaceutical industry is comprised of companies and the end-in-itself for companies is profit.

3.6.3. **No Lying**

Discoveries that pharmaceutical companies have tried to conceal their research findings are becoming more frequent[653] and studies produced by pharmaceutical companies present data that is biased towards the safety and effectiveness of their medicines.[654] Moreover, because of the

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[653] Okie, S. 'Missing Data On Celebrex' (August 5, 2001) *Washington Post* A11; King, R. T., 'How a Drug Firm Paid For University Study, Then Undermined It' (April 25, 1996) Wall Street Journal A1

[654] Amir, E., Seruga, B., Freedman, O., Tannock, I.. 'Lapatinib plus Paclitaxel as first-line Therapy for patients with human epidermal growth factor receptor 2-positive metastatic breast cancer: Inappropriate conclusions from a company-sponsored study?' (2009) 27 JCO 1919; Smith, R., 'Conflicts of interest: how money clouds objectivity' (2006) 99 JRSM 292-297; Bodenhiemer, T., 'Conflict of Interest In Clinical Drug Trials: A Risk Factor For Scientific Research' (August 15, 2000) Paper presented at the NIH Conference on Conflicts of Interest in Scientific Research. Available at: <http://www.hhs.gov/ohrp/coi/bodenheimer.htm> (Last Accessed: 1st July 2009); Friedberg, M., Saffran, B., Stinson, T. J., Nelson, W., *et al.* 'Evaluation of Conflict of interest in Economic Analyses of New Drugs Used in Oncology' (1999) 282 *Journal of the American Medical Association* 1453-1457; Stelfox, H., Chua, G., O'Rourke, K., Detsky, A., 'Conflict of interest in the debate over calcium-channel antagonists' (1998) 338 N Engl J Med 101-106; see Baker, D., and Chatani, N., Promoting Good Ideas on Drugs: Are Patents the Best Way? The Relative Efficiency of Patent and Public Support for Bio-

availability of financial rewards or research sponsorship for those whom produce favourable results some researchers may take falsification into their own hands.[655]

There are worse case scenarios whose propensity to reoccur remains perversely unaddressed and will remain so until the patent and regulatory system is rebalanced so that the human being, or a particular property thereof, i.e. human health, becomes the end-in-itself.

The Vioxx example illustrates how unsatisfactory it is for the agency certifying a pharmaceutical to be safe for the treatment of human beings to rely on data provided by a pharmaceutical applicant and then providing overview supervision of that company's monitoring of the approved drug. Pressure from physicians and independent researchers was put on the FDA for its perceived failure in monitoring the blockbuster painkiller Vioxx after serious side effects had been noted. In 2001 after independent studies had revealed that Vioxx had a statistically significant increase in myocardial infarctions compared to older painkillers the FDA was urged to mandate further clinical safety testing.[656] However, it did not do so.[657]

Medical Research (2002) CEPR Briefing Paper [Centre for Economic and Policy Research, Washington] 10

[655] Katz, D., Mansfield, P., Goodman, R., Tiefer, L., *et al.*, 'Psychological Aspects of Gifts From Drug Companies' (2003) 290(18) JAMA 2404-2405; Eichenwald, K., and Kolata, G., 'A Doctor's Drug Studies Turn Into Fraud' (May 17, 1999) New York Times A1

[656] Topol, E. J., 'Failing the public health - rofecoxib, Merck, and the FDA' (2004) 351 N Engl J Med 1707–09

[657] Horton, R., 'Vioxx, the implosion of Merck, and aftershocks at the FDA' (2004) The Lancet 1-2, at 1

Unfortunately the failure of post approval FDA monitoring is not an anomaly. Unless there are changes to the present system then institutionally a similar crisis is likely to occur again. Dr Graham, the FDA Safety Officer as a result of the crisis advised that,

> "...The FDA, as currently configured, is incapable of protecting America against another Vioxx." [658]

3.6.4. **We Have Change**

In black letter terms, the principal problems in the USA and the UK are the same for regulatory authorities working alongside the pharmaceutical patent regime. However, there are fewer regulatory instruments to muddy the picture in the USA, than there are in the UK, so to begin with we shall consider the USA. The principal problems are two fold: Firstly, that the Prescription Drug User Fee Act (PDUFA)[659] instituting the arrangement where pharmaceutical companies pay the FDA to review their pharmaceutical products made no provision for funding for the FDA to continue to review the pharmaceutical product once approval for it to enter the market is granted. During the second reenactment of the PDUFA through the Public Health Security and Bioterrorism Preparedness and Response Act in 2002, amendments were made to permit some funding of

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[658] Online NewsHour: Drug Safety. Available at: <http://www.pbs.org/newshour/bb/fedagencies/july-dec04/fda_11-23.html> (Last Accessed: 1st July 2009)

[659] The FDA maintains an informative website on the PDUFA, currently in its fourth re-enactment. Available at: <http://www.fda.gov/oc/pdufa/> (Last Accessed: 1st July 2009)

post market-approval appraisal, but the ability of the FDA to monitor all drugs adequately post market-approval cannot be realised on its present budget. Secondly, there is considerable pressure when an apparently important breakthrough product reaches the approval stage and appears to behave positively for it to become available. As most drugs are promoted as significant or breakthrough then the rapidity of review has been formally constrained to speed. For the FDA to retain the ability to continue collecting application fees from pharmaceutical applicants on submission of New Drug Applications (NDA), the FDA is required to meet performance benchmarks. The primary benchmark is the speed by which the components of the NDA review process are carried out. Especially where a therapeutic breakthrough has purportedly occurred then there is pressure on the agency to approve the medicine as quickly as possible so that patients can benefit from it. Since implementation of the PDUFA the median approval time for non-priority new drugs fell from 27 months to 14 months.[660]

In the UK, a good example of the pressure that drug safety regulatory bodies undergo is provided post Herceptin. The results are clear: The MHRA regulatory approval system was adapted, resulting in a fast track scheme. Whilst MHRA does not carry out its own trials and relies on the data from others studies, including those by the proprietor pharmaceutical company, MHRA does posses funding for ongoing review of

[660] GAO-02-958 Effect of User Fees on Drug Approval Times, Withdrawals, and Other Agency Activities. Available at: <http://www.gao.gov/new.items/d02958.pdf> (Last Accessed: 1st July 2009)

pharmaceutical safety. However, as with the FDA the MHRA budget is inadequate to monitor all pharmaceuticals on the market and its dependence on others' studies and feedback mean that its interventions are not as expedient as desirable.

Another problem that affects the FDA, and might be shared by other regulatory authorities is the concealment of information deemed commercially sensitive, yet which may present important indications of the safety of a medicine. It has been suggested that the FDA routinely conceals information it considers commercially sensitive.[661] For example the FDA suppressed essential information concerning Cox-2 inhibitors.[662] From one of its NDA files the FDA removed twenty-eight pages of data about Cox-2 inhibitors.

Moreover, Peter Juni, a clinical epidemiologist at the University of Berne and one of investigators responsible for revealing to the public the elevated cardiac infarction risk of Cox-2 inhibitors, claimed that his work had been obstructed by the FDA. His team had found "that many pages and paragraphs had been deleted because they contained trade secret

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[661] Dobson, R., and Lenzer, J., 'US regulator suppresses vital data on prescription drugs on sale in Britain' (June 12, 2005) *The Independent*. Available at: <http://www.independent.co.uk/life-style/health-and-families/health-news/article493903.ece> (Last Accessed: 1st July 2009)

[662] Editorial. 'Vioxx: an unequal partnership between safety and efficacy' (2004) 364 Lancet 1287–1288

and/or confidential information that is not disclosable."[663] David Graham, associate director of the Office of Drug Safety within the FDA, is reported to have had his results, indicating that patients taking Vioxx suffered five times as many heart attacks as patients taking the generic painkiller naproxen did, suppressed by his superiors in the FDA. Furthermore Graham's supervisors are reported to have refused him permission to present his findings and tried to prevent him from publishing them in the Lancet.[664]

Richard Horton, editor of the Lancet, summarised this problem "Too often the FDA saw and continues to see the pharmaceutical industry as its customers, a vital source of funding for its activities, and not as a sector of society in need of strong regulation... with Vioxx, Merck and the FDA acted out of ruthless, short-sighted, and irresponsible self-interest. "[665]

3.6.5. **Grey Markets**

Unsurprisingly the existence of large patent mark-ups endow pharmaceutical manufacturers with the potential to achieve high profits,

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[663] Dobson, R., and Lenzer, J., 'US regulator suppresses vital data on prescription drugs on sale in Britain' (June 12, 2005) *The Independent*. Available at: <http://www.independent.co.uk/life-style/health-and-families/health-news/article493903.ece> (Last Accessed: 1st July 2009)

[664] Dobson, R., and Lenzer, J., 'US regulator suppresses vital data on prescription drugs on sale in Britain' (June 12, 2005) *The Independent*. Available at: <http://www.independent.co.uk/life-style/health-and-families/health-news/article493903.ece> (Last Accessed: 1st July 2009)

[665] Horton, R., 'Vioxx, the implosion of Merck, and aftershocks at the FDA' (2004) The Lancet 1-2

and thereby create a strong incentive for the emergence of grey markets and counterfeit pharmaceuticals.[666] The Center for Medicines in the Public Interest, New York, predicts that global sales of fake medications will by 2010 be worth an estimated $75 billion.[667] As counterfeit drugs and pharmaceuticals sold on a grey market may not meet safety standards, nor present an honest account of their contents or dosages, they are another safety issue that needs to be addressed. The World Health Organization (WHO) estimates that 5-8% of drugs worldwide are counterfeit.[668]

The WHO's observation of the types of pharmaceutical counterfeits available in wealthier and poorer countries is supportive of the profit motivating factor for pharmaceutical counterfeiting. According to the WHO the most frequently counterfeited drugs in poorer developing countries are pharmaceuticals used to treat life-threatening conditions such as malaria, tuberculosis, and AIDS, whilst in wealthier countries counterfeits tend to be

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[666][666] Counterfeit drugs are usually pharmaceuticals 'sold under a product name without authorization, where the identity of the source of the drug is knowingly and intentionally mislabelled in a way that suggests that it is the authentic approved product. This definition can apply to brand name, generic products, or the bulk ingredients used to make the product.' Lutter, R. W., FDA (USA) Congressional Testimony on Counterfeit Medicines, November 1, 2005. Available at: <http://www.fda.gov/NewsEvents/Testimony/ucm112670.htm>

[667] Schenker J. L., "MPedigree's Rx for Counterfeit Drugs," Business Week, December 3, 2008. Available at: <http://www.businessweek.com/globalbiz/content/dec2008/gb2008123_027994.htm>

[668] Capell, K. & Timmons, S. 'What's in that Pill?' Business Week, June 18, 2001. Available at: <http://www.businessweek.com/magazine/content/01_25/b3737076.htm>

new and expensive lifestyle medicines; such as hormones, steroids, and antihistamines.[669]

Many mechanisms by which counterfeit pharmaceuticals can be excluded from consumers have been put forward and these range to recommendations that consumers buy only from authorised pharmacies and stockists, to the implementation of a unique coding that can be checked by the consumer. One such code system is mPedigree,[670] where the pharmaceutical manufacturer packages medicines embossed with a unique code recorded in mPedigree's database. Consumers purchasing the drug are able to scratch off a panel on the product's packaging to reveal the code. The consumer can then text this code from their telephone to the mPedigree's servers and after a short delay receive a text response indicating whether the product is authentic. Whilst such methods may be highly useful in countries with developed economies, stable infrastructures for drug distribution, and a viable text messaging service, for the majority of the world's population they are technologically and uneconomically viable.

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[669] Voice of America News, 'WHO Battles Counterfeit Drugs in Asia.' November 12, 2003. Available at: <http://www.voanews.com/english/archive/2003-11/a-2003-11-12-43-WHO.cfm?moddate=2003-11-12>

[670] Schenker J. L., "MPedigree's Rx for Counterfeit Drugs," Business Week, December 3, 2008. Available at: <http://www.businessweek.com/globalbiz/content/dec2008/gb2008123_027994.htm> (Last Accessed: 1st July 2009)

3.7. Availability of Pharmaceuticals

One of the main miscomprehensions about the accessibility of pharmaceuticals is that access to pharmaceuticals is a poor person's problem. This is only partially true. As we have indicated the rate of pharmaceutical innovation is likely retarded. Therefore medicines, which in the absence of the present system would be available, are not. Thus, such drugs are unavailable regardless of an individual's wealth.

Moreover, there are many drugs approved as safe and effective, on the basis of proprietary data, that are subsequently, through the misfortune of users, found to have no therapeutic utility to the target group or to exacerbate symptoms sometimes leading to mortality. As a result uptake, in new medicines does always not occur the moment that a pharmaceutical becomes available on the market. In some countries, For example the UK, lack of confidence in the safety of new products causes a statistically significant lag in uptake, with respect to other European countries and the USA.[671]

Use of medicines by hospitals and physicians can frequently result in the most clinically effective medicine not being chosen, but rather one that will allow the institution to stretch its budget further. This is a point of controversy in many areas of medical practice. In particular the post-operative treatment of orthopaedic replacement patients with warfarin,

[671] PICTF, Competitiveness and Performance Indicators 2004, 10

rather than heparin, or warfarin/heparin.[672] It is estimated that this cheaper alternative might be the cause of 20,000 deaths annually in the UK. However, it is good to note that fifteen years on and approximately 300,000 deaths later that the patent has expired on Heparin I and Heparin I is less expensive and more readily used. There are currently no figures available as to the number of deaths that would be preventable through the use of the newer forms of Heparin that are still under patent. Other jurisdictions experience the same problems.

> "In the United States, in many healthcare systems salary bonuses are offered to those who prescribe cheaply, and salary 'withholds' await those who prescribe too expensively. This contributes to the patients' uneasiness that their interests and ours may at times be incompatible."[673]

Information is a key factor in the choice of which medicines to utilise as complement therapy, as treatment, or as a prophylactic. For even a medical practitioner to keep up to date on the latest drugs and new discoveries about those in circulation is a daunting task. For a non-specialist, finding and assimilating information relevant to their condition and then insisting that their doctors follow that course is unrealistic. Wealth may provide more treatment possibilities, but only if the relevant

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[672] O'Brien, B. J., Anderson, D. R., Goeree, R., 'Cost-effectiveness of enoxaparin versus warfarin prophylaxis against deep-vein thrombosis after total hip replacement' (1994) 150(7) CMAJ 1083-1090

[673] Avorn, J. Balancing the cost and value of medications: the clinician's dilemma. (2002) 20 Suppl. 3 *Pharmacoeconomics* 68

doctors and institutions have the required expertise and choose to make other treatment options available.

Admittedly there has traditionally been a great difference between funding for research on diseases which affect the wealthier nations, than those affecting poorer populaces. But there are diseases that significantly effect all populations that would benefit from increased coordination in research and resource sharing. For example cancer and Alzheimer's.

3.8. Accessibility of Pharmaceuticals

The two principle access barriers to pharmaceuticals already granted market approval are: the price of the medicine and the supply.

Supply is simply the amount of product made available for sale. Artificial scarcity plays a role in ensuring high drug prices. The artificial scarcity that permits prices to remain high usually occurs through the manufacturer producing only enough of the pharmaceutical to meet the expected demand curve for the price that they have decided on. However, the artificial scarcity is sometimes maintained after competitor products should have entered the market. There is a trend for some generic introductions to delay entry to a market, thereby leaving supply to the patented originator for a longer period. This occurs through a "pay-for-delay settlement" agreement between the generic manufacturer and the

manufacturer of the patented originator medicine. A payment from the manufacturer of the patented originator medicine creates artificial scarcity in the competitive generic product thereby permitting the out-of-patent originator medicine to continue to sell for high prices.

In the USA the Federal Trade Commission has been less tolerant of anticompetitive practices than competition authorities in the European Union. In 2003, a decision of the Sixth Circuit Court of Appeals held that payments by the patent owner of an originator medicine a to a generic firm that had filed a patent challenge were unlawful as an anticompetitive practice.

> "...it is one thing to take advantage of a monopoly that naturally arises from a patent, but another thing altogether to bolster the patent's effectiveness in inhibiting competitors by paying the only potential competitor $40 million [USD] per year to stay out of the market."[674]

In 2005 the Federal Trade Commission brought an action against Schering-Plough Corporation [675] alleging that agreements to eliminate potential competition and to share the resulting profits constitutes a violation of antitrust law and should be prohibited under the antitrust laws. Both the Second and Eleventh Circuit appellate courts upheld the legality

[674] In re Cardizem CD Antitrust Litig., 332 F.3d 896, 908 (6th Cir. 2003).

[675] Schering-Plough Corp. v. FTC, 402 F.3d 1056 (11th Cir. 2005), cert. denied, 548 U.S. 919 (2006)

of a pay-for-delay agreements.[676] Moreover, the Eleventh Circuit both rejected the Sixth Circuit's approach to pay-for-delay agreements[677] and refused to consider if there was an per se antitrust violation, or illegality by the rule of reason.[678]

In 2008, another pay-for-delay agreement case the Federal Circuit Court of Appeals further alienated the decision of the Sixth Circuit by holding that

"...absent fraud... or sham litigation the mere presence of a patent entitles the patent holder to purchase protection from competition until patent expiration."[679]

The decisions effectively grant impunity to patent holders for what would otherwise be anticompetitive practices for the duration of their patent term. Whilst this notion is limitative to the time a patent holder may contract to exclude competition from a market, it does permit enormous market distortion and a delay to reductions in pharmaceutical prices that would result from competition. Moreover, through clever patenting and enclosure it is possible to maintain patents on a pharmaceutical product for long periods. Thus, it may be possible for companies to split the proceeds of a monopoly for several decades. Even then when there were no remaining tweaks to be made to the invention in order to engender evergreening, the

[676] Schering-Plough Corp. v. FTC, 402 F.3d 1056 (11th Cir. 2005), 10 cert. denied, 548 U.S. 919 (2006); In re Tamoxifen Citrate Antitrust Litigation, 429 F.3d 370 (2d Cir. 2005)

[677] Schering-Plough Corp. v. FTC, 402 F.3d at 1056, 1065 (11th Cir. 2005)

[678] Schering-Plough Corp. v. FTC, 402 F.3d at 1065 (11th Cir. 2005)

[679] In re Ciprofloxacin Hydrochloride Antitrust Litig., 544 F.3d 1323 (Fed. Cir. 2008)

manufacturer might be able to simply cease to manufacture the out-of-patent pharmaceutical and then monopolise the market with another. Generic manufacturers providing that they benefit more from the monopolists pay-out and that φ^C is a sufficient motivation for their behaviour will be content to be paid to be a spectator.

Not all scarcity in supply is artificial. There may be particular reasons why the quantity of a medicine that can be produced is much lower than demand, or even the manufacturer's projected optimum profit. This would be the case where the active ingredient cannot yet be synthesised and thus, needs to be extracted from organic sources occurring in very limited supply.[680] Of course the publicised limitation might also be a fiction designed to maintain high prices even in the face of pandemic, we shall have to await the memo.

Other than a shortage in supply, the problem of artificial scarcity is price inflation. As a result of inflated prices populations that might have

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[680] According to Roche this is the case with Tamiflu (oseltamivir phosphate) that is manufactured from shikimic acid, which cannot be synthesised economically and was only effectively isolated from Chinese star anise. See GRAIN, 'Fowl play: The poultry industry's central role in the bird flu crisis' Briefing Document (2006) at 15. Available at: <http://www.grain.org/briefings_files/birdflu2006-en.pdf> (Last Accessed: 1st July 2009) Shikimic acid is now commercially extractable from modified E. Coli. See Johansson, L., Lindskog, A., Silfversparre, G., Cimander, C., Nielsen, K., *et al.*, 'Shikimic acid production by a modified strain of E. coli (W3110.shik1) under phosphate-limited and carbon-limited conditions' (2005) 92(5) *Biotechnology and Bioengineering* 541-552; Bradley, D., 'Star role for bacteria in controlling flu pandemic?' (2005) 4 *Nature Reviews Drug Discovery* 945–946; Krämer, M., Bongaertsa, J., Bovenberga, R., Kremera, S., *et al.*, 'Metabolic engineering for microbial production of shikimic acid' (2003) 5(4) *Metabolic Engineering* 277-283

otherwise been able to afford medicines are denied access to them. There are some medicines that are so necessary for human welfare that, as a minimum, all societies ought to have access to them.

3.8.1. **Essential Medicines**

> "Essential medicines[681] are those that satisfy the priority health care needs of the population. They are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford."[682]

The Essential Medicines List, in addition to providing the minimum medicine needs for a basic health care system, only lists the most efficacious, safe and cost-effective pharmaceuticals for priority conditions. Moreover the basis of identification of priority conditions also takes account of the potential for cost-effective treatment. Thus, extremely few patented drugs feature on the WHO Essential Medicines List. Out of the three-hundred and twelve listed medicines of the 14th edition list (2005)

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[681] A list of essential medicines is produced by the WHO annually, though each Nation is in principle responsible for compiling its own list. WHO Essential Medicines list available at: <http://www.who.int/medicines/services/essmedicines_def/en/> (Last Accessed: 1st July 2009)

[682] United Nations - Millennium Development Goal 8 Task Force Report 2008, 'Delivering on the Global Partnership for Achieving the Millennium Development Goals.' At: 36. Available at: <http://www.who.int/medicines/mdg/MDG8EnglishWeb.pdf> (Last Accessed: 1st July 2009)

there are only fourteen currently under patent.[683] Eleven of the fourteen are antiretroviral medicines designated for the treatment of AIDS.[684] Whilst the remaining three patented medicines are for other diseases.[685]

That so few patented drugs appear on the Essential Medicines List is not an indication that satisfactory therapies are mainly available from amongst medicines that are out of patent, but the price of patent medicines excludes almost all patented drugs from the list for two reasons. Firstly, the potential for cost-effective treatment means that unless a cheaper therapy is available then the condition is not designated as a priority condition, thus no medicines to treat that condition will be listed at all. Secondly, for designated priority conditions only the most efficacious, safe and cost-effective pharmaceuticals are listed. The consequence of this is that although the list provides extremely useful advice to governments and health agencies based on pricing and efficiency it does not provide an ideal list based on drug effectiveness or all conditions. Thus, the core selection of the 14th edition Essential Medicines List contains no anti-cancer drugs at all. Which makes the list very incomplete from an

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[683] Abacavir Antiretroviral, Didanosine Antiretroviral, Lamivudine Antiretroviral, Stavudine Antiretroviral, Efavirenz Antiretroviral, Nevirapine Antiretroviral, Indinavir Antiretroviral, Ritonavir Antiretroviral, Lopinavir and ritonavir Antiretroviral, Nelfinavir Antiretroviral, Saquinavir Antiretroviral, Proguanil Malaria prophylaxis, Levofloxin, Eflornithine Antiprotozoal. See United States FDA Orange Book (online). Available at: <http://www.fda.gov/cder/ob/> (Last Accessed: 1st July 2009)

[684] Abacavir Antiretroviral, Didanosine Antiretroviral, Lamivudine Antiretroviral, Stavudine Antiretroviral, Efavirenz Antiretroviral, Nevirapine Antiretroviral, Indinavir Antiretroviral, Ritonavir Antiretroviral, Lopinavir and ritonavir Antiretroviral, Nelfinavir Antiretroviral, Saquinavir Antiretroviral.

[685] Proguanil Malaria prophylaxis, Levofloxin, Eflornithine Antiprotozoal.

American perspective as cancer is the second highest cause of mortality in the USA after heart disease.[686] Moreover between 1980 and 2000, life expectancy for cancer patients across select cancer types has increased by 2.9-3.0 years (5.9–6.0 years for breast cancer), with 83 per cent of the increases due to new therapies, including new pharmaceuticals.[687] Another study indicates that since 1975, the improvements in the longevity of cancer patients are 50 to 60 per cent attributable to pharmaceutical developments.[688]

The United Nations Millennium Development Goal 8 (MDG8) Task Force Report 2008 indicated that amongst twenty-seven 'developing countries' the mean public availability of essential medicines was only 34.9 per cent.[689] Where medicines are not available publicly their private retail prices are many fold greater and lack of accessibility to them statistically significantly more pronounced. The report also highlighted the variations in public expenditure, finding per capita spending ranges among countries

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[686] Heron, M., Hoyert, D. L., Murphy, S. L., *et al.*, 'Deaths: Final Data for 2006' (2009) 57(14) National Vital Statistics Reports (DHHS Publication No. (PHS) 2009-1120), at 2, 3, 22-23. Available at: <http://www.cdc.gov/nchs/data/nvsr/nvsr57/nvsr57_14.pdf> (Last Accessed: 1st July 2009)

[687] Sun, E., Lakdawalla, D., Reyes, C., Goldman, D., Philipson, T., *et al.*, 'The determinants of recent gains in cancer survival: An analysis of the Surveillance, Epidemiology, and End Results (SEER) database' (2008) 26 (15S) *Journal of Clinical Oncology* 6616. Abstract of ASCO meeting with table of data.

[688] Lichtenberg, F., 'The Expanding Pharmaceutical Arsenal in the War on Cancer' (2004) National Bureau of Economic Research Working Paper 10328

[689] United Nations - Millennium Development Goal 8 Task Force Report 2008, 'Delivering on the Global Partnership for Achieving the Millennium Development Goals.' At: 37. Available at: <http://www.who.int/medicines/mdg/MDG8EnglishWeb.pdf> (Last Accessed: 1st July 2009)

of similar economic status to be $26.67 to $505.46 USD for 'developed countries' and $0.04 to $16.30 USD for 'least developed countries.'[690]

There are many diseases and conditions that are not addressed by the WHO Essential Medicines List.[691] With some patented medicines for conditions not on the WHO list, though extensively subsidised by the government compared to other patented products, that are priced at more than $300,000 USD per patient[692] even when medicines are available, they may be unaffordable for the majority of the population.

Under the present regime, there are two methods by which both factors can be directly addressed. One is agreement of a lower price through a pricing regulation scheme. The other is through compulsory licensing. Collective payments for pharmaceuticals might sometimes be suggested as a third, but whilst they spread the burden of who pays for a medicine, they do not directly affect the price or supply of a medicine. Parallel importing,[693] arising from price discriminations, does occur and can provide price relief for some populations. However it also creates

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[690] United Nations - Millennium Development Goal 8 Task Force Report 2008, 'Delivering on the Global Partnership for Achieving the Millennium Development Goals.' At: 37. Available at: <http://www.who.int/medicines/mdg/MDG8EnglishWeb.pdf> (Last Accessed: 1st July 2009)

[691] 15th edition list. Available at: <http://www.who.int/medicines/publications/08_ENGLISH_indexFINAL_EML15.pdf> (Last Accessed: 1st July 2009)

[692] For example, Cerezyme which is used to treat sufferers of Gaucher disease, an hereditary enzyme deficiency which if untreated can result in liver and spleen rupture, lung and more rarely kidney impairment.

[693]

regulatory problems and can assist in the establishment of a grey markets, thereby posing health and security risks.

CHAPTER 4

STEPPING AROUND MISALLOCATION

It is telling that there are so many proposals for improving access to medicines and refocusing research initiative. This chapter provides an examination of key well thought out proposals reflective of the different mechanisms raised by a much larger group of proposals than could be examined here.[694]

All the proposals share recognition that the price of pharmaceutical products is high and they seek to address the large gap between the price and marginal cost of the medicines. However, whilst some proposals are only focussed on improving access to medicines, others are concerned with research and thus impact on the availability of medicines. As a result, a natural division for this chapter is proposals that target accessibility of existent pharmaceutical technologies (4.1) and proposals that target availability of pharmaceutical inventions (4.2).

The factors by which we assess each proposal are derived from the problems identified in Chapter 3. These are issues of accessibility,

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[694] For example we have not discussed proposals that drastically flawed, i.e. those that seek to improve research focus by injecting additional government money into research for industry acquisition of patent rights, as these will only exacerbate analysed problems. Nor have we considered proposals suggesting changes that are already talking place and thus, whose components are discussed in detail elsewhere in this thesis. Consider the Open Innovation Drug Discovery initiative of Eli Lilly and similar programs by its competitors. This re-emerging paradigm, with the exception of the proposal's magical additional funding from government, closely resembles a proposal for the organisation of fee-for-service facilities within drug companies where academics and industry can collaborate and which is funded by both the users and government. See, Nathan, C., Aligning Pharmaceutical Innovation with Medical Need (2007) 13(3) *Nature Medicine* 304-308

availability and the safety of pharmaceuticals. For each proposal the discussion follows this form.

The proposals in this chapter do not envisage the disjoining of research and the pharmaceutical product, thus measures which impact on the price of an existent medicine, i.e. accessibility, may also impact availability. Bearing this in mind it is more practical to consider proposals targeting accessibility first.

4.1. Propositions for accessibility[695]

> "The large and growing gap between the price and the marginal cost of drugs is the most apparent problem of the current patent system."[696]

Control of the gap between the price and the marginal cost of medicines can be limited in several ways, none of which are mutually exclusive. Price setting limits the price at which a pharmaceutical can be sold (4.1.1), but there needs to be a method to assess what that price will be (4.1.1.1. Price Regulation Schemes). In some circumstances price limitation might be insufficient or inexistent, and yet medicines are needed (4.1.1.2

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[695] By accessibility we refer to the opportunity for as many people as possible to benefit from existent medicines.

[696] Baker, D., 'Financing Drug Research: What are the Issues?' (2004) Issue Brief, Centre for Economic and Policy Research. Available at: <http://www.who.int/intellectualproperty/news/en/Submission-Baker.pdf> (Last Accessed: 1st July 2009)

Compulsory Licenses). The existence of different markets for the same drug, even if they are all sourced from the same supplier, may have an incidence on price (4.1.1.3 Price Discrimination). Alternatively or concurrently price might be limited through strengthening the bargaining position of the buyer (4.1.2. Monopsony).

4.1.1. **Price Controls**

> "...governments have relied heavily on government fiat rather than competition to set prices, lowering drug spending through price controls applied to new and old drugs alike. Such controls, when applied to new drugs, reduce company compensation to levels closer to direct production costs, leaving less revenue for R&D."[697]

The above-normal profit, the result of a pharmaceutical patent monopoly,[698] is also a government fiat. As there is no competition during the "fiat" patent monopoly, mention of competition in the report must refer to competition during the innovation process, i.e. pre-patent, or after patent expiry. As innovation cost has little determination on the pharmaceutical's price,[699] and that patented pharmaceutical prices are driven by company

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[697] U.S. Department of Commerce International Trade Administration. Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation [Washington, December 2004] ix

[698] There is a caveat here in that not all patented pharmaceutical products will necessarily achieve abnormal profits. See, 3.3.9. Keeping Abnormal Profits.

[699] For historical example consider Figure 1. Pharmaceutical company distribution of revenue from 2000 to 2004; or Gagnon, M-A., Lexchin, J., 'The Cost of Pushing Pills: A

profit and shareholder expectation competition is not a determinative of price during the patent term of the pharmaceutical. Comparison of average ex-manufacturer patented pharmaceutical prices (2003 data), were between 18 and 67 per cent lower than patented drug prices in the USA.[700]

The prices of patented pharmaceuticals rise far above the level of inflation,[701] and the companies that own these medicines declare profits within the top fifth of Fortune 500 Companies.[702] Whereas only a fifth or less of revenue is spent on research and drug development.[703]

New Estimate of Pharmaceutical Promotion Expenditures in the United States,' (2008) 5(1) PLoS Med. Available at: <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0050001> (Last Accessed 7th April 2010); Lauzon, L-P., Hasbani, M., 'Analyse économique: industrie pharmaceutique mondiale pour la période de dix ans 1996-2005. Montreal : Chaire d'études socio-économiques de l'UQAM, 2006. http://www.cese.uqam.ca/pdf/rec_06_industrie_pharma.pdf

[700] U.S. Department of Commerce International Trade Administration. Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation [Washington, December 2004] 11

[701] From 2006 through to the first quarter of 2010 the overall rise in medical costs was 3.8 per cent per annum. For in-patent pharmaceuticals the annual increase was 8.3 per cent. Government Accountability Office (USA) Prescription Drugs: Trends in Usual and Customary Prices for Commonly Used Drugs GAO-11-306R [Government Accountability Office, February 2011, Washington] Available at: <http://www.gao.gov/new.items/d11306r.pdf> 4

[702] Fortune 500, May 2006 to May 2011

[703] See Section i10. Also see, Lauzon, L-P., Hasbani, M., 'Analyse économique: industrie pharmaceutique mondiale pour la période de dix ans 1996-2005. Montreal : Chaire d'études socio-économiques de l'UQAM, 2006. Available at: <http://www.cese.uqam.ca/pdf/rec_06_industrie_pharma.pdf> (Last Accessed: 13th February 2011)

"...during the 1980s, prescription drug prices increased by almost three times the rate of general inflation and certain drugs increased in price by over 100 percent in five years."[704]

Without price controls, it is claimed that pharmaceutical revenues would be higher and that resources available for research and development "could be significantly higher."[705] The Department of Commerce International Trade Administration (USA) 2004 report suggests that price controls result in lower revenues for medicines than would result from a competitive market.[706] It suggests that the range of diminished returns is between $18 billion USD and $27 billion USD per annum. Moreover, it holds that if the price reductions did not occur then revenues (2003 figures) would be increased by 25 to 38 per cent.[707] This is an incorrect view, in a

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[704] United States General Accounting Office. Prescription Drugs Changes in Prices for Selected Drugs (1992) GAO/HRD-92-128, at 1

[705] U.S. Department of Commerce International Trade Administration. Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation [Washington, December 2004] x

[706] Considering the magnitude of revenues after price controls, even though firms currently only invest between 8 to 20 per cent of revenues in research and development, this is historically and theoretically unlikely. See Rumelt, R., 'How much does industry matter?' (1991) 12(3) Strategic Management Journal 167-185; Jacobson, R., 'The persistence of abnormal returns' (1988) 9(5) Strategic Management Journal 415-430; Rumelt, R.. 'Theory, strategy and entrepreneurship'. In D. Teece (ed.), *The Competitive Challenge: Strategies for Industrial Innovation and Renewal* [Ballinger, 1987, 1st Ed., Cambridge, MA] 137-157; Mueller, D. *Profits in the Long-Run* [Cambridge University Press, 1986, 1st Ed., Cambridge, UK] 15-34

[707] U.S. Department of Commerce International Trade Administration. Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation [Washington, December 2004] x

competitive market pharmaceutical prices would be much lower than under the price regulated monopoly.

What the report perhaps intended to state was that price controls result in lower revenues for medicine monopolies, than would result from a monopoly not limited by price controls. This may be correct, but only to a point. As national pharmaceutical budgets are fixed, effectively raising the price of medicines by removing price regulation will lead to a redistribution of the pharmaceutical budget. There will be perhaps very little change in revenues across the pharmaceutical industry[708] whilst the availability of drugs will diminish as pharmaceutical companies find they can realise the same income on fewer introductions. Moreover, many pharmaceuticals in the UK would be reassessed by NICE and may fail cost-benefit assessment.[709] As a result of removing price regulation schemes, national expenditure on monopoly pharmaceutical products may decline as substitutes and generic medicines with better cost-benefit weightings replace them. This would not have a positive effect on health care with fewer drug introductions and newer more effective drugs being substantially delayed from entering use.

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[708] The report assumes that increasing drugs prices will have no effect on sales volumes; that funds would be available to pay the higher costs; and that replacements such as generics, could not be substituted. See U.S. Department of Commerce International Trade Administration. Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation [Washington, December 2004] xii

[709] Similar repositioning of coverage on pharmaceutical products may occur with health insurers in the USA.

4.1.1.1. **Price Regulation Schemes**

Price regulation schemes reduce the price of medicines and despite the enormous volume of literature stating that they reduce research and development there is no empirical data demonstrating that this is the case.[710] Price regulation schemes appear by themselves to be an inadequate solution to the problems engendered by a patent based system of innovation for pharmaceutical technologies. As other than altering the price paid for a pharmaceutical and the income of pharmaceutical companies that then feeds down into (research and development, marketing, profits... etc.), price control has no effect on medicine safety, on which drugs are innovated, or the efficiency of pharmaceutical innovation.

Within the European Union, Member States have autonomy over the mechanisms by which they choose to regulate pharmaceutical prices, provided that such provisions are in accordance with the Transparency Directive.[711] The UK's system of price controls is particularly influential in price setting both within the European Union and the Commonwealth.

[710] Empirically there are no falls in the number of approved NCE introductions from the normalised curve following changes in drug pricing policy.

[711] Directive 89/105/EEC sets out a legal framework to eliminate disparities between Member States which hinder or distort intra-Community trade in medicinal products

"The [UK] Pharmaceutical Price Regulation Scheme (PPRS) ensures the NHS has access to good quality branded medicines at reasonable prices, and promotes a healthy, competitive pharmaceutical industry."[712]

On the 18th of June 2008 the UK Department of Health issued a press release announcing progress in the negotiations with the Association of the British Pharmaceutical Industry (ABPI). On the same day the UK Government issued a consultation paper concerning the use of statutory powers to control prices of patented[713] medicines sold to the NHS from 1st September 2008.

It was clearly intended that the statutory powers would apply to pharmaceutical companies that did not join the new voluntary scheme or in the event that agreement over a new voluntary scheme is not reached[714] and thus serve as an incentive to opt for the new PPRS. The Statutory measures are proposed a 3.9 per cent price cut on patented pharmaceuticals and limited the price of patented pharmaceuticals, where

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[712] Department of Health PPRS information website. Available at: <http://www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpricregulationscheme/index.htm> (Last Accessed: 1st July 2009)

[713] Although the powers are clearly destined for use on medicines still under patent, there is scope for statutory price control of medicines not under patent. See Department of Health, Consultation on a statutory scheme to control the prices of branded NHS medicines. Launch date: 18 June 2008. Available at <http://www.dh.gov.uk/en/Consultations/Liveconsultations/DH_085523> (Last Accessed: 1st July 2009)

[714] Department of Health, Consultation on a statutory scheme to control the prices of branded NHS medicines. Launch date: 18 June 2008, at 13

there is an unpatented equivalent, to 1.5 times the price of the unpatented equivalent. [715]

In accordance with section 261 of the National Health Service Act 2006, on the 13th of August 2008 a new interim non-contractual PPRS[716] was agreed between the Health Departments of the United Kingdom and the ABPI. This agreement was effective from the 1st of September 2008 until the 31st of December 2008. The new PPRS although restating the cooperation of the Department of Health and the British pharmaceutical industry towards the 'provision of safe and effective medicines for the NHS at reasonable prices'; the promotion of 'a strong and profitable pharmaceutical industry...capable of...sustained research and development expenditure...[leading] to the future availability of new and improved medicines'; and to 'encourage the efficient and competitive development and supply of medicines to pharmaceutical markets...'. [717]

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[715] Association of the British Pharmaceutical Industry and the UK Department of Health, The Pharmaceutical Price Regulation Scheme. (2008) E-Publication, London. Available at: <http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/?IdcService=GET_FILE&dID=145977&Rendition=Web> (Last Accessed: 1st July 2009)

[716] Association of the British Pharmaceutical Industry and the UK Department of Health, The Pharmaceutical Price Regulation Scheme. (2008) E-Publication, London. Available at: <http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/?IdcService=GET_FILE&dID=145977&Rendition=Web> (Last Accessed: 1st July 2009)

[717] Association of the British Pharmaceutical Industry and the UK Department of Health, The Pharmaceutical Price Regulation Scheme. (2008) London: 1

Members opting into the new PPRS retained their rights under the 2005 scheme, particularly with respect to arbitration, but rather than the fixed 7 per cent price decrease under the 2005 scheme they are only subject to a 5 per cent price decrease, with a further 2% if an unpatented equivalent became available.

The price regulation scheme, as did previous schemes, whilst reducing the price the NHS spends on patented pharmaceuticals does not go far enough in delivering cost effective medicines to NHS patients. Indeed the savings achieved by the NHS through price modification of patented medicines is estimated at £310 million of the £9bn currently spent on patented medicines each year. Whilst this saving will go a little towards offsetting the reduced growth rate in NHS spending it will not remedy the failure of the PPRS to deliver cost effective drugs for the National Health Service (NHS).[718]

Moreover, it also applies direct pressure to sensitive funding sectors such as research and development. Pharmaceutical companies cannot afford to risk the loss of shareholder confidence. More pressure on revenues in this manner means more focus on blockbusters, line extensions and high profit lifestyle drugs and therefore less industry funded investigation of less profitable therapeutically advantageous medicines. Immediate responses

[718] Office of Fair Trading. The Pharmaceutical Price Regulation Scheme. An OFT Market Study. OFT. London: 2007. Available from: < http://www.oft.gov.uk/shared_oft/reports/comp_policy/oft885.pdf> (Last Accessed: 1st July 2009)

to reduced revenue will most likely be met by corporate restructuring to maintain investor interest and not increases in dynamic efficiency.[719] This problem will be further exacerbated by the tendency of other countries, particularly Japan, France, Italy, Canada, the Netherlands and Belgium, which directly follow UK drug pricing trends.[720] It is suggested, that "[i]n total, countries totalling some 25 per cent of global demand link the prices of some of their pharmaceutical products to those in the UK."[721]

4.1.1.2 **Compulsory Licensing**

The Patents Act 1977, as amended,[722] makes compulsory licenses available under UK law. A distinction is drawn between patents with WTO patent holders and patents without WTO patent holders;[723] the compulsory licensing of patents without WTO patent holders being far less onerous.[724] However, considering the scarcity of WTO non-members, this distinction is rather redundant.

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[719] For example consider Pfizer, which from 2009 to 2011 has reduced its research and development budget by reducing the diversification of its research and number of research staff and facilities.

[720] Timothy Fitzgerald, Bridgehead International Chief executive officer, quoted in 'The Pharmaceutical Price Regulation Scheme Survives Again, UK' *Medical News Today* 13 June 2008 Available at: <http://www.medicalnewstoday.com/articles/111049.php> (Last Accessed: 1st July 2009)

[721] Office of Fair Trading, Annexe D, Global overview of the pharmaceutical industry (February 2007) OFT885d, at 4. Available at: <http://www.oft.gov.uk/shared_oft/reports/comp_policy/oft885d.pdf> (Last Accessed: 1st July 2009)

[722] In particular see Patents and Trade Marks (WTO) Regulations 1999, S.I. 1999 No. 1899

[723] §48 Patents Act 1977 (as amended)

[724] Compare the conditions of §48A Patents Act 1977 (patents with WTO patent holders) with the conditions required by §48B (patents without WTO patent holders)

According to §48A Patents Act 1977, compulsory licences are available where domestic demand for the patented invention is not being reasonably met,[725] where the patent owner's refusal to grant a license on reasonable terms either; effectively blocks later improvement,[726] or prejudices commercial or industrial activity in the UK.[727] Or where the conditions imposed with the grant of a license limit the use of the patented invention or patented process to an extent that commercial or industrial activity in the UK is unfairly prejudiced.[728]

Prima facie, the grounds to make an application for a compulsory licence seem quite broad. However, there are qualifications of reasonable and unreasonableness to be taken into account.[729] Moreover, the discretionary power exercised by the comptroller is subject to an extensive list of 'purposes' and 'factors' that the comptroller ought[730] to take into account when exercising their discretion. It is feared by the industry that use of compulsory licenses by countries too poor to purchase a medicine at the set price will allow those countries to obtain medicines that can then be re-sold on grew markets in countries where the medicines are

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[725] §48A(1)(a) Patents Act 1977

[726] §48A(1)(b)(i) Patents Act 1977. See Article 82 EC; and *Intel Technologies* v *Via Technologies* [2003] FSR 574, where the Court of Appeal rejected Laddie J's (*Philips Electronics* v *Ingman* [1998] 2 CMLR 1185), until then persuasive, suggestion that *Magill* (*RTE & ITP v EC Commission* C241-91, C242-91 [1995] ECR 808) might not be applicable to a patent.

[727] §48A(1)(b)(ii) Patents Act 1977

[728] §48A(1)(c) Patents Act 1977

[729] §50 Patents Act 1977

[730] *Monsanto's CCP Patent* [1990] FSR 93, at 97

purchased at their set price. This fear has been frequently couched in other terms.

> "Poor countries will not eradicate diseases by compulsory licensing certain pharmaceuticals. In fact the opposite is more likely because of the negative signal that such a decision would send to companies contemplating investment in knowledge-based industries. It would be a tragedy if long-term economic development and consequent improvements in the health of the poor were to be undermined by short-sighted policies aimed at placating narrow vested interests."[731]

Compulsory licences are available under Article 31 TRIPS, which limits medicines produced under compulsory license to those destined for the domestic market.[732] Criteria that must be met are set out by Article 31 TRIPS. In the case of countries without domestic facility to manufacture pharmaceuticals Article 31(f) TRIPS is in effect amended, so that such countries can import drugs manufactured under compulsory license in other countries.[733]

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[731] Morris, J. TRIPS and Healthcare: Rethinking the Debate (2001) International Policy Network. Available at: <http://www.policynetwork.net/main/press_release.php?pr_id=39> (Last Accessed: 1st July 2009)

[732] Article 31(f) TRIPS

[733] WTO, Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health (1st September 2003) WT/L/540 (General Council decision 30th August 2003)

There is further scope under trips to implement control of pharmaceutical access under Article 27 TRIPS. Where an argument could be made by a country for actions to achieve the health goal for its people of providing affordable and essential drugs to its population. Nevertheless for Article 27 permission, the medicine must feature on the WHO's list of Essential Medicines, and the use of Article 27 TRIPS must be validated by a WTO panel.[734] The use of Article 27 TRIPS as a means of appropriating pharmaceuticals for their populace requires the WTO signatory seeking the compulsory licence to persuade the WTO panel that there was no other measure less inconsistent with the treaty in order to supply affordable drugs. In this case it might be argued that price controls would be a more reasonable measure. However, the economic bargaining power of a country is likely a significant factor in determining the extent of price regulation beyond the extent of indexing undertaken in other countries. Which may be an insufficient reduction in price for the country that has to seek a compulsory licence.

Scherer suggests that a flexible compulsory licensing policy that could be fine tuned to circumstances is preferable. Moreover, he holds that 'technical progress would not grind to a halt if a uniform policy of compulsory licensing at 'reasonable royalties'... were implemented."[735]

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[734] WTO, Report of the Panel on Thailand: Restrictions on Importation of an International Taxes on Cigarettes, Nov 7, 1999, GATT B.I.S.D (37th Supplement) at 216

[735] Scherer, F. M., *The Economic Effects of Compulsory Patent Licensing* [New York University Press, 1977, New York] at 85. But also see 67-75.

4.1.1.3. **Price Discrimination**

Price discrimination arises where a supplier is able to sell the same product in separate markets at different prices. Whilst Price discrimination[736] may be an effective tool of positive publicity for a pharmaceutical company, it is problematic for the pharmaceutical company for two principal reasons. Firstly, it highlights to people the difference in price at which the company can still afford to market its product and the highest prices at which the company markets its product. It does not matter to the wealthier buyers whether their higher premiums are necessary in order to fund the poorer person's access to the medicine. [737] Secondly, as the designated wealthier population seek to purchase the medicine at the cheaper rate, they introduce competition. This was one of the major objections, antiretroviral pharmaceutical patent holders had, to the selling of cheaper AIDS drugs in Africa at the beginning of the new millennium. [738] It was feared that the cheaper antiretroviral drugs sold in Africa would be bought up and then imported to the lucrative USA and European markets.

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[736] In economic terminology this would be 3rd degree price discrimination, or direct segmentation. Bearing in mind that the principle of exhaustion has severe limitations on co-ordination, see: Nalla, V. R., Venugopal, V. and Van Der Veen, J. A. A., "Coordination with Supply Chain Contracts in the Presence of Two Different Consumer Segments" NRG Working Paper Series No. 07-07 (2007)

[737] A justification of the price difference on the basis that market paying the highest price is subsidising the lower price market is not favourable to buyers in the high price market, though it might be morally accepted.

[738] Copson, R. W., Issue Brief for Congress - AIDS in Africa (7 January 2003) Congressional Research Service, The Library of Congress. Code IB10050. At CRS-10

Even within Europe there are differences the pricing of medicines either due to price regulation schemes or the different purchasing power of national sickness insurance.[739] Thus, parallel importing does occur,[740] though pharmaceutical producers have attempted to control parallel importing through various means,[741] such as: agreements with undertakings that effectively limit geographic distribution, but are exempted from competition provisions under Article 81(3) EC; forbidding product repackaging;[742] supplementary protection certificates;[743]

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[739] See Case T-168/01 *GlaxoSmithKline Services Unlimited v. Commission*

[740] Article 6 TRIPS leaves the rules for exhaustion of intellectual property rights for national determination. See Schmiemann, M., Exhaustion of patent rights and the European union (1998) 20 *World Patent Information* 193-195; *Centrafarm BV v Sterling Drug Inc.* Case 15/74 [1974] ECR 1147; *Laserdisken ApS v Kulturministeriet* Case C-479/04 12 September 2006; Griffiths, J., Principle of Community exhaustion upheld by Court of Justice (2007) 2(1) *Journal of Intellectual Property Law & Practice* 15-16. The EU and many countries, including the USA and Canada, have adopted a principle of international exhaustion. Thus, the owner of the intellectual property rights cannot prevent the resale of a non-counterfeit product anywhere in the world on the basis of their intellectual property rights, almost regardless of where the product was first placed on the market. Where a license is involved in the use of a product preventing resale of that use then the principle of international exhaustion may not apply.

[741] Jack, A., 'EU drug industry to clamp down on repackaging for sale abroad' (1 June 2007) *FT.com.* Available at: <http://www.ft.com/cms/s/0/30f3c532-0fdd-11dc-a66f-000b5df10621.html> (Last Accessed: 1st July 2009)

[742] To comply with national requirements for packaging and labelling information, particularly with regard to language, or to adapt the product to different consumer preferences, parallel importers frequently repackage pharmaceuticals before distributing them in other member states. However, this must involve reapplication of the manufacturer's Trade Mark. For the EU position of reapplication of Trade Marks in parallel importing see: *Boehringer v Swingward* Case C-143/00 [2002] ECR I-3759 172; *Merck, Sharp & Dohme v Paranova* Case C-443/99 [2002] ECR I-3703 152

[743] Where the parallel import pharmaceutical originates from an EU Member State that does not yet award supplementary protection certificates, then the pharmaceutical manufacturer can exert their patent rights or supplementary protection certificate to prevent the import and of that product in an EU Member State where supplementary

adaptation of quota allocation systems;[744] and the imposition of shorter best before dates.[745]

Various measures have been implemented over the years to prevent parallel importing, but most have failed and grey markets, and so-called grey markets, in medicines flourish.[746] For health and safety reasons

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protection certificates are available. For example, from 1993 to 2000 AstraZeneca successfully extended their monopoly through the use of misleading information to national patent offices in concerning the supplementary protection certificate status of Losec and thereby prevented Losec parallel importing. See Anonymous, 'Competition: Commission fines AstraZeneca €60 million for misusing patent system to delay market entry of competing generic drugs' (15 june 2005) IP/05/737 *EUROPA (Rapid Press Releases)* Available at: <http://europa.eu/rapid/pressReleasesAction.do?reference=IP/05/737> (Last Accessed: 1st July 2009)

[744] This involves distribution through subsidiary wholesalers where allocation is assessed on consumption trends and produce is then allocated by quota to ensure that there is no surplus for parallel importing, thereby theoretically securing the most profitable outcomes. In practice secure allocation of quotas is difficult and expensive, thus imposing dead weight and still permitting some parallel importing.

[745] A shorter best before date means that parallel importers have less time flexibility to purchase, repackage and market the pharmaceutical in another EU Member State. Customers, particularly pharmacists and stockists will factor into their sales management the expiry of the medicines. Thus, if the medicines in the Member States, where the pharmaceutical medicines are more expensive, have a significantly longer best before date then they may become preferable in spite of the price variation. This technique could be considered analogous to degradation of the product in the expensive market for resale in the cheaper market (For example, business and home software). Some people critique this marketing strategy as risking the manufacturing company's goodwill. This however, in my opinion is an incorrect view. Nevertheless see Goodbody, A., and Goodbody, L., 'How to Protect Your Business Against Parallel Imports - Legally!' (17 February 2005) *HG.org.* Available at: <http://www.hg.org/articles/article_1174.html> (Last Accessed: 1st July 2009)

[746] See Criminal Intelligence Service Canada. Available at: <http://www.cisc.gc.ca/pharmaceuticals/pharmaceuticals_e.html> (Last Accessed: 1st July 2009)

allowing pharmaceutical grey markets to thrive presents a danger to public health and security,[747] therefore regulation to prevent parallel importing has to be carefully thought out. There are however instances where some governmental sympathy to the buyers has led to a relaxation in customs seizures.[748] Nevertheless, as buying pharmaceuticals abroad becomes easier and vendors' websites become increasingly persuasive[749] it will be extremely interesting to see the effect on the European and USA national markets.

4.1.2. **Monopsony**

The idea of the monopsony in the pharmaceutical market is to combine buyers into a monopolistic body to counter the effect of the monopolistic seller. Whilst the monopolistic seller retains their price-setting power and can continue to try and obtain above-normal profit, the seller is constrained by the highest price that the monopolist buyer is willing to pay.

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[747] World Health Organization, Fact Sheet № 275 (14 November 2006) Available at: <http://www.who.int/mediacentre/factsheets/fs275/en/> (Last Accessed: 1st July 2009)

[748] USA consumers have for many years bought small quantities of prescription drugs either whilst in Canada or by order through the internet. It is illegal to import pharmaceuticals into the USA and tight customs regulations meant that in the past most of these 'supplies' were seized at the Canadian border by USA customs. Seizures of small quantities of medicines for personal use, have been relaxed. See: Kermode-Scott, B., 'US eases its restrictions on prescription drugs from Canada' (21 October 2006) 333 (7573) BMJ 824.

[749] Consider for example: www.CanadianPharmacyTrust.com - "...no hidden fees, shipping to all 50 states,... savings up to 80% off on all your prescriptions,..." Available at: <http://www.canadianpharmacytrust.com/> (Last Accessed: 1st July 2009)

Thus, the decision of price becomes a negotiation between the two determinant players. On the one hand the monopolist seller has a good that the monopolist buyer needs, but on the other hand the monopolist seller needs to recoup their investment and continue to find other products for the monopolist buyer.

> "...[W]hat creation of the second monopolist [(the monopolist buyer)] does is, not to bring prices to the natural, or competitive, point, but to render them indeterminate over a considerable range..."[750]

The monopolist seller has a time constraint and no other way to vend their goods or recover costs than through the monopolist buyer.

Negotiating experience also differs between the seller and buyer; the monopolist seller although they may bargain and make many substantial exchanges with the monopolist buyer, the monopolist buyer will make many fold the number of exchanges with sellers in other products.

Moreover, the monopolist buyer has limited resources to allocate and a time scale in which it may spend those resources. As the monopolist buyer cannot purchase therapies for all conditions they are forced to prioritise: Thus, increasing the pressure on the seller to achieve an agreed sale price rather than have their products bypassed for those of another product that the monopolist buyer also finds desirable.

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[750] Pigou, A. C., The Economics of Welfare [Macmillan, 4th Ed., 1932, London] 358

The monopolist seller is further limited by the application of competition rules to the distribution of their product. The monopolist buyer suffers no handicap through its concentration, on the contrary its concentration gives it an almost perfect monopsony. There is however the principle of exhaustion to contemplate. If different national markets within an economic union practicing free movement of goods negotiated different prices and the distribution of those medicines was not limited, then parallel importing would occur and a monopsony would not occur. However, the definition of a monopsony is sufficiently flexible for a buyer to agree to pay different prices in different places, but the essential factor is the existence of a singular buyer for the whole market.

In theory monopsony may reduce the deadweight within the pricing of pharmaceuticals. Monopsony though requires enlightenment by the buyer and frank disclosure of costs by the seller if it is going to move towards dynamic efficiency, otherwise it may only balance short run costs or at the other end of the spectrum allow excess profit.

In practice government might on some occasions be considered to employ monopsonistic leveraging when negotiating price regulation with industry representatives and manufacturers. Considering the statutory powers poised for application to pharmaceutical companies that do not join the new voluntary UK PPRS, the government wields more than monopsonistic bargaining power. Indeed because of the government's relationship and

responsibilities to its citizens, and government's financial interest in pharmaceutical industry funding, it would be an incorrect view to consider government, as is, a monopoly buyer. Certain agencies may be considered to have monopsonistic tendencies, but again these through the lack of a strict administrative separation of powers bargain through a set of parameters arising through a complexity of political, as well as economic factors. Even without consideration of the political distortions government wields on behalf of their national health schemes and government's interest in funds from pharmaceutical companies, within the present system there is not monopsony; large buyers such as the National Health Service are in a stronger position than other buyers, but there are concurrent buyers overseas, over the counter, and private professional health organisations.

Furthermore, setting one price for all sectors of demand for a product may not be practicable, or may be disadvantageous to particular sectors. When considering the different sectors of demand that might exist for a product there are two which illustrate the difficulties in determining the price. Firstly, the economic prosperity of the population will determine what people can pay for a medicine or the funds available in a government purchase scheme. Consider that in April 2008 the median weekly pay for an employee in the UK was £479 GBP,[751] whilst in the following poorest countries: Burundi, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Georgia, Guinea, Guinea Bissau, Kenya, and Uganda, there are populations that

[751] Office of National Statistics, Annual Survey of Hours & Earnings 2008. Available at: <http://www.statistics.gov.uk/StatBase/Product.asp?vlnk=13101>

live on less than one dollar USD a day.[752] The magnitude of the disparity between the available resources is staggering. Moreover, in these poorest countries the prevalence of disease is much greater than the UK, as a result of climatic, education, and developmental factors. Consider the differences in available capital for both the population of the UK and the population of these poorest countries to receive the same medicines would require considerable price discrimination, with some form of subsidy scheme. Practically the monopsony would be extremely difficult to implement if it attempted to promote health care on a basis of equality. Moreover, ensuring pharmaceutical access in the poorer countries may engender further problems from the monopsony. More than one buyer, but only one per sector might alleviate some of the difficulties in decision policy. But in effect this would be third degree price discrimination and as we noted above in some circumstances it would result in parallel importing.

Monopsony may increase the bargaining position of the buyer so that a clear accounting of innovation costs could be obtained, thereby removing some of the threat value from the 'research and development scare card.'[753] However, many of the advantages conveyed by monopsony might be better obtained through government intervention in the form of direct legislation on the points of interest. Improved safety of medicines

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[752] US Department of State – Human Rights Reports. Available at: <http://www.state.gov/j/drl/rls/hrrpt/index.htm> (Last accessed 1st March 2011)

[753] See Public Citizen, Rx R&D Myths: The Case Against The Drug Industry's R&D "Scare Card" 2001. Available from Public Citizen at: <http://www.citizen.org/documents/ACFDC.PDF> (Last Accessed: 1st July 2009)

and a more honest evaluation of a medicine's effectiveness and suitability would already be a considerable improvement. Indirectly this might be obtained through product liability under monopsony, but this would be unsatisfactory. As although the monopolistic buyer could seek redress from the monopolistic seller this would not remove deadweight from the monopolistic buyer's initial purchase of medicines for target groups in which they have little more, or less effectiveness than a placebo, or prevent the suffering resulting from the administration of medicines to groups that are unsuitable recipients of the medicines.

4.2. Propositions for availability.[754]

Most proposals principally target accessibility. However, both the Pharmaceutical Innovation Fund (4.3.1.) and Medical Innovation Prize Fund (4.4.1) recognise the dearth of industry focus on therapeutic improvements and utilise assessment of therapeutic improvement to determine the size of payouts for patented inventions. This is likely to have desirable results in stimulating more drugs that are therapeutic improvements and thus will have a positive impact on availability.

4.2.1 **Pharmaceutical Innovation Fund**

> "The key to unblocking the impasse of high drug prices is to reward drug innovators based on the therapeutic value their products

[754] By availability we refer to whether drugs are existent, thereby encompassing the development of new medicines, and by accessibility we refer to the opportunity for as many people as possible to benefit from existent medicines.

create through a national government-funded Pharmaceutical Innovation Fund."[755]

The objective of this proposal is to alleviate inefficiencies caused by high drug prices and to direct pharmaceutical research towards innovations that are more desirable to society. The pharmaceutical innovation fund is a scheme that runs alongside the patent system. It involves the establishment of a fund, supplied by government capital that is responsible for making payments based on the therapeutic advances that a qualified invention makes.

It is not clear if all pharmaceuticals qualifying for the fund are automatically subject to zero cost compulsory licensing of their patent, or whether this only occurs when the fund makes a payment.

Payments from the fund are specified as being large enough to be preferable to returns that a pharmaceutical company might receive through the patent system. A figure of $1.2 billion USD for yearly payments is provided as an indication. A yearly pool of $60 billion USD has been

[755] Hollis A. An Efficient Reward System for Pharmaceutical Innovation. 2005; 2. Available at: <http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf> (Last Accessed: 1st July 2009)

suggested to provide adequate incentives for invention in the USA,[756] or global funds of about $120 billion USD.[757]

> Qualifying medicines will be restricted to those "whose primary purpose is to improve health outcomes."[758]

One suggested method of measuring health outcomes is through the use of Quality Adjusted Life Years (QALYs). A government agency would assign a drug a QALY rating allowing the extent to which it improved the quality of life and/or extended life compared with the next best treatments available.

QALYs are based on the number of years of life that would be gained as a result of a therapeutic intervention. A number between 1.0 and 0 is awarded for the quality of health in a given year. 1.0 is awarded for a year of perfect health and 0 for death. Health that falls below 'perfect' receives a score between 1.0 and 0. They are often employed in Cost-utility analysis. For example, it is believed that from January 2005 that the National Institute for Health and Clinical Excellence (NICE) has operated a

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[756] Hollis A. An Efficient Reward System for Pharmaceutical Innovation. 2005; 15 Available at: <http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf> (Last Accessed: 1st July 2009)

[757] Hollis A. An Efficient Reward System for Pharmaceutical Innovation. 2005; 15 Available at: <http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf> (Last Accessed: 1st July 2009)

[758] Hollis A. An Efficient Reward System for Pharmaceutical Innovation. 2005; 2 Available at: <http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf> (Last Accessed: 1st July 2009)

cost-effective threshold at about £30,000 per QALY.[759] Thus, where a therapeutic intervention is considered to have an incremental cost of more than £30,000 per additional QALY gained the intervention will not be deemed cost-effective. Whereas, interventions with an incremental cost of less than or equal to £30,000 per additional QALY gained may qualify as cost-effective.

Although QALYs are sometimes suggested to enable standardised comparisons to be made between the therapeutic benefits of different drugs, they are often as a tool of standardised assessment vitiated by subjectivity.[760]

QALYs provide the best attempt so far to solve the problem of measuring health care outcomes but they still suffer from a number of serious problems. A key question is who is to make the subjective choices which determine the QALY? Is it health professionals, the general public or patients who have experience of the particular medical condition and treatment? Experiments have shown that the value of a QALY can change

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[759] Devlin, N.; Parkin, D. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. (2004) 13 (5) *Health Economics* 437-52

[760] Drummond, M. F., Output measurement for resource allocations in health care. (1989) 5 *Oxford Review of Economic Policy* 59-74; Gerard, K., Mooney, G., QALY league tables: three points for concern-goal difference matters. [Aberdeen: Departments of Public Health and Economics,
1992, University of Aberdeen] (Health Economics Research Unit discussion paper 04/92)

radically according to who is making the choices.[761] Other problems include the fact that the responses given are to hypothetical situations and so may not accurately reflect people's real decisions, and that valuations are influenced by the length of the illness and the way in which the questions are asked.[762]

Moreover, QALYs may in many cases undervalue the value of a particular therapeutic intervention because they do not take account of externalities, such as the gain for the patient's family and friends, as well as the value of a patient's labour which will be gained as a result of the therapeutic intervention.

Although the proposal has as an objective improvement in the efficiency of research and development its impact on deadweight factors is limited. It is more effective than the patent system at diverting resources into inventions that present therapeutic advances, because it increases the rewards for these inventions over beyond rewards otherwise available under the patent system. Assuming that the number of users of the

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[761] Loomes, G., and McKenzie, L. 'The Use of QALYs in Health Care Decision Making' (1989) 28 *Social Science and Medicine* 299-308

[762] Bell, C. M., Urbach, D. R., Ray, J. G., Bayoumi, A., Rosen, A. B., Greenberg, D., Neumann, P. J., 'Is Everything in Health Care Cost-Effective? Bias in Published Cost-Effectiveness Studies' (2006) 332 BMJ 699-703; Brauer C, Greenberg D, Rosen AB, Neumann PJ. 'Trends in the Use of Health Utilities in Published Cost-Utility Analyses' 2006 9(4) *Value in Health* 213-218; Hahn RW, Kosec K, Neumann PJ Wallsten S. 'What Affects the Quality of Economic Analysis for Life-Saving Investments?' (2006) 26(3) *Risk Analysis* 641-55; Talmor, D., Shapiro, N., Greenberg, D., Stone, PW., Neumann, P. J., 'When is Critical Care Medicine Cost-Effective? A Systematic Review of the Cost-Effectiveness Literature' (2006) 34(11) *Critical Care Medicine* 2738-2747

pharmaceutical product remained unchanged then the Pharmaceutical Innovation Fund would necessarily be more expensive in developing pharmaceuticals than the present patent system. However, because the price of the manufactured pharmaceutical under the fund is much lower than it would be under the present patent system, then the number of users may increase. As the number of users increases then the unit cost of the product under the Pharmaceutical Innovation Fund falls. Thus, despite the cost of the fund it may present a more efficient system for research and development inducement for some conditions, than the present patent system.

Unfortunately, this proposal retains the costs of the patent institutions and perhaps the correlative cultural legacy of litigation as a method of determining what is a valid invention, the state of the art or the distribution of rewards from the fund. All of which are costs that are unnecessary to the invention of pharmaceutical technologies. The Pharmaceutical Innovation Fund does not modernise knowledge generation or take into account organisational paradigms that improve the efficiency of pharmaceutical innovation. Nor, does the fund make improvements to the safety of new pharmaceutical innovation products. It may well create additional incentive for ghost written reports and bogus clinical trial data.

"Governments also intervene in pharmaceutical markets in most countries through extensive regulation, price controls and purchases. In the proposed system, government would not be involved in the market at all,

but would retrospectively determine the therapeutic benefit of an innovation in order to make a payment to the patentee."[763]

One of the suggested factors in the government's evaluation of the payout that a pharmaceutical will receive are, in addition to the QALY, the annual sales figures for the pharmaceutical: The more units sold the greater the size of the payout for the pharmaceutical.[764] If this is the case, then this proposal is likely to exacerbate marketing expenditure and safety.[765]

4.2.2. **Medical Innovation Prize Fund**

The medical innovation prize fund[766] is another incentive system that is very similar to the Pharmaceutical Innovation Fund. It also retains the patent system and has no direct incidence on the process of research and development. Patents over pharmaceutical technologies are obtained as they are now. However, the pharmaceutical patent no longer grants a

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[763] Hollis A. An Efficient Reward System for Pharmaceutical Innovation. 2005; 2 Available at: <http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf>

[764] "...the innovator... would have an incentive to market the drug so as to increase the volume of sales on which it could earn points." Hollis A. An Efficient Reward System for Pharmaceutical Innovation. 2005; 11-12 Available at: <http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf>

[765] Baker, D., 'Financing Drug Research: What are the Issues?' (2004) Issue Brief, Center for Economic and Policy Research. Available at: <http://www.who.int/intellectualproperty/news/en/Submission-Baker.pdf>(Last Accessed: 1st July 2009)

[766] Love, J., and Hubbard, T., 'The Big Idea: Prizes to Stimulate R&D for New Medicines' (2007) 82 (3) *Chicago-Kent Law Review* 1519-1546. However, the proposal is still actively under development. See, Love, J., and Hubbard, T., 'The Big Idea: Prizes to Stimulate R&D for New Medicines' (Revised 26th March 2007) Available at: <http://www.keionline.org/misc-docs/bigidea-prizes.pdf> (Last accessed 12th December 2011)

monopoly right by excluding competitors from utilising the invention. Instead the patent ensures that the patent holder will receive a reward from a large public fund. The suggested period for this reward is ten years, and the size of the reward is to be determined on the basis of the therapeutic benefit that the new medicine conveys. It has been suggested that such a fund would be 0.6 per cent of GDP.[767]

The particular objective of the fund is to encourage the development of more medicines that constitute therapeutic advances. As a result it presents a considerable refinement to the patent system's utilitarianist ambition of directing resources into the channels of greatest usefulness. It is also likely to be more effective than the pharmaceutical innovation prize fund, from which it was perhaps conceived, as it applies to all pharmaceutical patents not merely to those whose purpose is 'to improve health outcomes.'

This has the result that pharmaceuticals which pose no therapeutic advance will receive no money from the fund and yet be available for all manufacturers to produce without the payment of royalties.

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[767] Love, J., 'Would cash prizes promote cheap drugs?' (2007) 2629 The New Scientist (online). Available at: <http://www.newscientist.com/article/mg19626296.100-would-cash-prizes-promote-cheap-drugs.html> (Last Accessed: 1st July 2009). The HR417 proposal sets the Fund total at 0.5 per cent of the U.S. GDP Love, J., and Hubbard, T., 'The Big Idea: Prizes to Stimulate R&D for New Medicines' (Revised 26th March 2007) Available at: <http://www.keionline.org/misc-docs/bigidea-prizes.pdf> (Last accessed 12th December 2011) at 13

An interesting question is why the patent system features in the mechanism of the fund at all? As monopolist rights are eschewed in favour of promoting competition to drive down the price of the manufactured product, the presence of the patent system in the chain is dead weight. Moreover, the fund fails to address another important problem of the present pharmaceutical system, i.e. the small percentage of the price of pharmaceutical products that is reinvested in research. Whilst the fund shifts the burden from the consumer and perhaps lowers the overall cost to society in providing the medicines, a large portion of the fund's payouts will still not be directed towards further research.

Moreover, some nations are better equipped both in resources and expertise to conduct pharmaceutical research, as always some markets will be of greater reward than others. Will assessment of the pharmaceutical's therapeutic advance be performed with respect to conditions within the national jurisdiction, or will it be a global assessment? For example sleeping sickness is not normally experienced in the USA, thus a medicine that is extremely effective against sleeping sickness compared to the current state of the art treatments, would receive little or no payout from the fund if the assessment is for USA conditions only. On the other hand if the fund takes account of conditions globally, will the principal source of the fund's capital, the American citizen be content to

pay out? If the fund is global then political and national issues may be factors.[768]

Currently the patent fails as an 'index of social usefulness' although rewards and prizes do constitute encouragement for activity to take place. If the inventive genius of the inventors is to be considered as an *iff* of the innovation occurring, the patent system suggests that the inventive genius is less valuable than the capital of the investor. We see this in the ownership rights an employer exerts by default over employee's inventions.[769] As well as in the differing remuneration the inventor and investor receive. Since the innovators receive less return than the manufacturer, who is in the pharmaceutical patent system both the employer and the cumulative body of the investor.[770] The use of patents as an index for prizes is unlikely to be straightforward. The person or team that made the breakthrough, on which the prize winning patent was based, might not be the owners of the patent or even mentioned on the patent application except as prior art. Furthermore, which should be the qualifying patent, as the active ingredients of the winning pharmaceutical will most likely be the subject of multiple patents? There will certainly be patents on the aspects of the product, as well as on its manufacture and

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[768] Baker, D., 'Financing Drug Research: What are the Issues?' (2004) Issue Brief, Center for Economic and Policy Research. Available at: <http://www.who.int/intellectualproperty/news/en/Submission-Baker.pdf> (Last Accessed: 1st July 2009)

[769] See §39(1) Patents Act 1977

[770] Outsourcing of manufacture which has recently become possible is increasingly being adopted by larger former research manufacturers, as well as very small biotechnology companies.

its manner of administration. If these patents lie in different hands which owner will qualify for the prize? The Medical Innovation Prize Fund has a clever answer to the problem of evaluating prize payments to particular patents. Patents on FDA approved products would be usable by generic manufacturers and the inventor (is this used synonymously with patent holder or refer only to the names listed as inventors within the patent application?) would use the frequency with which their patents were used to make a prize claim from the Fund.[771] However, when deciding prizes will any additional weighting be given to the patent holders who funded the clinical trials that enabled FDA approval? Or will patent holders on the approved therapy only benefit from the frequency by which generic producers utilise their patents?

The patent system places the onerous of determining the utility of a pharmaceutical invention, and the value of particular patents, on the patent owners through the medium of legal contention and market reception. That legal contention is expensive and this in turn increases the costs of patent filing as applicants attempt to make their positions as strong as possible. Thus, even with the complications of deciding the allocation of funds amongst different patent holders of the chosen therapy, the Medical Innovation Prize fund may constitute a cheaper method of determining utility.

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[771] Love, J., and Hubbard, T., 'The Big Idea: Prizes to Stimulate R&D for New Medicines' (Revised 26th March 2007) Available at: <http://www.keionline.org/misc-docs/bigidea-prizes.pdf> (Last accessed 12th December 2011) at 16

Marketing has a strong incidence on demand and is another drain on possible investment in research and development and a contributor to the reduced accessibility of medicines. The criteria used to determine utility will be extremely important regarding the incentives of competitors for the prize fund to create an impression of utility through marketing and false reporting of safety and therapeutic value. The assessment criteria are also significant for interest in diseases, such as Orphan diseases, which effect a small proportion of populations.

HR 417 is a practical suggestion of the Medical Prize Fund and the general rules under which the fund would administer prizes.[772] The general rules state that companies who register new medicines with the FDA will compete for rewards by providing evidence of the inventions benefit patients based on measured improvements to health outcomes. Assessment criteria include,

> "(1) The number of patients who benefit from a drug, biological product, or manufacturing process including (in cases of global neglected diseases, global infectious diseases, and other global public health priorities) the number of non-United States patients. (2) The incremental therapeutic benefit of a drug, biological product, or manufacturing process, compared to existing drugs, biological

[772] Love, J., and Hubbard, T., 'The Big Idea: Prizes to Stimulate R&D for New Medicines' (Revised 26th March 2007) Available at: <http://www.keionline.org/misc-docs/bigidea-prizes.pdf> (Last accessed 12th December 2011) at 13

products, and manufacturing processes available to treat the same disease or condition.

(3) The degree to which the drug, biological product, or manufacturing process addresses priority health care needs, including:

a. Current and emerging global infectious diseases;

b. Severe illnesses with small client populations (such as indications for which orphan designation has been granted under section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb)); and

c. Neglected diseases that primarily afflict the poor in developing countries.

(4) Improved efficiency of manufacturing processes for drugs or biological processes."

Since the fund pays out over 10 years, there is scope for assessment of a pharmaceuticals true effectiveness, rather than overly optimistic proprietary trial data. Thus, although early payments may be made, later payments could be withheld as changes in the number of patients taking the medicine or the incremental therapeutic benefit is revealed to be less. This might be the case anyway if new assessments and rankings of medicines are made each year.

Moreover if the HR417 Medical Prize Fund has legal capacity, prize payments based on false indicators and data about the drugs from the

company registering the new product can be recouped with damages. Legal capacity will also mean that the Medical Prize Fund has liability in formulating its decision. Which may not be a problem if the sources of information and manner of deliberation are clearly set out and followed.

Love and Hubbard argue for a 'non-voluntary' scheme.[773] Whether the scheme is voluntary or compulsory also has an impact on the liabilities of competitors. Whether the compulsory or voluntary nature would effect the liabilities of the Medical Prize Fund are beyond my knowledge of USA constitutional and administrative law. In the UK if such a scheme were compulsory then the Medical Prize Fund would be subject to judicial review of its operation and decisions. This would be in addition to the contractual undertakings that it made in operating the prize fund.[774] A compulsory scheme would make more sense: Consider, the circumstance where the scheme is not compulsory and the patents on an FDA approved product are held in different hands. If one of those patent holders does not wish to be part of the scheme, this would affect payments to the volunteering patent owner and undermine the scheme's effectiveness.

Although the Medical Innovation Prize Fund makes no direct changes to market approval regulation, it may have consequences for the party funding the drug trials and the time taken to reach market approval might

[773] Love, J., and Hubbard, T., 'The Big Idea: Prizes to Stimulate R&D for New Medicines' (Revised 26th March 2007) Available at: <http://www.keionline.org/misc-docs/bigidea-prizes.pdf> (Last accessed 12th December 2011) at 15

[774] Carlill v Carbolic Smoke Ball Company [1893] 1 Q.B. 256

be an important factor. Moreover, would data exclusivity conditions still apply? Considering the objective of the fund to promote early competition it is likely that data exclusivity restrictions would be abridged or discontinued. As the fund pays out after therapeutic advances have been determined, does the fund shift the burden of clinical trials into the hands of companies with sufficient capital to afford the clinical trial outlay? If it does then it continues the present status quo rather than stimulating small sized patent holders to undertake clinical trials and product approval. The effect of the Fund in terms of borrowing and investment must be considered. Investors in pharmaceutical companies are familiar with the share impact a patent might have; how will the Fund alter their investment behaviour?

Contractual relations between the Fund and competitors may drain Fund resources particularly where incorrect data allows a new product applicant to earn a prize when they should not have done. Thus, the scheme would benefit from a clause requiring the Fund's legal costs in recovering wrongly claimed prizes to be automatically met by the product applicant who submitted misleading information. However this is complicated by payments that have been made to third party patent holders on the qualifying product. Whilst these parties were not party to the data submitted in support of FDA approval they will have received prize payouts. Since a significant component of FDA application information is subject to confidentiality, the Fund's access to this information needs to be

considered. Unless the fund can recover wrongly made payments then the fund poses no positive indicia for the safety of products.

Some products may not initially qualify for prizes, and although they later would the assessment may occur too late to permit sustainable development of medicines within that company's environment. This may or may not be a desirable outcome as the failure of that competitor would suggest inefficiency. However the failure may be based in a lack of success securing interim capital, rather than research and development inefficiency. This might be the case if the invention was targeted at poor populations.

Furthermore, there is no indication that the fund will have consequences on the submission of data and the accuracy of reporting. However, it would present the advantage that the FDA would be less likely to consider information concerning significant negative indications commercially sensitive, and thus not reveal it to consumers.[775]

4.2.3. **Tax Incentives**

Differences in the taxation of company profits have been noted to influence company decisions on where to locate their activities. As a

[775] Dobson, R., and Lenzer, J., 'US regulator suppresses vital data on prescription drugs on sale in Britain' (June 12, 2005) The Independent. Available at: <http://www.independent.co.uk/life-style/health-and-families/health-news/article493903.ece> (Last Accessed: 1st July 2009)

result, tax rates and tax incentives have a rich history of being used to attract company activity.

The UK's basic rate of corporate taxation is thirty per cent, which is lower than corporate taxation in most of its developed competitor countries. In addition to lower corporation tax the UK also offers significant inducement for research and development through research and development tax credits. These are particularly pertinent to pharmaceutical companies whose activities may include some research. The available incentive varies with the size of the company. For small or medium sized companies 150 per cent tax relief for research and development expenditure is available on staff and material costs. Large companies can claim 125 per cent tax relief for research and development expenditure on staff and material costs.[776]

As a means of encouraging research activity within the corporate sector, tax incentives are utilised in the USA, Canada and by all the member states of the European Union. They are not however, ubiquitously without critics.[777]

The obvious method of utilising tax credits to improve the availability of medicines has been through alterations in the magnitude of the incentive.

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[776] HM Revenue and Customs (UK). Available at: <http://www.hmrc.gov.uk/randd/> (Last Accessed: 1st July 2009)

[777] Griffith, R. (2000) 'How important is business R&D for economic growth and should the government subsidise it?' Briefing Note No. 12, The Institute for Fiscal Studies. Available at: <http://www.ifs.org.uk/bns/bn12.pdf> (Last Accessed: 1st July 2009)

This however, must be considered in the broader context of national attempts to resituate research and development industries within their own dominion and the perception of the benefits that increases in national research and development have on national welfare, rather than a legitimate interest in promoting research and development globally. The use of tax credits to improve the accessibility of pharmaceuticals is not as straightforward.

A proposal has been made to utilise a tax credits to encourage pharmaceutical companies to lower drug prices. Which would make the proposal an attempt to improve the accessibility of medicines. It does not replace the patent system, rather companies would receive a rebate on the tax due on their profits for that product based on the changes that they make to the price relative to the marginal cost of drugs.[778] How clearly these changes can be assessed is unclear, as is the body that will administer the credits and the qualification criteria.

Moreover, the gains in the reduction of pharmaceutical product prices are translated into a deficit in the receipt of money that the government would receive. Whilst the net income of the pharmaceutical company on the product will be increased, or stay the same. Thus, generation of the pharmaceutical products would not necessarily become more effective or cheaper. What happens under this system is that there is a slight change in the sources of revenue for the qualifying pharmaceutical company. The

[778] Lybecker, K. M, and Freeman, R. A., 'Funding pharmaceutical innovation through direct tax credits' (2007) 2 *Health Economics, Policy and Law* 267-284

essence of the proposal is that customers pay less and the government receives less money in tax. Where this scheme becomes attractive is where companies that intend to market products abroad qualify. This makes the State offering the tax credits more favourable as a discount is only required on the national product and the tax credits can be earned without restriction of product pricing in other countries.

Another proposal utilising tax credits involves redirecting research towards medicines that present therapeutic advances, rather than regulation of prices. Instead of receiving tax credits for all research, the tax credits would only be available for research on designated conditions. [779] However, there are a number of difficulties. With no limitation mechanisms for pricing, the loss of tax incentives from research and development on non-designated conditions would be transferred to product prices for medicines on designated conditions. Non-designated conditions would still present attractive markets and continue to be researched, most likely within the same facilities and by the same staff as designated conditions. Moreover, it is likely that many medicines for non-designated conditions would be found, at least until independent research demonstrated otherwise, useful for prophylaxis of designated conditions.

[779] The report specifically talks about WHO Essential Medicines, indicating that the author has no knowledge of how WHO Essential Medicines are identified. I have taken the liberty of substituting 'designated conditions.' What constitutes a 'designated condition' is best left to a National Health authority based on their disease demographics.

CHAPTER 5

TOWARDS OBLITERATION OF MISALLOCATION

"All too often, the production of financial capital seems to occur at the expense of social and natural capital."[780]

As seen in the previous chapter, the creation of a less problematic and effective system for generating and distributing medicines is difficult to envisage where innovation incentives are focused on the economic value derivable from the medicine itself rather than the wider impact of that medicine on human life. Managing incentives in a system as complex as pharmaceutical innovation is not a straightforward task. The main failing of the proposals in Chapter 4 is that they are primarily focused on post-patent supply and do not alleviate safety concerns or modernise our research methodology for pharmaceuticals.

The material in this Chapter takes a different approach, to improving accessibility, availability and safety, to the proposals in Chapter 4. In many ways it is radical, because it seeks to move away from proprietary methods of controlling inventive pharmaceutical knowledge. It is focussed on reducing the difference between the price and marginal cost of available medicines (5.1), modernising pharmaceutical research on the basis of contemporary technologies and historic lesson (5.2), and on improving safety (5.3). Thus, it is organised along the same line as

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[780] Senge, P. M., *The Fifth Discipline: The art and practice of learning organization* [Random House Business Books, 2006, London] xiii. Within the context of pharmaceutical innovation this quotation is a provocative stimulation for a speculative thesis: Consider, without being constrained to the institutions which exist today, how pharmaceutical innovation might be achieved with the wealth of technologies available and humankind's immense ingenuity.

Chapter 4's proposals were organised and assessed; that is accessibility, availability and safety.

5.1. Improving accessibility

Early freedom in the uptake of pharmaceutical technology ought to be facilitated if the objective of pharmaceutical innovation is to provide new or improved therapies for people suffering conditions. As we saw in Chapter 4 the significant proposals to improve the accessibility of medicines were mechanisms of forcing lower prices. Our solution for lowering the prices of available pharmaceuticals is completely different. Our methodology is to unlink the pressures of availability and accessibility (5.1.1. Research Disjoined) and our methodology for doing this is to extinguish property rights over pharmaceutical knowledge (5.1.2. Abandoning Pharmaceutical Patents) and thereby promote competition between manufacturers.

5.1.1. **Manufacture Disjoined**

Uncoupling the cost of research from the price of medicines is initially very difficult to conceptualize. Throughout our lifetimes our indoctrination has been that the cost of innovating and testing pharmaceuticals must be recouped in the sale price of pharmaceuticals or no one would do it. As we have seen there are examples that show this is not the case, but the discussion of how decoupling manufacture from research impacts on research, the systems of incentive for generating new pharmaceutical knowledge, and the systems for testing that knowledge will be discussed

in 5.2. For the moment we are concerned with the legislative reforms necessary for the decoupling and their effect on accessibility.

5.1.2. **Abandoning Pharmaceutical Patents**

There is a lot of legislation concerning pharmaceutical ownership and intellectual property rights. There is more than for any other patentable area. The most significant legislation however, are the national Patent Acts. For example, in the UK this would be the addition of pharmaceuticals to the 'are not inventions' list of §1(2) Patent Act 1977[781] and removal of entries specifically concerned with pharmaceuticals, such as §2(6), from the rest of the Act.[782] Depending on whether the transition is instant (with rights on currently patented pharmaceuticals extinguished) or a gradual phasing out (with no new patents for pharmaceuticals being awarded)[783] then it may not be necessary to retain National use requirements.[784] However, even if an instant change is adopted if other nations retain patents for pharmaceuticals provisions relating to the National services will be useful.[785]

Textual alteration of the leading international treaties on patents is straightforward even if organising the political consensus is not.

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[781] Also see Schedule A2 UK Patent Act 1977 as amended.

[782] The relevant sections for the UK Patent Act 1977 as amended are: §§1(2); 56(2)(b); 56(4); 128A(1);

[783] Historically the addition of technology areas to non-patentable subject matter has been done by ceasing to grant new patents on the technologies and by revoking granted patents with compensation. See, 42 USC § 2181 - Inventions relating to atomic weapons

[784] For example, §56(4) UK Patent Act 1977 as amended.

[785] For example, §56(2)(b) UK Patent Act 1977 as amended.

TRIPs[786] as the leading international agreement on intellectual property certainly requires amending,[787] as does the Paris Convention for the Protection of Industrial Property 1883.[788] More complicated are multilateral and bilateral trade agreements, and unified markets. For example removal of patents for pharmaceuticals within the European Union would require the amendment or annulment of 14 Directives[789] and 26 Regulations.[790]

However without pharmaceutical patents and exclusory practices, such as data exclusivity, we would expect competitive pharmaceutical manufacture to exaggerate the positive trends of old therapeutic areas in current day generic pharmaceutical markets, such as first generation analgesics. Thus, we would expect lower medicine prices, increased quality, and removal of inefficient producers from the market. Moreover, because process patents would not be available over pharmaceutical manufacture, dissemination of ideas should be more rapid which would lead to swifter improvements in pharmaceutical manufacturing, storage and distribution.

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[786] Agreement on Trade-Related Aspects of Intellectual Property Rights 1994

[787] Part I Article 39(3); Part II Articles 27(3) – on matters excluded from patentability; 39(3) – on data exclusivity encompassing pharmaceuticals; Part V may require renegotiation if some nations retain patents for pharmaceuticals.

[788] Article 1(3) Paris Convention for the Protection of Industrial Property 1883

[789] 2011/62/EU; 2010/84/EU; 2009/53/EC; 2009/120/EC; 2008/29/EC; 2005/28/EC; 2004/27/EC; 2004/24/EC; 2003/94/EC; 2003/63/EC; 2002/98/EC; 2001/83/EC; 2001/20/EC; 89/105/EEC

[790] EU/1235/2010; EC/668/2009; EC/249/2009; 2009/219/EC; 2008/29/EC; 2008/C243/01; EC/1234/2008; EC/312/2008; EC/1394/2007; EC/658/2007; EC/1902/2006; EC/1901/2006; EC/507/2006; EC/2049/2005; EC/1905/2005; EC/726/2004; EC/494/2003; EC/1085/200; 3EC/1084/2003; EC/847/2000; EC/141/2000; EC/2743/98; EC/2141/96; EC/1662/95; EC/540/95; EC/297/95

Moreover, the production methods employed to manufacture and package medicines generally follows a constant returns to scale relation. That is that the cost of producing five-hundredth batch is almost the same as producing the second or third. The absence of artificial limitations on supply will have important connotations for the least economically wealthy nations, where even if local pharmaceutical manufacturing is unviable philanthropic assistance will have greater purchasing power.

Employment in the pharmaceutical manufacturing sector will also be affected by reinstating pharmaceutical inventions as public goods. Without the pharmaceutical patent, and with the cost of research disjoined from the price of purchasing a medicine, the individuals earning many millions USD each year may no longer do so,[791] and pharmaceutical manufacturers might not perpetually remain amongst the top five most profitable industries each year. However, there would likely be no loss in the number of jobs within the pharmaceutical manufacturing industry. If the Indian experience is indicative of the effect of abolishing the patent, then there would be an increase in the number of jobs in the pharmaceutical

[791] For example, Miles White - Abbott - $33.4M; Fred Hassan - Schering-Plough - $30.1M; Bill Weldon - Johnson & Johnson - $25.1M; Bob Essner - Wyeth - $24.1M. Data from: Staton, T. and Martino, M., 'Top 17 Paychecks in Big Pharma' (19 May 2008) FiercePharma. Available at: <http://www.fiercepharma.com/special-reports/top-17-paychecks-big-pharma> (Last Accessed: 1st July 2009)

manufacturing industry and an expansion of the industry's industrial capacity.[792]

Furthermore, the incentive to innovate under a monopoly is not necessarily greater than the incentive to innovate in a competitive market.[793] Amongst the least economically wealthy nations, the countries not adopting strict patent policies have developed stronger domestic research facilities and been more innovative than the least economically wealthy nations that did.[794]

Whether pharmaceutical knowledge is a public or artificially private good is a choice of society. As we have stated knowledge is by nature a public

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[792] Lanjouw, J. O., 'The Introduction of Pharmaceutical Product Patents in India: "Heartless Exploitation of the Poor and Suffering"?' (1998) National Bureau of Economic Research Working Paper, W6366.

[793] Ng, Y.-Q., 'Competition, Monopoly and the Incentive to Invent' (1971) 10 *Australian Economic Papers* 45-49. Paper re-establishes Arrow's conclusion showing that the incentive to invent is greater under competition than monopoly. The analysis has some conditions that need to be considered in context of pharmaceutical innovation, such as the ability of the second inventor to reverse engineer a product, or the value of pre-invention incentives for non-drastic inventions. Unlike Davis, I find that the model is acceptable, with relation to pharmaceuticals, for both drastic and non-drastic inventions, admittedly pharmaceuticals can present a more complex situation as prices are also a function of marketing. See: Davies, K. 'Competition, Monopoly and the Incentive to Invent: A Comment' (1971) 14 *Australian Economic Papers* 128-131; Ng, Y.-Q., 'Competition, Monopoly and the Incentive to Invent: A Reply' (1977) 16 *Australian Economic Papers* 154-156

[794] Brazil and India are examples of countries that were poor but did not implement strong pharmaceutical patent rights initially. Whilst Thailand and South Africa were poor, but implemented strong pharmaceutical patent rights. Also see, Davidson Frame, J., National Commitment to Intellectual Property Protection: An Empirical Investigation (1987) 2 *Journal of Law and Technology* 209-227

good. Neither pharmaceutical companies, nor patents, are natural persons; they are not endowed at birth with unalienable rights from God.[795] They are created by governments and as such can be ended by governments, modified or adapted to best fit the needs of society. Such is the purpose of government to organise the rapports of society in society's best interests. What those interests are is not always clear or even easy to decide. However, it is clear that the pharmaceutical patent system currently makes pharmaceutical prices exclusive of many people who need them.

5.1.3 **Reduced Delay**

Any delay to availability or accessibility of medicines may have mortal or long-term detrimental consequences for people suffering the target condition. In this light it is preferable that available pharmaceutical therapies are accessible as soon as they are considered safe.[796]

There are substantial economic rewards for society in decoupling research from manufacturing and removing the patent from pharmaceuticals. We can currently see an indication of this from Germany and the UK. Both Germany and the UK pharmaceutical industries make significant gains

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[795] Jefferson, T., (1776) ME 1:29, Papers 1:315. Transcription copy available at: <http://www.princeton.edu/~tjpapers/declaration/declaration.pdf> at 2

[796] Nelson and Merges argue that early freedom to use inventions should be an essential component of intellectual property, in the context of pharmaceutical therapies their arguments are especially poignant. See Merges, R., and Nelson, R. R. On the Complex Economics of Patent Scope. (1990) 90 *Columbia Law Review:* 839-916. Particularly at 908.

from the manufacture of medicines without patents.[797] This creates jobs, increases supply security and helps to converge supply and demand.

In a market where competition on patentless medicines occurs, the centralised buyer, i.e. the NHS, is able to invest savings, from only paying research, development, clinical testing and manufacturing related costs for medicine innovation, improvement and supply. Moreover, a significant component of the public funds input will not be reallocated into private hands.[798] Which will have a consequence on grey markets and the degree of risk manufacturers are willing to undertake to increase profits through illegal or dangerous practices. Moreover, even in these conditions pharmaceutical manufacturing may remain lucrative as the full extent of demand for pharmaceuticals is met.

5.2. Improving Availability

If research and manufacture are uncoupled, the costs superfluous to research removed, (for example marketing, lobbying and shareholder dividends). Moreover, if the same level of funding is directed to research

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[797] Competitiveness and Performance Indicators 2004, PICTF. Available at: <http://www.advisorybodies.doh.gov.uk/pictf/2005indicators.pdf> (Last Accessed February 2006)

[798] "Tracking government-funded research to develop new treatments, a Spotlight team investigation revealed a billion-dollar taxpayers' subsidy for pharmaceutical companies already awash in profits. The investigation also documented a pattern of scientists and universities cashing in on government-funded inventions." See Dembner, A., 'Public handouts enrich drug makers, scientists' (April 5, 1998) *The Boston Globe* A1

and development then research productivity should increase as a result of efficiency gains. This may entail other methods of collecting some of the funding that the population would save on medicine prices and channelling it into research and development to make up the previous industry investment on research. This could be done through a small increase in taxation. It would be an unpopular move, but the advantages in the instant change to the accessibility of medicines might offset its general unfavourable reception. Within the UK reductions in pharmaceutical prices would be less than in the USA which would mean that the UK would need a higher level of taxation than the USA to recuperate enough of consumer spending on pharmaceuticals to sustain research levels.

There may be a slight shift from private health care in the UK to the NHS if savings allowed expansion of NHS services into areas where previously only private treatments were available. Changes in the USA would be viable without significant legislative intervention in domestic health insurance or Medicare. Both in the UK and USA there may be savings in health insurance premiums.

Restoring pharmaceutical knowledge to a public good has more advantages than the increased purchasing power of capital spent on pharmaceuticals for both production and research. It permits implementation of the most productive pharmaceutical invention paradigm.

We explained that the degree of testing necessary to achieve a successful dye disfavoured the single chemist.[799] This is true of pharmaceutical and biotechnology research today. Nearly all researchers work in a laboratory they share with other researchers. Whilst they may conduct all the experiments of their research they will at some point interact intellectually with the ideas of the other researchers. Most likely they will even work in small teams. However, because knowledge that might lead to a pharmaceutical patent is potentially extremely valuable there is an innate bias towards secrecy and avoiding any collaborations that are not absolutely necessary.

This same patent focused mentality also causes another loss to society.

> "The current innovation system encourages researchers to patent and commercialize discoveries that in an earlier era were considered basic science insights."[800]

Without the potential for pharmaceutical patents, basic science insights can exist again. Furthermore, with the loss of reticence to share knowledge collaborations and inter linking of expertise becomes preferable.

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[799] Section 1.2.1. New Research Paradigm

[800] Taylor, P. L., 'Research sharing, ethics and public benefit' (2007) 25 *Nature Biotechnology* 398 - 401

5.2.1. **Research Networking In the Digital Era**

According to DiMasi's uncertain estimates, 23 per cent of NCEs are granted FDA approval.[801] Kettler providing an update of DiMasi's cost estimates to 1997 values notes that the "cost of new drug development is critically dependent on the proportion of drugs that fail in clinical testing."[802] Comanor utilises these propositions to infer that,

> "If recent scientific advances could reduce the proportion of failures, then the overall research costs would decline substantially."[803] Knowledge sharing has been noted to reduce the cost of knowledge creation, with knowledge spill over an important component of industrial progress.

Research networking and restoration of focus on the generation of high quality basic science will not be fully achieved in the field of pharmaceuticals in the presence of a pharmaceutical patent. There is too

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[801] DiMasi, J. A., Hansen, W., Grabowski, H. G., Lasagna, L., Cost of Innovation in the Pharmaceutical Industry, (1991) 10 *Journal of Health Economics* 107-142, at 121-126

[802] Kettler, H. E., Updating the Cost of a New Chemical Entity, [Office of Health Economics, 1999, London] at 26

[803] Comanor, W. S., The Pharmaceutical Research and Development Process, and its Costs. (1991) *UCLA Research Program in Pharmaceutical Economics and Policy*, paper 99. At 4.
Available from the eScholarship Repository at: <http://repositories.cdlib.org/pep/99-1> (Last Accessed: 1st July 2009)

large a self-interest. However, we have strong indications that increased research networking improves pharmaceutical innovation productivity.[804]

Some economic models of knowledge transfer assume the cost of transferring knowledge to be zero. Practically this is not the case. Knowledge transfer in the pharmaceutical and chemical industries is not costless. Primarily there are costs involved in data storage, data transfer and then the expertise required to understand the data.[805] Moreover where data is incomplete or requires experimentation to be fully understood there are other costs inherent to the transfer of knowledge which must be accounted for. Indeed amongst a survey of British firms knowledge transfer has been highlighted as the main reason for patent licensing agreements.[806] This is not the information and technical specifications provided in the patent application, but rather the know-how

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[804] If the trends in the number of NCEs compared to R&D investment are plotted, then European research productivity as a proportion of investment has increased, whilst USA pharmaceutical innovative productivity as a proportion of investment has fallen, becoming almost flat. Donald Light suggests this difference is the result of the European initiative of bringing applied research scientists together. Such a view is supported by changes in the behaviour of the large better performing pharmaceutical companies over 2011, with their forging of strong collaborative links between academic research departments under a forum controlled and monitored by the pharmaceutical company (For example, the Open Innovation Drug Discovery Platform). See, Light, D., 'Global Drug Discovery: Europe Is Ahead' (2009) 28(5) *Health Affairs* 969-977

[805] Gambardella, A., 'Competitive advantages from in-house scientific research: The US pharmaceutical industry in the 1980s (1992) 21(5) *Research Policy* 391-407

[806] Taylor, C.A., and Silberston, Z.A., The economic impact of the patent system: A study of the British experience [Cambridge University Press,1st Ed., 1973, Cambridge] 23.

and expertise of the inventors.[807] Utilisation of the patent for this purpose adds another dimension of complexity and expense to the acquisition of information, where a contract would have been sufficient, [808] a contract and patent licensing agreement are required.

With utilisation of digital media and the global infrastructure of internet communications the initial expense of establishing a system and maintaining it can be offset by the extremely low marginal costs of connecting more users, the increased ability of a larger group of specialists to contribute to research progress, the greater availability of information.[809] There are many examples of where successful collaborations, with varying degrees of technology, are being routinely performed over the internet.[810]

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[807] Allen, T., and Cohen, S., 'Information Flow in Research and Development Laboratories' (1969) 14(1) *Administrative Science Quarterly* 12-19

[808] Arora, A., 'Licensing tacit knowledge: Intellectual property rights and the market for know-how" (1995) 4 *The Economics of Innovation and New Technology* 41-59

[809] Bitzerab, P., and Schrder, J., 'Open Source Software, Competition and Innovation' (2007) 14(5) *Industry & Innovation* 461-476

[810] For example: Alliance for Cellular Signalling; BioBricks; BioForge; Biojava; BioPerl; BioPython; BioRuby; Bio-SPICE; GMOD; Human Genome Project; Simple Molecular Mechanics for Proteins; and the SNP Consortium. If these examples are not persuasive then consider the improvements that expanding research and development more broadly across an industry has compared to merely in-house research and development. For an analysis of Germany see, Becker, W., and Dietz, J., 'R&D cooperation and innovation activities of firms—evidence for the German manufacturing industry' (2004) 33(2) *Research Policy* 209-223

5.2.2. **Transaction Costs**

By allowing sustainable data sharing the internet has dramatically lowered transaction and technology transfer costs.[811] It has also provided more powerful retrieval tools and permitted the generation of much larger databases. It would be surprising if employment of its technologies in modernising, interlinking and opening research did not yield further advantages than have already been experienced over closed proprietary models of research.[812]

There are three points of concern when trying to establish a specialist research network across the internet and these have been the subject of much study.[813]

Firstly, there are the intermeshed issues of quality control and moderation of the database, which are also integrated into the parameters of who can contribute and the structure in which those contributions are added to the system. The degree of access to be granted might be based on being a member of a nationally recognised profession, or part of an institution, with all additions and amendments id stamped and dated. Security against malicious users and saboteurs has been utilised in many different open

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[811] Wellcome Trust. 'Costs and Business Models in Scientific Research Publishing' (2003) Available at: <http://www.wellcome.ac.uk/doc_WTD003185.html> (Last Accessed: 1st July 2009)

[812] Taylor, P. L., 'Research sharing, ethics and public benefit' (2007) 25 *Nature Biotechnology* 398 - 401

[813] An excellent resource on research collaboration via the internet is: Olson, G., Zimmerman, A., and Bos, N., (Eds.), *Scientific Collaboration on the Internet* [MIT Press, 2008, 1st Ed., Cambridge, Massachusetts]

contribution projects. It has been found that such systems can be made robust by requiring authors to log in, so that their id stamp appears on the edit; flagging new content and amendments for a probationary period and / or until they are approved by another author; and by keeping a back-up archive that allows fine tuned reversion. The most useful current form of reversion is considered to be by author, by date or both.

5.2.3. **Content Quality**

Moderators pose another difficulty entirely. However, within the research communities and the medical profession there are already established hierarchies, where more senior members are responsible for the conduct of their lab members or clinical staff. Extending the responsibility to them of moderating their teams contributions would not in most cases be a great burden. Particularly as in the current climate of 'publish or perish' they are likely to be party to publications by their team members. Once posted, material should be flagged so that database users know that it is uncorroborated. The work would be unflagged once it was confirmed by the findings of a group independent of the initial entry, whose data would expand the statistical significance of the data. Moreover, a second author to unflag database contributions is not a burdensome requirement as there are most likely other researchers in the same or very similar field that will read the contributions and utilise or repeat experimental components. A further advantage of this system is that it advertises the work of a research group intimately allowing for more frequent collaborations that are far less onerous to organise. The ability of other groups to expand or comment on

research findings also increases the quality of the data. Only the authors submitting the paper and the journal editor see most reviewer comments for peer review journal publications. Such comments may be of interest to a wider audience, particularly when they impact on the validity of the experimental results. Importantly reviewer comments and entries by other research groups are likely to expand the interest of the work and increase the linkages with other spheres of knowledge.

Omotani comments that,

> "...two processes, dialogue and implementation -...reflection and action – moving in parallel, and feeding each other..."[814]

were responsible for the improved student performance within a learning community. There are parallels with that community and scientific research communities.[815]

> "It wasn't any one thing that happened that enabled this or that innovation to occur. It was definitely the result of those conversations. It was all about developing a capacity to talk together

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[814] Senge, P., The Fifth Discipline: The Art and Practice of the Learning Organisation [Random House Business Books, 2006, 2nd Ed., London] 308

[815] There are fewer similarities with non-hard science areas of research which lack pretence of objectivity, such as philosophy. Non-hard science questions are distinct through the inapplicability of the Popperian falsifiability criterion. Non-hard science disciplines lack the need to accept contentious theoretical ideas, instead they are rather 'intuitive.' Thus, in non-hard science disciplines it is less important to find a convention that can be regarded as objective.

in very diverse groups, developing a collaborative network of people who were supportive of one another..."[816]

Improving research methodology is more readily effected by subjecting work to the attention of other groups in the same field and perhaps related fields. By creating a database where such communities may undertake a conversation would improve the quality of research, create a natural system of rating significance and improve transparency. This would be exceptionally useful for clinical trial data, where subsequent independent findings too often present a different picture to the data generated by the pharmaceutical company applying for market approval.

5.2.4. **Simple Or Complex**

Secondly, there is the issue of sophistication. The more advanced the search and archival systems, the more sophisticated the imaging and graphical interfaces, then the higher the specification of computers required. Not all countries have access to advanced computing facilities. Thus, either alternative less demanding retrieval and archival platforms would concurrently be needed, or some gradual initiative to facilitate access and contribution to the datasets. There is balance to be achieved in limiting the sophistication of databases to improve accessibility of the data. Limiting the sophistication of a database too greatly may create problems for the presentation of information, the establishment of a community 'conversation' and thereby prevent the technological platform

[816] Senge, P., The Fifth Discipline: The Art and Practice of the Learning Organisation [Random House Business Books, 2006, 2nd Ed., London] 308

being used to full advantage. The database needs to be viable, manageable, and yet at the same time prospective enough not to be limitative or retardative of the research effort. Indeed, the database should be a precursory 'conversation' to the database's creation.

5.2.5. **Upkeep**

The third problem is the expense, upkeep, and ownership of the superstructure. There are many solutions available from the studies of collaborative research projects. Many merely consider the interface of the parts of knowledge being interchanged and are more concerned with the allocation of the fruits of success rather than sustained ongoing collaboration. In such cases each collaborator has management, responsibility for their own resources. This would be an unsatisfactory position for a global research effort and might shift the burden of research to particular nations, thereby reintroducing the 'free-rider' objection to voluntary contribution and support systems. This however need not be the case. Obligatory proportional contribution could be required and complete dataset copies housed in more than one location, with all of them belonging to the global community or occupying server space leased from a national governments at cost. There are many possibilities for proportional contributions. For example, the cost of upkeep could be apportioned on the basis of GDP.

5.2.6 **Open Access**

A patent requires the inventor to disclose details about the invention, which are then placed on publicly accessible databases. The patent databases can provide a rich source of information that can facilitate in the development of new products. However, the patent entry may also require knowledge and understanding of the state of the art to understand and build on the invention. Or whilst the entry describes an invention it may be part of an incomplete mosaic that needs to be understood as an ensemble in order to embody the invention usefully. We should also remember the strategies of the German dyestuff manufacturers; who employed both secrecy and misleading patent data to extend their lead times. Indeed, a patent is no guarantee that the information filed is correct. Today, clever patenting of complex substances may indeed involve a dozen misleading patents, containing erroneous or untested knowledge.[817]

Patent databases can require specialist knowledge to navigate and use effectively, although basic searches are fairly easy to conduct. Moreover, the manner in which information is filed is not necessarily researcher friendly or sufficient. Neither is there any guarantee that the information is useful or accurate. It is common practice following discovery of what may be a successful medicine candidate to file patents on every drug of the same family. Many, if not all of these drugs will be less effective than the candidate chemical, not effective, or even detrimental for target group if its specification even mentions a target group.

[817] Informal discussions with patent attorneys (2004-2005)

Moreover, the restrictive effect of patents on the access to information on research methods and results may impose substantial efficiency losses in addition to the deadweight loss of monopoly.[818] To understand the mechanism claimed in a patent, investigators might need to conduct their own experiments in order to verify that the information is correct and to understand the mechanics of what is taking place. Whilst poorly drafted academic literature reporting experimental results can sometimes be lacking in the information that others need to replicate or fully appreciate the experiment, patents if it is possible to give the appearance of sufficiency invariably are.[819] As little information as possible is supplied and as long as the patentee is able to argue sufficiency and secure their claim, then their patent attorney has done their job.

In the absence of a defacto monopoly on the employment of information the data itself loses its economic value except in the very limited context of first mover advantage. Thus, data pooling becomes a greater possibility and with the excellent and growing information networking possibilities it would have a substantial impact on primary research. Moreover, since the

[818] David, P. A., 1992, "Intellectual property institutions and the panda's thumb: Patents, copyrights, and trade secrets in economic theory and history", Working paper #287, CEPR, Stanford, CA.

[819] Remember that a patent application must disclose the invention sufficiently clearly and completely that a person skilled in the art could replicate it. However, the notional addressee to substantiate or contest a patent is a complex construct that may be an interdisciplinary team (EPO T 460/87 - CLBA 1996 – VISCOSUD) of specialists (EPO T 164/92 - OJ 1995/305 - ROBERT BOSCH) and it may be possible to narrow down particular specialists to a very small number of people.

research is to be carried out by groups disconnected from the manufacturing and sales of the pharmaceutical, lead time is irrelevant, except as an advantage for the researchers to gather enough data for their publication. Optimistically, with the establishment of an open access global research database, then journal publications might become obsolete as the nature of publishing research findings changes to database contributions. The move from proprietary journals to free-access databases[820] would present substantial savings for research communities and educational institutions.[821]

5.2.7. **Tried And Excelled**

Successful collaborative projects utilising web based architecture for information exchange and joint publishing[822] present optimistic indications for the aptness of this medium for global collaborative research. Although none has yet existed on the proposed scale the historical antidotes suggestive that the methodology of open information sharing would be highly successful.

Moreover, the success of the German dyestuff pioneers was the institution of highly organised industrial research.

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[820] *Free* in the sense that a subscription is not required. The architecture of access, i.e. the cost of a computer, may be inhibitive of access. However, the deadweight or artificial scarcity in the price of access would be eliminated.

[821] Educational institutions are particularly important for specialist labour – reducing education costs might improve the labour pool.

[822] For example the Human Genome Project. See Arzberger, P., Schroeder, P., Beaulieu, A., Bowker, G., *et al.* 'Science and government. An international framework to promote access to data' (2004) 303 *Science* 1777-1778

> "The Germans had realised something the others had not - nature would only give up its chemical secrets under a collective assault by a large group of scientists."[823]

Unlike the 19th Century dyestuff chemists we now have access to technologies that allow us to communicate across the planet. To store, share and search an enormous quantity of data within seconds. Moreover, the cost of connecting others to that system has negligible marginal costs for those connected. The survey has not been done, but it seems highly likely that if medical researchers were asked if their work would benefit from their ability to access the research work of all other medical researchers in the world, to share ideas and perspectives freely without the institutional fetters of proprietorship, and to examine data of clinical trials (successful and unsuccessful) that they would respond affirmatively.

> "Data sharing is essential for expedited translation of research results into knowledge, products and procedures to improve human health."[824]

Even if an individual is capable of forming abstract relations between multiple sources of information and thereby realising practical benefits,

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[823] Drahos, P; Braithwaite, J., Information Feudalism: Who Owns the Knowledge Economy? [Earthscan Publications Ltd, 1st Ed., 2002, London] 40

[824] <http://grants.nih.gov/grants/policy/data_sharing/> (Last Accessed April 2007)

such linkage is not possible without the simultaneous awareness of the multiple sources of information.[825] Moreover, the greater the number of people exposed to information and/or the greater the available information the greater the likelihood of useful correlations being made.

As most inventive steps are arrived at on the basis of existing bodies of knowledge or by the serendipitous use or combination of existing technologies, it has been common throughout human experience for inventions to be achieved by different individuals unbeknownst to one another within a short time period. Three well documented and interesting examples are the hot air balloon[826], radio and penicillin, but there are many others. A global pharmaceutical research dataset would eliminated serendipitous duplication and channel such energies into collaborative research or later improvements. Moreover, the search through the database is no longer to discover what research directions have already been claimed around your research trajectory, but rather what useful results, expertise and possible assistance there is available.

With data from experimentation and clinical trials, both successful and unsuccessful, made available the greater the likelihood that the utility of the idea and the trial information can be put to further use. An argument

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[825] Kingston, W., *The political economy of innovation* [Nijhoff Publishers, 1984, The Hague] 26

[826] Lourenço de Gusmão, B. {1709} Fac-similé d'un dessin à la plume de sa description et de la pétition adressée au Jean V. (de Portugal) en langue latine et en écriture contemporaine. [Réunies S. A., 1917, 1st Ed., Lausanne] 7-17

along this line for collaborative input into innovation is well supported empirically by initiatives such as the GNU Project and Wiki.

Furthermore, if data pooling occurs then the practical elements of the innovation to production chain are free to focus on improvement, and if there is competitive behaviour without defacto monopoly each competitor must strive to be as effective and savant in their choices as they are able. The information gathering research institutions, on the other hand, are free to continue data pooling.

There is another advantage of data pooling across institutions. Burns and Stalker found that firms with mechanistic forms of organisation and hierarchic structures of control and communication were poorer innovators than firms that were organised in an organic form in an environment of consultation rather than command.[827] Presently where firms, research organisations and clinics enter into collaboration, the organisation is usually clearly hierarchically defined by non-disclosure agreements, intellectual property licenses and other collaborative contracts. If data is pooled but authorship is fully detailed, then the establishment of collaboration with useful partners is facilitated and whilst institutions can

[827] Burns, T., and Stalker, G. M. The management of innovation [Tavistock, 1st Ed., 1961, London] 6. See: Nordhaus, W. R., Invention, Growth and Welfare [MIT Press, 1969, 1st Ed., Cambridge, Massachusetts] 56; Aiken, M., Bacharach, S., and French, J., Organizational structure, work process, and proposal making in administrative bureaucracies (1980) 23 Academy of Management Journal: 631–652; Covin, J., and Slevin, D., Strategic management of small firms in hostile and benign environments (1989) 10 Strategic Management Journal: 75–88

maintain their agendas and hierarchical structures, the specialist can form organic consultative collaborations with relevant specialists across the world.

5.2.8. **Benefits Unbound**

Undeniably the 19th Century dyestuff leaders skilfully employed patents in conjunction with secrecy to deter entry and preserve market leadership. However, their growth, dyestuff expertise, and initial leadership of the market, were a direct result of their industrial research organisation. In a world where there are no pharmaceutical patents, where medical and medicinal knowledge is unowned there are no requirements for gatekeepers other than quality. In fact utilisation, development and production of others' research would be for the betterment of populations. Time stamped, author attribution on database entries would provide a stronger universal recognition system for insight and work than any existent today.

There are further benefits available from a non-proprietary system of global medical and pharmaceutical research. One of the problems amongst contemporary drug development teams is identifying key stages in their objectives. For example, where the team identifies a chemical with a minor therapeutic advance, should they continue their research in the hope of finding a major therapeutic advance, or should they direct their efforts into the commercial development of the minor advance.

Within my proposed system the development concern is not significant. Once the minor advance is identified then the research group can look for the major therapeutic advance, confident that their addition to the database will have already enriched global knowledge and been author attributed. Moreover, should a group find that the minor therapeutic advance beneficial in the treatment of a condition then it can set up and begin clinical testing. Moreover because of the openness of the information system, there is no inhibitory factor preventing the initial research group participating in the clinical trials. This would allow a closer interface between breakthrough research and clinical testing.

The sharing of information and the ease of collaboration should have important effects on reducing the cost of realising safe NCEs. It will also lead to a greater acquisition of expertise as researchers are subject to much more data and know how than they would have experienced working in small groups behind walls of secrecy and under the burden of creating blockbuster medicines. It is likely that reorganising pharmaceutical research in the way we have suggested will have a cut off point where investment in research starts to become less productive. However, amongst a larger pool of expertise and where all investigations are logged this point of diminishing breakthroughs with increasing funds should take much longer to reach.

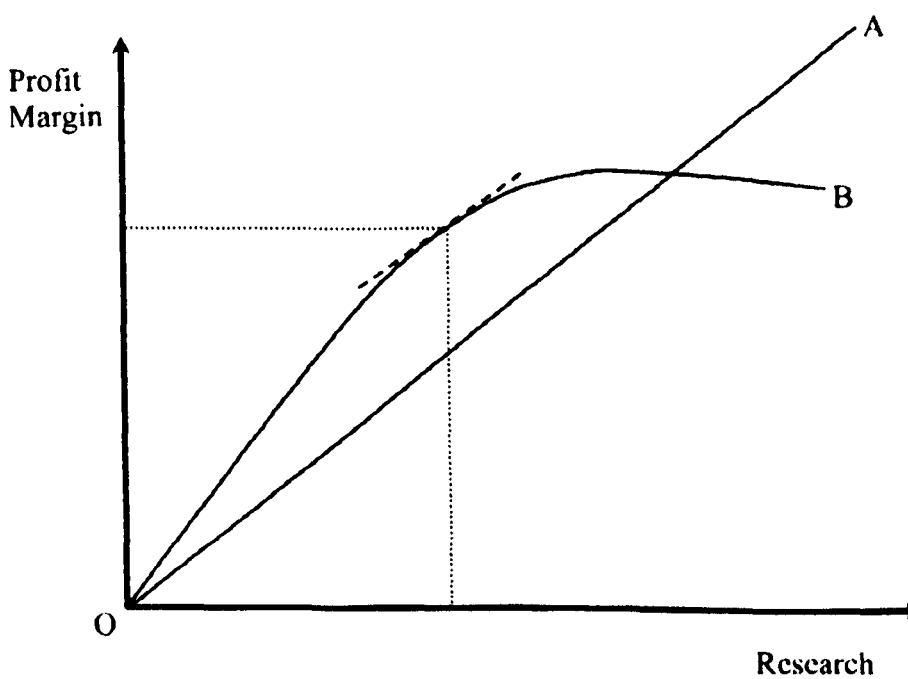
The Findlay extension of the Heckscher-Ohlin model that attempts to describe the production of two final goods (and an untradable product) in a

small open economy suggests that in the real world there is an optimal extent to which research can be utilised in the production of a good thereby realising a profit. Further research results in a loss of profit. Whilst this model seems to *prima facie* provide an argument for the strengthening of a patent monopoly with respect to research, it does not however suggest that with a longer monopoly more research would be conducted, or that there would be a greater focus on research before a product was released to the market. Indeed with the preference for as lower costs to profit margin as possible as the favourable *modus operandi* of manufacturing, it is in fact a very strong argument for the disjoining of research from manufacturing. Thereby permitting both research and manufacturing to be ends in themselves.

The Findlay extension considers capital and labour to be constants. The untradeable product consists of research that has been conducted, but that has at present no opportunity for profit. Within the model this will comprise all information that the manufacturer obtained through research investment, but is not positioned to exploit. Considering the possibility of employing licensing and non-disclosure agreements to supplant relations between firms, this research outcome must be considered to be without realised value. Within the context of pharmaceuticals, there may also be a more sinister interpretation: Indeed the information may contain safety contraindications and therefore affect the value of a product. However, forming a linkage between the untradeable research findings and the

products is an unnecessary complication to the clear simplicity of Findlay extension of the Heckscher-Ohlin model.

FIGURE 2. The Finlay extension of the Heckscher-Ohlin model comparing the profitability of two products, where one product (B) varies with increasing technological knowledge as a result of further research by the manufacturer, whilst the other product (A) develops as a result of technological diffusion to the market.[828]



This figure suggests that there is an optimal point for research investment and incorporation of research into a product. The dotted line indicates where increased research investment no longer adds to the profit margin of product B.

[828] Based on a figure in Findlay, R., Factor proportions and growth [MIT Press, 1st Ed., 1995, Cambridge, MA] 89

Consider two goods: For the purpose of Figure 2 let these be A and B. Where good A is the product of technological diffusion into a market with little or no innovation on the part of the manufacturer. Good B is the product of technological implementations resulting from research conducted by the manufacturer.

We label the abscissa simply as research and it should be borne in mind that B comprises a substantially larger research investment than A. [829] Thus as the degree of research incorporated into a good increases with the state of technology on the market, so does the research investment and cost of producing a more sophisticated product B.

In the absence of pharmaceutical patents and other exclusory rights this will only be true for manufacturing, although full disclosure of the manufacturing and quality control process as part of a licence as a pharmaceutical manufacturer will reduce the profit margin available from research into manufacturing. This will occur as disclosure reduces lead-time on the introduction of improvements in manufacture. However, the returns gained to the industry as a whole from access to almost all improvements in manufacturing and access to the research network should more than compensate for loses that a higher level of investment at an individual level might have inspired.

[829] For a full treatment of Findlay's extension of the Heckscher–Ohlin theorem see Findlay, R., Factor proportions and growth [MIT Press, 1st Ed., 1995, Cambridge, MA].

Profit margin does not apply to a public good in itself, only into products incorporating it. However, as applications are produced there will be savings to society with fewer and shorter hospitalisations and lower mortality. Whilst knowledge in itself is a public good, the labour of researchers and the database are private goods and thus, a Findlay extension may also present a valid general description that a cut of point in increasing returns on research investment will occur.

One of the main points with forcing research into academic research environs such as universities is that even when the research department does not discover potential blockbuster pharmaceutical, the university researchers publish their results in the data base. Thus, knowledge is continuously driven forward at lower marginal and transactional costs. The standards of research in a scientific community subject to peer review can be high, and though fraudulent claims of success are known in such environs they are invariably short lived. In clandestine research departments where scientists require management and legal authorisation to publish results or make statements to the press, the standards of primary research remain unknown elements. Whilst the research may be of a quality on par with peer reviewed institutions, it may well be otherwise. Openness and thoroughness are of crucial importance not only to science, but also with respect to clinical safety testing. There are many pharmaceuticals that have caused death and endangered people because they were purported to provide therapeutic benefit, when in fact they were

more harmful and no more effective for the target condition than a placebo.[830]

5.2.9. **More Expertise**

Maintaining and training medical researchers can be expensive and with the change in the nature of funding for university research facilities and the increasing dependence of universities on industrial partnerships, funding and training opportunities for postgraduate researchers are limited to very small spheres of specialisation. One of the most expensive components of the postgraduate researcher's development will be their access to knowledge and skill training. Secrecy plays an important part here, with the financial gains the university or researcher will obtain from devising a blockbuster drug, few risks of information leak are tolerated.

State conducted clinical trials in the absence of a patent would produce more reliable and fully available trial data. Moreover, there would by no need for the substantial expenditure on marketing and product promotion

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[830] Wagner, K. D., Kowatch, R. A., Emslie, G. J., Findling, R. L., Wilens, T. E., McCague, K., D'Souza, J., Wamil, A.,. Lehman, R. B., Berv, D., Linden, D., A double-blind, randomized, placebo-controlled trial of oxcarbazepine in the treatment of bipolar disorder in children and adolescents. (2006) 163 Am J Psychiatry 1179–1186; Hewitt, R. G., Yiannoutsos, C. T., Higgs, E. S., Carey, J. T., Geiseler, P. J., Soave, R., Rosenberg, R., Vazquez, G. J., Wheat, L. J., Fass, R. J., Antoninievic, Z., Walawander, A. L., Flanigan, T. P., Bender, J.F., Paromomycin: no more effective than placebo for treatment of cryptosporidiosis in patients with advanced human immunodeficiency virus infection. AIDS Clinical Trial Group. (2000) 31(4) Clin Infect Dis. 2000 1084-1092; Pande, A. C.; Crockatt, J. G., Janney, C. A., Werth, J. L., Tsaroucha, G., Gabapentin in bipolar disorder: a placebo-controlled trial of adjunctive therapy (2000) 2 (3 Pt 2) Bipolar Disord. 249–255

that presently occurs. Information regarding the use, risks, and effectiveness of medicines, including trial data, could be provided on an open and searchable database. Thus, not only would health practitioners have more information, more readily available there would be greater transparency towards the public as well. Furthermore, because the data presentation could be systematised the health professional or member of the public would be able to perform a direct comparison. There are costs involved in wrongly medicating, open access to accurate data on medicines should be expected to reduce, even though not eliminate, these costs.

Perhaps this is something that we need to remember when public or private research laboratories and organisations make even small seeming contributions to knowledge: However small, each advancement should be lauded. Nevertheless, all gains would be multiplied if the work and expertise of every other practicing researcher and clinician were available. Within this global scale of knowledge production even the largest research laboratories and networks of today would be considered tiny.

5.2.10. **Local Medicines**

Moreover, in the absence of patent restrictions knowledge migration and the establishment of fledgling pharmaceutical industries in countries where there is a large demand for medicines to treat indigenous diseases, but little foreign investment may occur. Historically, the absence or weakness of patents for pharmaceuticals has permitted the development of local

pharmaceutical industries. Whilst that will contribute to improvements in accessibility of some medicines, it will not address local endemic diseases by itself. As labour costs within the manufacturing industry within that country will be lower, these fledgling industries might perform well competing with manufacturers in economically wealthier countries. Indeed because of the cheaper labour pool foreign corporations may be stimulated to make direct investment in developing a local industry. Moreover, the savings, revenue, and development of technical skill derived by the society from its new industry may feed into application of science from other parts of the World into local problems. Furthermore as the industry increases the wealth of the nation there may eventually be sufficient resources to establish research facilities focused on endemic diseases.

Whilst knowledge may poses an irrepressible power and be difficult to contain expertise is more readily restricted, especially where the state of the art is particularly complex. Without education an open database of technical information is not as useful as it should be, which is a failing of our proposal. In an economy with rich research facilities the training of new generations of research scientists, clinicians and medical personnel would be facilitated by our proposal. Thus, education would not be an inhibitory factor in interaction with the database. However, in a country where there are no research facilities and only rudimentary education, the database would be incomprehensible. There may also be other applications, than education and endemic disease research, where invested capital would

have more health impact, such as the supply of clean drinking water and food security.

Nevertheless even in these circumstances our proposal has advantages over the present pharmaceutical patent system. The patent is by design restrictive of the establishment of local industries and expertise through both the property sovereignty function statement[831] and the knowledge feudalism function statement.[832] For a determinant player in the pharmaceutical industry to permit a country to develop a national pharmaceutical manufacturing and research industry would be to allow a potential threat to be established. Even if the fledgling industry catered to markets outside of the established companies' ambit there would be potential for that industry to eventually usurp parts of established pharmaceutical markets. This is as always reinforced by the lessons learned following the World Wars, the development of the Swiss pharmaceutical companies, and even the Italian pharmaceutical industry. In all cases the ability to absorb and exploit the knowledge of industries in other countries permitted these companies to begin manufacture, build expertise and then become global competitors.

5.2.11 **Utilising Potential**

Since intellectual property became an essential component of University science research funding and resources were diverted to establish intellectual property transfer offices the amount of documented knowledge

[831] See 3.1.

[832] See 3.2.

transfer from UK universities has increased. Many of the UKs world-class research universities have seen their research commercialised thus forming high-technology clusters around departments.[833] Following funding changes in Higher Education the UK suffered a large reduction in its supply science graduates, however incentives are being taken to renew numbers in some disciplines. That these graduates are of good quality relative to competitor nations and available at reasonable cost is a major attraction to research and development investment in the UK.[834]

Moreover, it is clear that along with foundations, hospital research facilities and public sector research agencies, that universities are responsible for discovering and financing the majority of the most innovative and health significant medicines.[835] Thus, they would be able to adopt and benefit from my proposed system with rapidity.

> "Private firms alone, in seeking to maximise their returns, will undertake less research than is socially optimal."[836]

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[833] Sainsbury Review. The Race to the Top: A Review of Government's Science and Innovation Policies. [HMSO October 2007] 5

[834] Pharmaceutical Industry Competitiveness Task Force, Competitiveness and Performance Indicators 2005, 8

[835] ABC News May, 29th 2002. Available from: <http://abcnews.go.com/onair/ABCNEWSSpecials/Pharmaceuticals_020529_pjr_feature.html> (Accessed 4th January 2004) (ABCNews.com page has moved or no longer exists.)

[836] Sainsbury Review. The Race to the Top: A Review of Government's Science and Innovation Policies. [HMSO October 2007] 23

Masters and doctoral students could provide a cheap and highly skilled research support community. Together with the openness and interlinkage within the research community, this would have immediate impact on knowledge generation and the acquisition of expertise. Furthermore, it would contribute to an enhancement in the teaching of science and technology at lower levels, especially where the disciplines were related to medicines and pharmaceutical technologies.

> "Demand for science, technology, engineering and mathematics (STEM) skills will continue to grow. The UK has a reasonable stock of STEM graduates...."[837]

Moving research back into universities, making it open and having the funds available to increase the number of researchers will improve job prospects for STEM graduates and may create an increased interest earlier in the education chain.

Systems of prizes and accolades could be implemented for breakthrough research leading to a scientific discovery, but it is not necessary. Since pharmaceutical knowledge is a public good and the database provides a forum for that knowledge generation, storage and retrieval all discoveries immediately enter into a global knowledge commons.

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[837] Sainsbury Review. The Race to the Top: A Review of Government's Science and Innovation Policies. [HMSO, October 2007] 6

> "[A]ny information obtained... should, from the welfare point of view, be available free of charge (apart from the costs of transmitting information). This insures optimum utilisation of the information but of course provides no incentive for investment in research."[838]

In practice all markets have inherent incentives for research this is true even when the market is not formalised or acknowledged; these include lower production costs, the ability to perform new tasks, access or creation of a new market, greater efficiency. However, incentives directed at the act of discovery, providing all unfavourable incentive generation is avoided, may facilitate knowledge sharing.

It has to be remembered that researchers are not just cogs in an innovation mechanism, they are people with interests, complexities and ambitions. Advancement within research institutions will hopefully be based on merit, which should provide some incentive.

In addition history supports Taussig's assertion that "...the race of contrivers and inventors does obey an inborn and irresistible impulse."[839] This is an experience that is already apparent in the research laboratory, it is just that under the pressures imposed by privatising pharmaceutical

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[838] Arrow, K. J., "Economic Welfare and the Allocation of Resources for Invention," R. R. Nelson (eds.) *The Rate and Direction of Inventive Activity: Economic and Social Factors* [Princeton University Press, 1962, New York] 616-617

[839] Taussig, F. W. Inventors and Money-Makers [Macmillan, 1930, New York] 21

knowledge priorities are shifted with a consequence for inventiveness and working relations.

If there were to be rewards for researchers, these could be based an assessment of literature produced by researches with respect to date. The first to disclose an important hypothesis in a manner that makes it persuasive as a hypothesis will be awarded a prize. If a researcher laid down an important part of the framework, but did not make the breakthrough they will be eligible for some share of the prize if not the prize itself. Prize could be of two parts consisting of financial reward and public accolade. Since the prize is awarded only after the knowledge provided by the hypothesis has been utilised successfully in the production of a result. The difficulty will be the breakdown of a discovery into discrete parts and then an assessment of each parts importance to the integrity of the thesis.

Scientific hypothesis would be available to be used by public research centres all over the world. These centres would be connected via fully accessible research intranet and database (the 'Commons'). All nations of the world could pay for these research centres as a proportion of GDP. Where they would be established would need to take into account resource access, e.g. availability of technical knowledge, transport and communication connectivity. Other factors such as corruption, infrastructure costs and civil stability are also important. Resources should be maximised, with as little waste as possible.

Closer interrelation between universities for research and hospitals for conducting clinical trials should be organised with relation to research centres. Postgraduate students conducting research into the life sciences could be employed part time. This would subsidise their own research expenses, provide low cost skilled labour and create a new generation of researchers for the centres. Universities, government laboratories and non-profit research institutions already play an essential part in developing new knowledge and knew embodiments of that knowledge.[840]

The revenue to pay for the dramatic increase in government sponsored research would have to come from taxes, however considering that the costs of research and the price of pharmaceuticals would be phenomenally lower there may be no need for significant increases in taxes. Indeed the median disposable income of the average citizen might increase despite a slightly raised tax rate.

Moreover, if the new methodologies of research were successful then the resultant increases in employment and quality of life might permit redistribution of funds to other projects, further increases in research, or a reduction in taxes. Moreover individual and corporate income taxes cause far less distortion than excise taxes like the patent system. Some deadweight, such as marketing and lobbying, would be entirely eliminated.

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[840] Nelson, R., R., US Technological Leadership: Where did it come from and where did it go? (1990) 19 *Research Policy* 119-132

5.3 Safer Medicines

It is clear that the magnitude of rents from pharmaceutical patents incentive patent holders to create health risks. Market approval could be based on a requirement of sufficient disclosure, i.e. the information required by a good scientific paper describing experimental results, which would include sufficient instruction for other scientists in the field to repeat the experiment. Imposing such a requirement would serve several purposes. Since most research would be the issue of research institutions before being taken up by development centres, such as teaching hospitals, the practice of keeping clear experimental accounts that permit others to verify scientists' work is both good practice and the usual requirement of research beyond undergraduate level. For reasons of safety it is preferable that detailed unbiased clinical trial records are taken. The results from a particular phase test may also indicate other applications for the chemical, or highlight little known conditions where a greater degree of monitoring and caution are required.

A sufficient disclosure requirement would also have significance for pharmaceutical compositions and manufacturing processes that producers under the present system would desire to keep secret. As we described,[841] even though a pharmaceutical product patent is taken early in the development of the pharmaceutical product, patents on the manufacturing of the product are usually taken much later, potentially

[841] Section 1.5

expanding the effective monopoly on the pharmaceutical.[842] A sufficient disclosure requirement would mean that all information necessary to the safety assessment of the pharmaceutical and its obtainment would be disclosed. The sufficient disclosure requirement would also ensure that the information discernable from a patent was available much sooner and in a form more convivial to technology transfer.

With patents for pharmaceuticals abolished and with research and manufacturing disjoined, clinical trials could be undertaken by university research groups and teaching hospitals.[843] Teaching hospitals are already responsible for the provision of much independent and sponsored clinical performance data for pharmaceuticals and the uptake of further reporting would create two important benefits. Firstly, because of the close interlinks between academic faculties and teaching hospitals, standardising reporting tools and databases would be expedited. Secondly, reporting would be more detailed and unbiased. Thereby permitting thorough monitoring of drug safety.

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[842] For example Oseltamivir, where patents on synthesising shikimic acid from Chinese star anise lagged product patents on Oseltamivir by nearly a decade. This might have endured for longer but with the threat of a pandemic and an apparent shortage of supply, third parties saw an investment opportunity. See, US Patents: 5952375 (Oseltamivir 1996); 6613552 (synthesis from star anise 2003); 6436664 (microbial synthesis 2002).

[843] For example in the UK Sheffield Teaching Hospital is notable for its trials on cancer drugs and Leeds Teaching Hospital for its clinical trials on Haematology products. Addenbrooke, Cambridge University's Teaching Hospital, currently has over 1000 projects and 400 clinical trials in progress.

The present system is particularly concerned with the speed at which pharmaceuticals progress to the market, this rush is partially based on the need to make the medicines available, and partially because every moment that the medicines spend being sold is generates income. In conjunction with this regime of speeded approval is an unsatisfactory post approval surveillance.[844] Elimination of pharmaceutical patents and clinical testing undertaken by teaching hospitals and public research institutions with full documentation made openly accessible in an online database would drastically improve the openness, and clarity of drug safety scrutiny.

Moreover, there is no indication that conducting clinical trials in this manner would delay pharmaceutical approval. It is more feasible that the increased number of specialists available to supervise trials would lead to faster approval times.

Post approval monitoring could be accumulated from data on all users of a medicine and uploaded onto the database making potential adverse indications more readily identified and loss of life kept to a minimum. Moreover, because every drug's full clinical history would be available to everyone, doctors would be able to make a fully informed decision as to which therapies would suit their patient.

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[844] Online NewsHour: Drug Safety. Available at: <http://www.pbs.org/newshour/bb/fedagencies/july-dec04/fda_11-23.html> (Last Accessed: 1st July 2009)

As drug safety is an extremely important failing of the current system improved impartiality and reporting of findings would be a considerable improvement. Open reporting in a standard reference database may also reduce the number of patients receiving incorrect diagnoses. This would reduce the instances of medication with the wrong medicines, which is a particular problem in some less wealthy countries, and lead to savings in all society's labour pools and resources.

Currently, proprietor generated clinical safety data and FDA regulation is unsatisfactory and many proposals have been made to improve it.[845] Foremost amongst these proposals is a legal requirement that pharmaceutical companies disclose to the public adverse effects as soon as they are discovered. Such a requirement would theoretically constitute a significant improvement legislatively.[846] But in practice if the penalty came in the form of a fine, would it be effective in prompting disclosure? Considering the pharmaceutical industry's past behaviour a fine would be insufficient deterrent and would in effect be deadweight transmitted to purchase of the company's pharmaceuticals. Criminal penalties might be more effective, but this is not a certainty. There is already a Corporate Manslaughter and Corporate Homicide Act in the UK and criminal measures against misadvertising neither has prevented loss of life arising

[845] National Public Radio, 'Experts Call for Changes to FDA Drug Approval' (Online Broadcast). Available at: <http://www.npr.org/templates/story/story.php?storyId=6226295> (Last Accessed: 1st July 2009)

[846] Actions currently are based on product liability and tort law, such as clinical negligence.

from pharmaceuticals being marketed when it was known internally to the company marketing them that they increased mortality. Adoption of legal requirements to disclose adverse effects have often been raised, but so far no measures have been taken to ensure that adverse indications are reported.[847] It is preferable that rather than tweaking a system that is skewed in its comportment towards profit in preference to safety, that a system promoting safety with little scope for distortion be adopted.

Moreover, in the absence of the pharmaceutical patent, and in a system where the mechanisms of research, development and clinical trials are separated from manufacturing then a disclosure incentive function statement[848] is unnecessary.

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[847] For example Peter Juni, a clinical epidemiologist at the University of Berne and one of investigators responsible for revealing to the public the elevated cardiac infarction risk of Cox-2 inhibitors see, Dobson, R., and Lenzer, J., 'US regulator suppresses vital data on prescription drugs on sale in Britain' (June 12, 2005) *The Independent*. Available at: <http://www.independent.co.uk/life-style/health-and-families/health-news/article493903.ece> (Last Accessed: 1st July 2009)

[848] See, Section 2.3.

Discussion

"The welfare of the people shall be the supreme law"[849]

We know that innovation occurs in the absence of a patent and that pharmaceutical innovation under a patent incentive is expensive. The balance between short run costs and long run sustainability of research in the Pharmaceutical Industry is skewed towards static efficiency. This is reflective of the diminishing numbers of new medical introductions.

Governments, the main purchasers of medicines, pay many fold the cost of innovating a medicine within its purchase price. Therefore, we know there would be more money to spend on innovating other therapeutic breakthroughs in the absence of a patent. We are also aware that a significant proportion of pharmaceutical inventions, which are later characterised as constituting therapeutic breakthroughs, originate in public institutions or institutions heavily subsidised by Government.

We know that scientific knowledge is essential to the development of new medicines and we know there is a growing trend for research scientists to withhold any knowledge that might have a practical application until they, their industrial partners, or their institutions secure a patent. Data sharing except within strict collaboration agreements is not practiced.

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[849] *Salus populi suprema lex esto.* Cicero, *De Legibus* III.viii.8.

The swiftness at which community research products develop is astounding, when compared to the slow rate of therapeutic advancement in the pharmaceutical industry. Moreover, the quality and diversity that can be achieved in community research products surpasses the accomplishments of individual private firms and inter firm collaborations. Historical paradigms suggest the validity of reorganising pharmaceutical research to include larger populations of researchers, and to promote knowledge sharing, to improve pharmaceutical innovation productivity.

Currently the cost of new medicines means that an enormous proportion of humanity are unable to afford the latest therapy regardless of the mortality of their condition. Health organisations avoid using more effective drugs because they are expensive leading to inefficient health outcomes and social cost. Drugs are not developed for conditions that afflict significant populations if those populations are poor. Patients have ongoing drug therapies changed or stopped as a result of monopolist price squeezing.

Safety information and disclosed indications for medicines are unreliable leading to thousands of deaths each year.

Marketing, lobbying, large dividends and legal expenses drain resources which might have been invested in innovation and jobs. Reduced medicine development and access to research inhibits national economic growth within the medical sector and has severe economic consequences for all employment sectors.

In addition to being expensive, pharmaceutical patents are an ineffective method of technology transfer.

Despite the overwhelming number of empirical examples describing the detrimental effects of the current patent based system of pharmaceutical innovation, positive reform is sidetracked, insufficient or bought to argue for a stronger patent system. Assuming that politician's motivations for a pharmaceutical patent system are not related to personal assets or party funding then it is likely that they believe that a strong patenting system provides convenient inducement for private investment in research and development.[850] Thus, stimulating technological progress and thereby improving health care and the welfare of their citizens.

However, if the mechanism of innovation favoured retards innovation and the size of the incentive distorts the behaviour of the investor to harm society's natural persons, then that incentive has failed. Moreover, its existence is a travesty - a breach of the special relationship that government has with the people of its society.

Moreover, considering the scale of the indicia and the frequency with which the disadvantages are manifested, it is doubtful that anyone could be unaware that the system is not working. Thus, we have to suspect that whilst pharmaceutical companies remain wealthy and their pockets

[850] Mazzoleni, R., Nelson, R., 'The benefits and costs of strong patent protection: A contribution to the current debate' (1998) 27 *Research Policy* 273-284

captivate politician's hearts, there will be no effective reform of the inefficient, retardative and unsafe method of generating new pharmaceutical therapies that the pharmaceutical patent system engenders. As things stand all the determinative players form an interlinked system of self-interest.

Aside from personal investment, politicians have substantial dependence on pharmaceutical industry funding for party funds and personal campaigns. The pharmaceutical industry is dependent on legislative bodies for its rights and government agencies for enforcement of those rights. The morality of a pharmaceutical company is a footnote to the returns on shareholder capital. Rights over pharmaceuticals, including the function of human genes, will continue to wax until there is a crisis and a different self-interest perturbs the balance. By the time that arrives we may well be dead. In the meantime the unnecessary loss of longevity and quality of life will continue.

> "The way we use and protect knowledge and ideas has never been more relevant to everyone. New ideas are... vital if we are to tackle global issues like climate change, shortages of resources and to develop better medicines."[851]

It is malignantly paradoxical that knowledge, inexhaustible and a necessary requirement of technological advancement, should need

[851] http://www.ipo.gov.uk/career/career-workforus/career-workforus-vacancy/career-workforus-vacancy-policy911.htm (Last Accessed: October 2008)

defending or guarding, especially when it could convey the ability to significantly improve lives globally. That use of knowledge is the chosen tool for retarding the access and availability of medicines is deplorable and darkly ironic.

APPENDIX 1

Summary of Signified Characters

φ^{A} presupposes the advantage of the patent system as a source of innovation incentive, compared to the absence of such a system. It holds that without the patent system the incentive for innovation will be insufficient to meet minimal community requirements.

φ^{A1} is the compound distortion of the assumption that without the patent system the incentive for innovation will be insufficient to meet minimal community requirements and that without the patent there would be no disclosed innovation

φ^{B} holds that inventors perform research leading to non-rivalrous inventive steps

φ^{B1} the longer the duration of a patent the greater the magnitude of incentive and thus, the greater the number of potential inventors persuaded to innovate

φ^{B2} the larger the breadth of entities capable of being patented the greater the domain of inventors to which the patent system provides incentive

φ^{C} assumes that an economic return is the most important incentive for inventive activity to occur

φ^{C1} assumes inventive activity occurs for the ability to perform new tasks, more effective performance, lower production cost, renown, the natural creativity of humankind, a rent in the innovation, patent circumvention, and altruism

φ^D the inventor and patent holder are the same natural person, or group of natural persons

φ^E Serendipitous invention, it is not a necessary condition for invention incentive, but it is a sufficient condition

φ^F that the invention may have more applications than the inventor anticipated

φ^G reinvestment of resources gained from an earlier invention, this is envisaged as a magnitude expressed as a proportion of the return on the earlier invention

ρ^A where a firm dominates a given market in the absence of rivalrous potential there is a tendency towards inventive indolence

ρ^B where competitive potential exists regardless of the limited number of rivalrous firms there is still incentive to innovate more rapidly than if there were no potential competitive provider to that given market

ρ^C increasing the fraction of the community exposed to knowledge of the invention increases the number of useful embodiments of the invention that might be discovered

λ inventive activity

λ^I inventive activity as a result of the invention incentive function statement

W^P is the cost of duplicated research and development project expenditure on existing technology

$W^{\partial P}$ is the cost of creating an additional forum or providing the necessary training so that duplicated research and development project expenditure on existing technology tends towards zero.

Invention incentive function statement: $\varphi^{A} \bullet \varphi^{B} \bullet \varphi^{C} \bullet \varphi^{D} \supset \lambda^{I}$

Disclosure incentive function statement: $\varphi^{A1} \supset \varphi^{F} \bullet \rho^{C}$

Investment Incentive function statement: $\varphi^{c1} \bullet \varphi^{C} \supset \lambda$

Organised derivative innovation function statement: $\lambda([\varphi^{G}] > [\varphi^{F} + \rho^{B} + \rho^{C}])$

APPENDIX 2

Survey on the Statistical Significance of Research Sources in Industry and University Pharmaceutical Research Environments.

820 questionnaires were addressed to researchers connected with pharmaceutical research in universities, biotech companies and pharmaceutical laboratories in the UK, France, USA and Canada. 221 completed questionnaires were returned (27 per cent). 156 declined to take part (19 per cent) and 396 did not respond (48 per cent). 47 replies (6 per cent of questionnaires) were discounted because they provided conditional responses, did not complete all sections of the questionnaire, or requested further information that may have lead their responses.

Although this survey provides some substantively important relations, the sample is small and may if a much larger population was examined be shown to be statistically insignificant. I was unable to identify the total population of pharmaceutical researchers in the sampled countries and therefore the level of confidence of this sampling is uncertain.

Bibliography

Since the bibliography is more extensive than generally found in a thesis of this length, it was considered easier to find and use material from the bibliography if the sources were categorised. Thus, biographical materials are arranged according to material type; books, articles, government and organisation reports, web based resources and newspaper articles are all referenced in separate sections within the bibliography. These sections are then arranged in alphabetical order by author and then, where an author has more than one cited publication, by date.

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