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A Critical Analysis of DG
Competition's Preliminary
Pharmaceutical Sector Report

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ANNO XXXII.
HENRICI OCTAVI

IN THE PARLYAMENTE BEGON
at Westm. the .xxviii. of Aprill, the .xxxii. yere of
the regne of the moste excellence, most hight, and moste
myghty prince, HENRYE the eighth by the grace of
GOD, King of ENGLAND, & FRANVCE
defendoure of the faythe, lorde of Ireland, and in earth
vnder CHRIS TIE supream head of the church of Englande, our
most redoubted souerayne lorde, there holden and afterwaies continued
by diuers prorogacions vnto the .xii. daye of Aprill in the sayde yere, & in
the last session thereof begon the same .xii. daye of Aprill, and from the same
holden vnto the .xi. daye of May, in the .xxxii. yere of his maiesties
most prosperous reigne, fro the which it was by prorogacion con-
tinued vntil the .xxv. of the same moneth of May, and holden
vntil the .xxiiii. daye of Iulie the sayde .xxxii.
yere: At which daye the sayde parlyament
was by his graces auctorite finished and
dissolued. Amonges many other the
actes folowing by his highnesse
with chasset of the lordes spi-
ritual and temporal, and
the commons assembled
in the sayd parlia-
ment, haue bene
established,
ordere
ned
and enacted.

ANNO, M.D. XI

The title page of 'The Pharmacy Wares Drugs and Stuffs Act 1540' (32 Henry VIII c 40) (© 2004 Blackwell Publishing)

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Abstract

This paper examines the Pharmaceutical Sector Inquiry initiated by the Commission on January 15, 2008 and the resulting Preliminary Pharmaceutical Sector Report issued November 28, 2008. It examines the Sector Inquiry's initial premises and its change of direction as reflected in the Sector Report. The paper performs a critical analysis of four areas of the Preliminary Report: 1. The Report's failure to address why fewer NME's were coming onto the market; 2. Litigation between originator and generic manufacturers; 3. The Report's failure to examine generic manufacturers' "Tool Boxes"; and 4. The Report's recommendations. Finally, the paper makes recommendations with the object of balancing incentives for innovation in the pharmaceutical sector with conditions for the effective entry of generic drugs into the market.

Summary

On January 16, 2008 DG Competition announced the initiation of a Sector Inquiry¹ into the Pharmaceutical Industry which it had begun by conducting unannounced “Dawn Raids”² the day prior at a number of Pharmaceutical companies. The key premise for the Inquiry as announced by Commissioner Neelie Kroes³ was the Commission’s concern that innovation in the industry was not proceeding as “it should” as measured by a drop in the introduction of novel medicines from previous years. Although the Commission has not alluded to earlier governmental investigations of the issue this appears have been a case of “Deja vu, all over again”⁴ (a phrase attributed to baseball player Yogi Berra.) The Commission surmised that the decline in bringing NME’s to market might be due to potentially anti-competitive actions by originator companies⁵. The Commission also sought information regarding whether anti-competitive commercial practices were used to delay generic competition with originator companies. The Commission’s allusions to unilateral abuses of dominant position, misuses of public procedures and vexatious litigation in speeches and press releases were generally understood to mean that the Commission suspected the existence of widespread abuses of public procedure such as it had found in its case

¹ Council Regulation (EC) No 1/2003 of 16 December 2002 on the implementation of the rules on competition laid down in Articles 81 and 82 of the Treaty (Text with EEA relevance) OJ L 1, 04/01/2003 p. 1 (“Regulation 1”) Article 17.

² See Regulation 1 Article 20.

³ Neelie Kroes, *Commission launches sector inquiry into pharmaceuticals*, Introductory remarks at press conference, Brussels, 16th January 2008, SPEECH/08/18 (the “January 16 Speech”). Found at

<http://europa.eu/rapid/pressReleasesAction.do?reference=SPEECH/08/18&format=HTML&aged=1&language=EN&guiLanguage=en> Last visited April 5, 2009.

⁴ See e.g. U.S. Government Accountability Office, *New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts 1*. Found at <http://www.gao.gov/new.items/d0749.pdf> Last visited March 26, 2009 (“GAO Report”) (Investigating possible causes of decrease in FDA submissions for NME’s since 1995 despite 147% increase in R&D spending.) October 2006 Congressional Budget Office Study Pub. No. 2589, *Research and Development in the Pharmaceutical Industry*. (the “CBO Study”) (Examining reasons for decline.) See also, Arti K. Rai, Jerome H. Reichman, Paul F. Uhlir, Colin Crossman, *PATHWAYS ACROSS THE VALLEY OF DEATH: NOVEL INTELLECTUAL PROPERTY STRATEGIES FOR ACCELERATED DRUG DISCOVERY*, 8 Yale J. Health Pol’y, L. & Ethics 1 (Winter 2008) (“Valley of Death”).

⁵ See the January 16 Speech at p. 3.

The information gathered will be used to look at two particular questions relating to the sector.

First, the inquiry will look at agreements between pharmaceutical companies, such as settlements in patent disputes, to see whether they infringe the EC Treaty’s prohibition on restrictive business practices.

Second, the inquiry will look at whether companies have created artificial barriers to innovative or generic product entry, through the misuse of patent rights, vexatious litigation or other means, to see whether such practices infringe the EC Treaty’s ban on abuses of dominant positions.

(Emphasis added.)

against AstraZeneca⁶. On November 28, 2008 the Commission released its 426 page Preliminary Sector Report⁷.

The Preliminary Report did not make any findings as to its original question, the alleged slowdown in the introduction of novel medicines. The only finding related in any way was the somewhat counterintuitive argument that originator firms created “patent thickets” of secondary patents to prevent other originators from patenting similar medicinal products. This appears to be an elision of the original problem namely, why fewer New Molecular Entities (“NME’s”) or New Chemical Entities (“NCE’s”) were coming to market. (Surprisingly, notwithstanding an abundance of evidence of the same pattern of decline in the approval of NCE’s in the US, the Sector Inquiry did not examine the US experience for evidence of some other causal factor⁸.) Secondary patents, the subject of the alleged Patent Thickets, appear to have nothing to do with NME’s. The Report failed to show how Patent Thickets could block anything other than minor changes from the originator drug or manufacturing processes. The fact that more patents are being filed would also appear to indicate that innovative improvements of some kind are being made.

The Preliminary Report also failed to mention any abuse of dominance cases similar to AstraZeneca by other Originators and did not investigate instances of vexatious or at least aggressive litigation by Generic producers. Instead, it analyzed originator/generic disputes and litigation from the point of view of originator commercial practices which the Commission named “tool box” whose purpose, (according to the Commission) was to deter originators from creating “me too” drugs and generic market entry. This change in focus resulted in a number of recommendations and hints by the Commission with respect to its taking action against the use of such “tool boxes”⁹. The outgoing FTC Commissioner has already made a public

⁶ The Commission’s Press release dated 16 January 2008 MEMO/08/20 *Antitrust-sector inquiry into pharmaceuticals-frequently asked questions Why has the pharmaceuticals sector been selected for such an inquiry* states “Through its own monitoring of the sector as well as through specific cases (e.g. the AstraZeneca case...the Commission has become concerned that competition may not be functioning optimally in the pharmaceutical sector.” Found at

<http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/08/20&format=HTML&aged=0&language=EN&guiLanguage=en> Last visited April 1, 2009. (“Commission 16 January Press Release”).

⁷ *Pharmaceutical Sector Inquiry Preliminary Report (DG Staff Working Paper) 28 November 2008*. Found at

http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/exec_summary_en.pdf (Last visited March 1, 2009) (the “Sector Report”).

⁸ See, e.g., The GAO Report and the CBO Study. See also, Frederic M. Scherer, *Pharmaceutical Innovation*, AEI-Brookings Center for Regulatory Studies Working Paper 07-13 (June 2007) Figure 2 at p. 47. Found at <http://ssrn.com/abstract=902395> Last visited April 1, 2009. (“Scherer.”) (Graph showing approval of NCE’s in the US 1970-2005.)

⁹ The Commission previously perjoritized normal business practices by using a similar term “toolkit for dominance” to describe GE’s access to capital in Commission Decision 2004/134/EC of 3 July 2001 in Case No. COMP/M.2220 General Electric/Honeywell OJ 2004 L 48, p. 1. The use of the term “toolkit” unleashed a storm of criticism, not the least from the U.S Department of Justice. See, William J. Kolasky, *Conglomerate Mergers and*

speech regarding the Report's "tool boxes" distinguishing between anticompetitive and lawful uses of its tools¹⁰.

The recommendations include changes to the patent system and restrictions on originators' abilities to use commercial practices such as IPR strategies.

The Preliminary Sector Report's changed focus appears to regard increased originator versus generic competition as an appropriate commercial model for innovation. This is puzzling as the generics' business model is to manufacture drugs after the originator's Exclusive Marketing periods end. The Report approaches the innovation problem by wishing to level the playing field between Originators and Generic producers during even the Originators' exclusive IPR periods. While decrying various originator practices as "tool boxes" to deter generic entry the Report fails to examine similar practices by generics. The Commission's recommendations appear to discourage, rather than encourage, investment in innovation in the name of lowering consumer prices.

While the Commission has no competence to alter patent law it makes recommendations for significant changes to it. It eschews, as outside of its competence, any attempt to examine the cost of pricing and marketing regulations in the 27 Member States (except to examine originator actions.) The Sector Report makes no examination of generic versus generic competition, an area that is within its competence and relevant to the sector's operation. Finally, the Report fails to distinguish between New Chemical Entities and Biologic Entities, the fastest growing segment of new therapeutics in which a substantial role is played by SME's. These acts and omissions in an ostensibly objective inquiry are puzzling and create questions regarding the information upon which the Report's recommendations are based.

It appears to me that the Commission had not read Aesop's Fable "The Goose That Laid the Golden Egg"¹¹ before it espoused its model of originator/generic competition.

Range Effects: It's a Long Way from Chicago to Brussels, Address before the George Mason University Symposium, November 9, 2001. Found at <http://www.usdoj.gov/atr/public/speeches/9536.htm> (Last visited February 8, 2009.)

¹⁰ J. Thomas Rosch, *THE EC'S PHARMACEUTICAL SECTOR INQUIRY PRELIMINARY REPORT--WADING INTO THE THICKET OF THE ANTITRUST/INTELLECTUAL PROPERTY LAW OVERLAP*, FIW - Innsbruck Symposium on Innovation and Competition Law, February 26, 2009, Found at www.ftc.gov/speeches/rosch/090226innsbruck.pdf Last visited April 15, 2009, 2009 WL 576145 (F.T.C.) ("Wading into the Thicket") (Commissioner Rosch interprets some of the Report's originator tools as consisting of such elements as "repeated meritless infringement" actions.)

¹¹ I confess to emulating the Rt Hon. Sir Robin Jacobs, whose November 29, 2008 Speech at DG Competition's presentation of the Preliminary Sector Report cautioned those arguing after the fact that pharmaceutical prices are too high by quoting "The Pied Piper of Hamelin". See, e.g. Rt. Hon. Sir Robin Jacobs, *Patents and Pharmaceuticals-A Paper given on 29th November 2008 at the Presentation of the Directorate General Competition's Preliminary Report of the Pharma-sector inquiry*. Found at <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/index.html> Last visited

Preface

I wish to express my gratitude to Professor Hans Henrik Lidgard for his example as a scholar, his infectious passion for getting to the bottom of things and for his boundless patience. I am not quite sure how he managed to turn me into a competition /IP/pharmaceutical lawyer without my being aware of it but I am pleased that he did. He is one of the most remarkable persons I have met and I hope to continue my association with him. His impartiality won't be tested by the fact that he is also grading this thesis but I'm sure that he will smile when he reads this.

I am also grateful for the friendship and collegiality of my friends Doctorands Tu Nguyen and Timo Minssen. They are brilliant scholars and damn nice people.

I can't list all of the fine people who taught or participated in this program but they will definitely make their marks on the world. I would, however single out Asta Aleskute as someone of particular promise.

I also want to thank the people of the Kingdom of Sweden whose taxes made it possible for me to attend Lunds Universitet.

March 23, 2009) (the "Sir Robin Jacobs Speech".) Milord, I plead guilty - with an explanation.

Abbreviations

Abbreviation	Explanation
API	Active Pharmaceutical Ingredient
ATC	Anatomical Therapeutic Classification
Biologic or Biopharmaceutical	Medicinal product produced by using biotechnology
Biosimilar	Medicinal product approved as comparable to a biopharmaceutical
Blockbuster medicine	Medicinal product achieving annual revenues over one billion dollars
CBO	Congress of the United States Congressional Budget Office
Data Exclusivity	Period during which a generic product may not use clinical information submitted by originator in connection with obtaining marketing exclusivity
DG Competition	Directorate General for Competition of the European Commission
EMA	European Medicines Agency
EPC	European Patent Convention
EPO	European Patent Office
FDA	US Food and Drug Administration
GAO	United States Government Accountability Office
Generic	Medicinal product containing the same active ingredient or equivalent of an originator's medicinal product
INN	International Non-proprietary Name for pharmaceutical substances
IPR	Intellectual Property Right-right to the exclusive use of information
LoE	"Loss of Exclusivity" the period after a medicinal product loses IP, data and marketing exclusivity
MA	Marketing Authorisation-regulatory approval to sell a medicinal product
Marketing Exclusivity	Period granted by regulatory authorities during which no other entity may sell a specific medicinal product the jurisdiction regulated by that authority
NCE	New Chemical Entity-a new chemical substance that has not previously been authorised as available for therapeutic use in humans
NME	New Molecular Entity a new chemical or biological substance that has not previously been authorised as available for therapeutic use in humans
PCT	Patent Cooperation Treaty
Preliminary Sector Report, Sector Report, or Report	Pharmaceutical Sector Inquiry, Preliminary Report DG Competition Staff Working Paper, 28 November 2008

PTO	US Patent and Trademark Office of the US Department of Commerce
R&D	Research and Development
RMP	Reference medicinal product
RMS	Reference Member State
SEC	US Securities and Exchange Commission
SPC	Supplementary Protection Certificate

1 Introduction

Innovation is the lifeblood of the Pharmaceutical sector. If pharmaceutical companies do not provide more, better and safer medicines they are supplanted by those that do. Innovation also requires that originator companies sink vast amounts of capital into research in exchange for hoped for returns from successful innovation. The unique nature of medicinal products, that they be safe and effective for use in the human body, requires that a large proportion of these sunk costs be expended in meeting the many legal and regulatory requirements of commercialization. As a result, general economic welfare is advanced. However, in the case of the pharmaceutical sector one cannot advance general economic welfare without considerations of consumer welfare. This model necessarily creates tensions between the need to insure return on investment, incentives to capitalize the search for more innovation, and the benefits of providing them to consumers at affordable prices.

The Commission's Sector Inquiry initially focused on a perceived need to stimulate the introduction of Novel Medicines into the EU Market. It also sought to determine whether there were any anticompetitive bottlenecks deterring entry of cheaper generic copies into the market. The Preliminary Sector Report however, demonstrates a greatly changed focus to Originator versus Generic competition. At the end of its 426 pages the Report left its initial question unanswered. I reframe the question to distill its essence, much as the European Court of Justice will reframe a question referred by a National Court. To wit: "How can the Community encourage medical innovation yet at the same time provide a mechanism to provide cheaper medicinal products to the public."

2 Background

The pharmaceutical industry is large, global, and vital to the well being of the human race. The story of modern medicinal products is one of the great triumphs of innovation in modern times. It has been estimated that about 40% of the two-year increase in average life span for the period from 1986-2000 may be attributed solely to the launch of new drugs¹² and pharmaceuticals have played a dominant role in adding 30 years to average life expectancy over the last century¹³. It has recently been estimated that the introduction of just one new drug reduces overall *per capita* health care spending by 0.063%, (or US \$1 Billion) short-term, and 0.183%, (or US \$3 Billion) long-term¹⁴. A self-evident addition to consumer welfare.

Medicines enhance societal productivity¹⁵ by emulating, the words of Luke 7.22 “that the blind see, the lame walk, the lepers are cleansed, the deaf hear...”¹⁶

In modern times, drug development became highly regulated as governments sought scientific assurance that medicinal products are safe, pure, and effective. Developments in the Community have paralleled developments in the US regarding enactment of strict standards for marketing approval for medicinal products.

The Pharmaceutical Industry encompasses highly complex interrelationships between the Scientific Community, the Business Community and Government. The interaction embraces a number of different types of Intellectual Property, and a plethora of regulations

¹² See, Frank R. Lichtenberg *The Impact of New Drug Launches on Longevity: Evidence from Longitudinal, Disease-Level Data from 52 Countries, 1982-2001* (NBER Working Paper No. 9754 16 February 2003) (“Impact of New Drug Launches”) Found at http://www.rand.org/labor/seminars/adp/pdfs/adp_lichtenberg.pdf. Last visited March 17, 2009)

¹³ Michael Enzo Furrow, *PHARMACEUTICAL PATENT LIFE-CYCLE MANAGEMENT AFTER KSR v. TELEFLEX*, 63 Food & Drug L.J. 275, 319 (2008) (“Patent Life-Cycle”). (Citing, S.Hrg. 107-1081. Generic Pharmaceuticals: Marketplace Access and Consumer Issues, April 23, 2002. Prepared statement of Dr. Greg Glover, M.D., J.D., Pharmaceutical Research and Manufacturers of America, p. 49.)

¹⁴ Rexford E. Santerre, *The new drug offset effect: some national and international evidence*, MPRA Paper No. 13628 25 February 2009 at p. 19. (“Santerre”) Found at <http://mpa.ub.uni-muenchen.de/13628/> Last visited March 31, 2009.

¹⁵ Impact of New Drug Launches at p. 18 (According to Lichtenberg this averages out to a cost of approximately \$4,500 per life-year while delays in new product launches cost money in terms of delayed longevity increases.) This figure was later reappraised by Lichtenberg to \$6,750 with average figures for the value of a life year of between \$100,000 to \$150,000. Santerre at p. 5, (citing Frank R. Lichtenberg, *The Impact of New Drug Launches on Longevity Evidence from Longitudinal Disease-Level Data from 52 Countries, 1982-2001* Int. J. Health Care Fin. and Econ. 44:369-389). See also, Patent Life-Cycle at p. 319.

¹⁶ Luke 7.22, King James Bible. (The raising the dead department lies outside of the delimitations of this thesis.)

regarding governmental authorizations, and pricing. The system must also comply with various other legal regimes such as the securities laws¹⁷, product liability laws,¹⁸ and IPR. The latter is especially problematic in light of the exclusionary nature of IPR and the policies behind the competition laws. This complex mosaic of rights and obligations must then be repeated, with variations, in the 27 Member States of the EU. Because medical needs are universal, and the pharmaceutical market global, the Pharmaceutical Industry must also comply with a similar set of considerations in the US and indeed, worldwide.

2.1 Purpose

I want to explore how, on the one hand how to reward pharmaceutical innovation may be rewarded and future innovation encouraged, while on the other hand how to balance these interests against consumers' interest in obtaining cheaper and safer medical products.

Accordingly I perform a critical analysis of the Sector Report. I examine its premises, methodology, and conclusions. In order to do this I provide a brief description of the pharmaceutical market in the EU and the US, a summary of the Report, and analysis and criticism of representative areas of the Report and its methodologies. The length of the thesis is due to deficiencies in the Sector Report itself and because I intend to use the thesis as the basis for several articles.

Finally, I make some practical recommendations for improving the system and reducing the transaction costs of operating it. Hopefully this will help provide balance between encouraging investment in medical innovation and providing cheaper drugs to the public.

2.2 Delimitations

The Pharmaceutical industry is global and involves an enormously complex set of interrelationships between many scientific disciplines, and legal and regulatory regimes. This thesis does not attempt to make a full description of or investigation into, all of the sectors of law, regulation, and commerce in which the industry functions. The vast scope of such an endeavor is beyond the proper bounds of this thesis. I do not have either the linguistic tools or the space to perform more than a sampling of how the 27 individual Member States resolve various problems of internal law or litigation, how they implement relevant directives into their legal regimes, or how they

¹⁷ See, e.g. *Cozzarelli v. Inspire Pharmaceuticals, Inc.* 549 F.3d 618 (4th Cir. 2008) (Dismissal of Securities Fraud Class Action stemming from public statements made regarding clinical trials) and *In re GPC Biotech Securities Litigation*, 2009 WL 367534 (S.D.N.Y. February 13 2009) (Securities fraud class action complaint stated claim regarding public statements made about "fast track" clinical trials).

¹⁸ See e.g. *Wyeth v. Levine, _U.S._*, 2009 WL 529172 (U.S. Vt. March 4, 2009.) (Approval of warning label by FDA did not preclude State law failure-to-warn claims.)

resolve conflict with actions of the Commission and/or other Member States. Instead, I shall give a general description of the manner in which the industry works, and areas of intellectual property law, competition law, and regulation using EU and US statutory and case law to illustrate some the problems encountered in encouraging innovation and general welfare while simultaneously increasing consumer welfare.

The size of the Sector Report (426 pages), its many areas of inquiry and somewhat fragmented construction create additional limitations. I select, examine, and criticize four areas or representative arguments from the Sector Report. The Sector Report was originally to have been finalized in Spring 2009. I had expected to incorporate the final report but only examine the Preliminary Report here because the timetable for the final version has now been set back to some time in Summer 2009¹⁹.

2.3 Methods

I employ the following methods to examine the Preliminary Sector Report and its recommendations:

The Comparative Legal Method

Comparative law, with an emphasis on comparing the legal and regulatory regimes applicable to the pharmaceutical industry in the EU and the US. I shall refer to statutes, regulations, and case law as well as learned articles examining areas of inquiry.

Law and Economics Method

Law and Economics, dealing with the interplay of the various legal structures and how they affect innovation in the pharmaceutical industry. In so doing, I also utilize statutes, regulations and case law as well as articles examining areas of inquiry. I shall place special attention on applying some of the transaction cost principles underlying the Coase Theorem²⁰ to the question of the best method of cross-disciplinary dispute resolution.

Traditional legal (dogmatic) Method

I use the traditional legal method, also known as the dogmatic method to interpret and systemize applicable law. I shall utilize sources such as laws, case-law, preparatory work and doctrines and assign them value and analyze them in so as to shed light on the problem and find answers to the questions that have been posed.

¹⁹ See Pharmaceutical Sector Inquiry web site. Found at <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/index.html> Last visited April 7, 2009.

²⁰ See e.g. Ronald H. Coase *The Problem of Social Cost*, 3 J.L. & Econ. 1 (1960), (reprinted in, Kenneth G. Dau-Schmidt, Thomas S. Ulen, *Law and Economics Anthology* (1st Ed. Anderson Publishing Co. 2002).

2.4 Outline

The first part of the thesis (section 3) sets forth a short overview of how the Pharmaceutical Industry functions in the EU and the US. This includes a summary of the process from Innovator R&D through the various stages of IPR and Marketing Approval. I summarize how Generic pharmaceutical companies develop and bring to market generic versions of medicinal products which have lost their IPR protection. The summary includes a description of the regulatory regimes including Marketing Authorization, Pricing and relevant differences between the EU and US.

In the second part of the thesis (section 4) I summarize the Preliminary Sector Report and its recommendations.

In the third part of the thesis (section 5) I analyze and criticize four problems with the Preliminary Sector Report and its recommendations.

In the fourth part of the thesis (section 6) I make practical recommendations for resolving some of the main problems identified in the Preliminary Sector Report with the aim of balancing the interests of promoting investment in continued innovation and increasing general and consumer welfare.

3 THE PHARMACEUTICAL SECTOR IN THE EU AND THE US

3.1 The Organization and Function of the Pharmaceutical Industry in the EU and US

3.1.1 Historic Development of Regulatory Schemes

All has not been sunshine and light in the world of pharmaceuticals. What is invented by man may be subverted by man. Snakes exist outside of paradise²¹ and “snake oil” sales were some of the public health threats mandating imposition of governmental regulations and controls in the early Twentieth Century²². Regulations governing drug purity and efficacy became even more complex and exacting after several tragic incidents created intense public pressure for more and stricter testing prior to authorizing the sale of medicinal products to the public²³.

²¹ Indeed, it was thought that the antidote Mithradatium (© Mithradates VI of Pontus c. 120 B.C) without the requisite number of lizards, or Galen’s (c. A.D, 129-200) follow-on, Galene®, (a/k/a “theriac”) without the lizard’s bioequivalent number of snakes, negated their effectiveness. In Europe, only 1,300 years later, (1540) this resulted in the enactment of the Pharmacy, Wares, Drugs and Stuffs Act, (32 Henry VIII c. 40). *See*, J.P. Griffin, *Venetian treacle and the foundation of medicines regulation*, *Br. J. Clin. Pharmacol.* 2004 September; 58(3): 317–325 at pp. 317-318. However, it was only in 1718 that strict standards for Mithradatium’s manufacture were instituted in The London Pharmacopoeia. *See also*, Stata Norton, *The Pharmacology of Mithradatium: A 2000 Year Old Remedy*, *Molecular Interventions* 6:60-66, (April 2006).

²² *See, e.g.*, John P. Swann *History of the FDA*, Found at <http://www.fda.gov/oc/history/historyoffda/default.htm> (Adapted from *George Kurian, ed., A Historical Guide to the U.S. Government (New York: Oxford University Press, 1998)*)(Last visited March 5, 2009), *see also*, A brief History of the Center for Drug Evaluation and Research. Found at <http://www.fda.gov/cder/about/history/default.htm> (Last visited March 5, 2009). One example of a modern cure which never made it to the “Orange Book” was “Radithor, “a radium-containing tonic that sentenced users to a slow and painful death”. *See* History of the FDA website found at <http://www.fda.gov/oc/history/historyoffda/section2.html> Last visited March 24, 2009.) (Obviously the unfortunate victims did not take sufficient Mithradatium.)

²³ In 1938, in the aftermath of an incident involving the fatal poisoning of over 100 people the Federal Food, Drug and Cosmetic Act was passed (Codified as 21 U.S.C. §§ 301 et. Seq.) (the “FDCA”). In 1962 strict regimes for clinical drug testing were instituted after the sedative Thalidomide caused the birth of thousands of deformed babies in the U.K. (Pub. L. No. 87-781, 76 Stat. 780, Codified in Title 21 U.S.C.) *See*, Patent Life-Cycle at pp. 281-282 (2008) . *See also*, Adam R. Young, *GENERIC PHARMACEUTICAL REGULATION IN*

International harmonization is performed through a series of International Conferences on Harmonization in which representatives from the EU, the US, and Japan meet regularly for the purpose of harmonizing requirements for drug safety and efficacy and medicinal product registration²⁴. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was initiated in the 1980's by the European Union. Recently, DG Enterprise and Industry and the FDA entered into an agreed Transatlantic Administrative Action Plan to relieve unnecessary burdens of administrative practices and to permit more pharmaceutical industry resources to be focused on greater innovation and efficiency in the development of quality medicinal products²⁵.

The harmonization of pharmaceutical regulation has been a Community priority since 1965²⁶. In 1975 The Community formed the Committee for Proprietary Medicinal Products whose goal is to facilitate the adoption of a common position by individual licensing authorities²⁷. The process of holding clinical trials for medicinal products is presently harmonized via Directive²⁸.

The Commission has played an important role by developing Directives and Regulations aimed at harmonizing the procedures for determining the safety and efficacy of medicinal products and establishing examining bodies such as the EMEA²⁹.

THE UNITED STATES WITH COMPARISON TO EUROPE: INNOVATION AND COMPETITION, Wash. U. Glob. Stud. L. Rev., Vol. 8, Number 1, 2009, 165, 167-168. ("Generic Pharma. Reg.")

²⁴ See generally, The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) website. Found at <http://www.ich.org/cache/compo/276-254-1.html> Last visited April 5, 2009. (The last ICH meeting was held on November 14, 2008 in Brussels and the next meeting will be on June 12, 2009 in Tokyo.)

²⁵ Medicines Regulation: Transatlantic Administrative Simplification and Action Plan, 17 June, 2008. Found at http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/archives_en.htm Last visited April 17, 2009.

²⁶ Council Directive 65/65 EEC of January 26, 1965 on the approximation of provisions laid down by law, regulation, or administrative action relating to proprietary medicinal products, Official Journal (no. 22) 368, reprinted in 1965-1966 O.J. Sec. Ed. 20 (1972) ("Directive 65/65").

²⁷ Joseph G. Contrera, *THE FOOD AND DRUG ADMINISTRATION AND THE INTERNATIONAL CONFERENCE ON HARMONIZATION: HOW HARMONIOUS WILL INTERNATIONAL PHARMACEUTICAL REGULATIONS BECOME?* 8 Admin. L.J. Am. U. 927, 939 (Winter 1995).

²⁸ See, Directive 2004/10 EC of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of applications for tests on chemical substances OJ L 121, 1.5.2001 p.34-44 ("Directive 2004/10")

²⁹ Articles 55 *et seq.* of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Text with EEA relevance) OJ L 136, 30/04/2004 p. 1 ("Regulation 726/2004") set up the European Medicines Agency (the "EMEA"). The EMEA has the responsibility "for coordinating the existing scientific resources put at its

As will be noted in various citations herein the ECJ has been important to the implementation of Directives and Regulations aimed at harmonizing the issuance of Medical Authorization for medicinal products and the balancing of IPR issues.

More recently, DG Competition has asserted its competence examining, under Article 82 EC, the behavior of pharmaceutical companies in connection with regulatory compliance. Most notably its decision of 15 June 2005 found that AstraZeneca Plc. had abused its dominant position by misusing public procedures in the course of obtaining Member State Marketing Authority and the issuance of Supplemental Protection Certificates³⁰.

DG Competition, in its January 2008 Press release regarding the initiation of the Sector Inquiry cited AstraZeneca as typical of the abuses it expected to find in the pharmaceutical sector. The CFI heard the AstraZeneca appeal³¹ on November 26, and 27, 2008 and a decision is expected Spring 2009³². Perhaps not coincidentally, the Final Sector Report was originally set to be issued in Spring 2009 and has now been postponed to sometime in Summer 2009.

3.1.2 Research & Development

3.1.2.1 From Molecule through Market Approval

As a result of these stringent requirements for proving drug safety and effectiveness, the bulk of the time and money spent on bringing a medicinal product to market is expended upon compliance with regulatory requirements. The process is relatively similar throughout the industrialized world and operates generally as follows:

3.1.2.2 Compound Discovery and Decision to Commercialize

Typically, a new molecule with potential medically therapeutic effects is discovered through research and development (“R&D”) as opposed to

disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products.”

³⁰ See generally, COMMISSION DECISION OF 15 JUNE 2005 relating to a proceeding under Article 82 of the EC Treaty and Article 54 of the EEA Agreement Case COMP/A.37.507/F3-AstraZeneca (“AstraZeneca”).

³¹ Case T-321/05: Action brought on 25 August 2005 - *AstraZeneca v Commission* OJ C 271, 29/10/2005 p. 24

³² See Astrazeneca plc Fourth Quarter 2008 results, p. 7, Legal Proceedings, and Contingent Liabilities. Found at

www.astrazeneca.com/_mshost3690701/content/resources/media/investors/AZN-Q4-2008/q4-results-2008-figures.pdf Last visited April 7, 2009.

chance³³. More than 90% of the new molecular entities (“NME’s”) discovered between 1990 and 1999 came from originator pharmaceutical companies³⁴. This represented a change from the period 1965-1992 in the US when only 5 of 21 of the most influential drugs were developed by the private sector³⁵.

However, the process is fraught with difficulty, from the upstream research identifying promising genes, proteins, and biological pathways meriting further investigation to identifying downstream drug product candidates. Due to the high failure rate in determining if the substance is a good target candidate the process has been termed “The Valley of Death”³⁶. After deciding to go ahead and fund research, originator companies assess initial results of searches for new entities in terms of the likelihood of positive results.³⁷ At this point, pharmaceutical companies employ the first part of their patent screen, crossing off compounds that they believe cannot be protected by patents³⁸.

Small molecule drugs, the main focus of the Sector Report, typically work by affecting activity in human proteins (“Targets”)³⁹. Effective therapies have been developed for only a few hundred of the estimated 3,000 targets in the human genome⁴⁰. In recent years an average of only three drugs a year that act on novel targets have come to market⁴¹. Generally speaking the initial search for promising NME’s is done by pharmaceutical firms performing “high throughput screening” (“HST”) whereby promising compounds are robotically screened against target proteins⁴² (“Assays”). Initially, a class of compounds is isolated with potential for medical use. However, sometimes, as in the case of isomers, the compound may have the same atom to atom connectivity but a different spatial arrangement of the atoms which may have dramatically different biological activity (called “chirality”)⁴³. A subset of isomers, called enantiomers may involve only one

³³ One notable exception being Alexander Fleming’s discovery of the antibiotic properties of penicillium mold which had accidentally contaminated and killed bacteria he was culturing on a Petri dish. *See*, Scherer at p. 6.

³⁴ Patent Life-Cycle at p. 319.

³⁵ CBO Study at p. 27 FN 1.

³⁶ Valley of Death at p. 4 and FN 16 (Noting that “Valley of Death is a widely used term in scientific endeavors denoting the difficulties of translating an invention into a marketable product”)

³⁷ Drug Development at pp 162-163.

³⁸ Benjamin N. Roin, *UNPATENTABLE DRUGS AND THE STANDARDS OF PATENTABILITY*, 87 Tex. L. Rev. 503, 545-546 (February 2009) (“Unpatentable Drugs”).

³⁹ Valley of Death at p. 3.

⁴⁰ *Id.*

⁴¹ Valley of Death at p. 3. *See also*, GAO Report at pp. 17-18 regarding drop in submissions of applications for novel NME’s.

⁴² Valley of Death at 7-8 (citing *inter alia*, Konrad H. Bleicher, Hans Joachim Bohm, Klaus Muller, Alexander I. Alenine, *Hit and Lead Generation: Beyond High-Throughput Screening*, Nature Reviews, Drug Discovery, Vol. 2, 369-378 (May 2003).)

⁴³ Patent Life-Cycle at pp. 291-292 (Much of the information on these subsequent patents is derived from this article. Dr. Furrow is both a scientist and a lawyer. Martindale Hubbell, which lists affiliations and scholastic degrees for attorneys lists Dr. Furrow’s as: Harvard

the isomer with specific chirality having beneficial therapeutic effects⁴⁴. One example of how crucial this can be is that one enantiomer of the drug Thalidomide is effective against morning sickness while the other causes birth defects. The single enantiomer reformulation of selective serotonin reuptake inhibitor citalopram oxalate is nearly 100 times more potent than the original⁴⁵.

The process is extremely expensive and the risk of failure high⁴⁶. The high rate of attrition in recent years between initial discovery of a compound and its survival in HST tests as a viable candidate have resulted in reluctance among venture capitalists and pharmaceutical firms to invest in upstream research based upon early stage patents⁴⁷.

The process from drug compound discovery through the pre-clinical stage takes, on average about six and a half years⁴⁸.

It has been calculated that the average actual expenditure on new drugs, (whether successful or not) is \$17 Million per year for Phase I tests, \$34 Million per year for Phase II tests and \$27 Million per year for Phase II tests⁴⁹. NCE's average 12.3, 26 and 33.8 months and Biological Entities, 19.5, 29.3 and 32.9 months in Phase I, II and II clinical trials and 18.2 and 16 months respectively before obtaining final Regulatory approval⁵⁰. The process takes a great deal of time and thus the cost of capital must be assessed in addition⁵¹. Most pharmaceutical firms finance R&D and clinical trials from their cash flow and the real-cost-of-capital of roughly 11% per annum⁵² represents their assessment of a cost benefit analysis taking into

Law School, J.D., 2007, Harvard College, A.B., Chemistry, 1999; Harvard University, Ph.D., Chemistry, 2004.)

⁴⁴ Patent Life-Cycle at p. 292, Rebecca S. Eisenberg, *PHARMA'S NONOBVIOUS PROBLEM*, 12 Lewis & Clark L. Rev. 375, 425-427 (Summer 2008) ("Pharma's Nonobvious Problem".) (Describing the issue in *Forest Laboratories, Inc. v. Ivax Pharmaceuticals, Inc.* 499 F.3d 1293, 1303 (Fed. Cir. 2007) (*Forrest v. Ivax*) which involved a generic companies challenge to a patent on a (+) –enantiomer of the INN Citalopram unsuccessfully claiming that a prior patent on the racemic (all isomers) form rendered the subsequent patent obvious. It should be noted that Citalopram is one of the 219 INN's in the Sector Report.)

⁴⁵ Patent Life-Cycle at p. 293. (The reader is referred to Patent Life-Cycle for a more detailed scientific explanation.)

⁴⁶ GAO Report p. 8 Fig. 1. (Only 250 out of 10,000 compounds make it from initial discovery to the preclinical stage.)

⁴⁷ Valley of Death at pp. 9-10.

⁴⁸ GAO Report p. 8 Fig. 1.

⁴⁹ Spending on New Drugs at pp. 8-11.

⁵⁰ Henry Grabowski, *Data Exclusivity for New Biological Entities*, at Fig. 1. Working Paper June 2007. ("New Biological Entities") Found at <http://www.econ.duke.edu/Papers/PDF/DataExclusivityWorkingPaper.pdf>. (Last visited March 25, 2009.) (Grabowski Data Exclusivity".) See also, Spending on New Drugs at 10 Fn 11 (citing J. Di Masi, R. Hansen and H. Grabowski The Price of Innovation: New Estimates of Drug Development Costs *J. Health Econ.* vol. 22 pp 151-185 (2003). ("Drug Development") (12 months, 26 months, and 34 months spent on average on Phase I-III clinical testing.)

⁵¹ Drug Development at p. 163.

⁵² See Discussion in Drug Development at pp. 163-164.

account how much it will cost to bring a drug to market. The capitalized cost of bringing a drug to market thus averages out to a \$1.214 Billion development cost per new approved-drug⁵³. These costs have been estimated at higher or lower ranges depending upon databases and assumptions but they all point to huge costs for bringing a drug to market⁵⁴.

3.1.2.3 Comparison of R&D Spending in the US and EU

It is interesting to note that in 1986 R&D spending in the EU exceeded such spending in the US by about 24%. By 2004 EU R&D spending trailed US R&D spending by 15%⁵⁵. In 1990 European firms spent 73 % of their R&D in the EU and 26% in the US but by 2002 they spent 58% in the EU and 34% in the US⁵⁶. This calculates to \$4.96 Billion and 31,925 job years (or 1,680 research jobs) forgone in the EU from 1986-2004⁵⁷. The authors of European Price Regulation attribute this trend to price regulation in Member States and estimate that over the last 19 years this cost consumers 46 new medicines foregone (or 2.42 per year)⁵⁸. The Sector Report chose to analyze R&D from a Global perspective without any breakdown of EU R&D spending on the basis that pharmaceutical R&D was “global”⁵⁹.

3.1.2.4 Biologics

Biologics, (also referred to as “Biopharmaceuticals” or “Biological Medicinal Products”⁶⁰) are Medicinal products consisting of large molecules derived from biological processes as opposed to NCE’s which are small molecules, synthesized chemically⁶¹. The Commission has estimated that Biopharmaceuticals represented 9% of the 2005 EU pharmaceutical market⁶². In the US Biologics represented approximately 16% of new drug introductions in the 1993-2002 period with a strong “pipeline” of more than

⁵³ Spending on New Drugs at p. 13 (This includes spending on marginal drugs but not on new formulations of older drugs.) The cost per new drug includes the capitalized costs of drugs which did not make it through the approval stage.

⁵⁴ Sector Report para. 127 (Between US \$800 Million and \$1 Billion with some respondents suggesting lower costs.)

⁵⁵ Joseph Golec, John Vernon, *European Pharmaceutical Price Regulation, Firm Profitability, and R&D Spending*, (August 2006) at pp17-18. (“European Price Regulation.”)

Found at <http://ssrn.com/abstract=932989> Last visited April 6, 2009.

⁵⁶ European Price Regulation at pp. 18-19.

⁵⁷ European Price Regulation at p. 30.

⁵⁸ European Price Regulation at pp. 31-32.

⁵⁹ See Sector Report paras 53-62.

⁶⁰ See e.g., Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use (Text with EEA relevance) OJ L 136, 30/04/2004 p. 34 Recital 15.

⁶¹ See Annex to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Text with EEA relevance) OJ L 136, 30/04/2004 p. 1. See also, Grabowski Data Exclusivity at pp 3-5.

⁶² See, COM (200&) 175 Communication from the Commission to the Council, the European Parliament, The European Social and Economic Committee and the Committee on the Regions, on the Mid-Term Review of the Strategy on Life Sciences and Biotechnology 4 April 2007 at p. 4 FN 8.

400 Biologics under development as of 2006 (of which 200 biotech drugs were targeted for cancer treatment)⁶³. The number had increased to over 600 as of December 2008, two years later⁶⁴. Many Biologics are developed by SME's financed by venture capital financing, Joint Ventures with large pharmaceutical companies or mergers with them⁶⁵. Usually the biologic being developed represents their sole product⁶⁶. The cost to bring a Biologic to market is between \$1.24 Billion to \$1.33 Billion⁶⁷ and it takes significantly more time to bring to market than an NCE⁶⁸. There is no agreement on the use of INN's for follow on biologics while some stand-alone biologics do have the same INN⁶⁹. Most important is the fact that the regulatory pathway for biologics and biosimilars is different than that of NCE's. These facts and the decision not to examine them bring many statistical assumptions in the Sector Report into question. Assumptions regarding delays for follow-ons and the additional information required to market a biosimilar are ignored in the Sector Report while raw statistical information is handled the same way as the information regarding NCE's. Due to their production, using strictly designated and usually proprietary biological processes or strains of bacteria there are no truly generic⁷⁰ copies of biosimilars.

⁶³ Grabowski Data Exclusivity at pp 16-17 (citing Pharmaceutical Research and Manufacturers of America ("PhRMA") Report *Medicines in Development, biotechnology* (July 2006) Found at http://www.phrma.org/index.php?query=biotechnology&option=com_swishesearch&intMaxHits=20&intPageOffset=0 Last visited March 29, 2009.

⁶⁴ PhRMA Report, *Medicines in Development, Biotechnology*, (December, 2008). Found at http://www.phrma.org/index.php?query=biotechnology&option=com_swishesearch&intMaxHits=20&intPageOffset=0 Last visited March 29, 2009.

⁶⁵ Grabowski Data Exclusivity Discussion at pp. 18-20.

⁶⁶ Grabowski Data Exclusivity at p. 6.

⁶⁷ Grabowski Data Exclusivity at p. 12. (Using a real cost of capital of between 11.5 % and 12.5% for firms with publicly traded biotech firm. Small biotech firms without a marketed product but with one or more candidates in Phase II or III trials have an average real cost of capital of approximately 27.4%. Id at FN 8.)

⁶⁸ Grabowski Data Exclusivity at p. 11. (97.7 months compared to 90.3 months for an NCE.) (One example cited by Grabowski at p. 10 is Avastin, an anti-cancer treatment. Discovered in 1989 with Phase I trials in 1998, the drug was approved by the FDA in 2004. It was subsequently approved in the EU in 2005 as bevacizumab, rhuMAb-VEGF Roche Press release January 14, 2005. Found at <http://www.roche.com/med-cor-2005-01-14> Last visited March 29, 2009.)

⁶⁹ See e.g. World Health Organization Drug Information Vol. 19, November 2, 2005 pp 103-104 (Gene Therapy products) and World Health Organization WHO Informal Consultation on International Nonproprietary Names (INN) Policy for Biosimilar Products, INN Working Document 07.211 pp. 5-6 and 8. Found at www.who.int/entity/medicines/services/inn/BiosimilarsINN_Report.pdf Last visited March 29, 2009. (Noting difficulties in developing INN's for biological products due to their complexity and recognizing the difficulties posed for regulatory authorities.)

⁷⁰ Most biologicals in the US are regulated by the Public Health Services Act. 42 U.S.C. §§ 201 et seq., and not the process followed for NCE's under the HWA (codified at 21 U.S.C. §§ 355, 360 and 35 U.S.C. §§ 156, 271, 272 (as amended) (Presently, while there are Congressional bills pending considering the creation of a process for follow on "biosimilars" there is no procedure for generic biologics in the US. Similarly in the EU Directive 2001/83 Article 10(4) (as amended by Directive 2004/27) and Regulations 726/2004 and 1394/2007 govern the procedures for approval of biosimilars which require substantially more clinical information from applicants than do the abbreviated procedures

Biologics present significant challenges to establishing as similar mechanism (e.g. ANDA) as abbreviated application [sic] for chemical agents. Scientific methods for establishing equivalence are so different between chemical and biological agents that “even if the biosimilar has the same gene sequence, vector, host cell line, culture conditions, and purification methods as the innovative protein, it can still differ substantially in its biological and clinical properties”⁷¹.

These costs do not include the costs of obtaining basic patent protection or the costs of obtaining secondary or continuation patents which, as noted below, may run into considerable sums of money.

Some of the special problems of biosimilars, the off-patent follow-ons of biologics are dealt with *infra* in the section on generics.

3.1.3 Decision to commercialize an NME or Biologic

Most of the costs of bringing a medical compound to market represent the additional cost, in time and money of compliance with regulations designed to assure the safety and efficacy of drugs marketed to consumers. This is a very considerable investment decision for originators. Business decisions regarding drug development are subject to the pressures of avoiding risk while producing a high return on investment⁷² Patentability audits are standard procedure in the industry, and are performed at a number of points in the pre-clinical and clinical trial stages before substantial sums are committed to further development⁷³. They arise from concerns regarding the ability to protect capital investment. Interestingly enough in this Global industry most patent audits are focused upon a drug’s patentability under US law and will often disregard whether or not they can be protected *inter alia*, under EU law⁷⁴. This is due to the fact that half of all global profits come from the US market with other major markets generating much smaller market shares.

for generic NCE’s.) See also Jo Pisani, Yann Bonduelle, *OPPORTUNITIES AND BARRIERS IN THE BIOSIMILAR MARKET: EVOLUTION OR REVOLUTION FOR GENERICS COMPANIES?* at p. 5 Table 1. Found at

<http://www.ableindia.org/biosimilars.pdf> Last visited April 1, 2009. (The authors are pharmaceutical strategy consultants at PriceWaterhouseCoopers LLP).

⁷¹ Henry G. Grabowski, Jeffrey L. Moe, *Impact of Economic, Regulatory and Patent Policies on Cancer Chemoprevention, Cancer Prevention Research* 1, 84, July 1, 2008 at p. 27. Found at <http://cancerpreventionresearch.aacrjournals.org/cgi/content/abstract/1/2/84> Last visited April 1, 2009. (Citation omitted.)

⁷² See GAO Report at pp. 27-28 (Originators may even stop development of drugs if it becomes apparent that they will not satisfy shareholder expectations of Blockbuster profits in the range of US\$200 to \$500 million a year.)

⁷³ Unpatentable Drugs at pp. 545-546.

⁷⁴ Unpatentable Drugs at pp 547-548.

By way of contrast, the cost, in the US, to a generic manufacturer for demonstrating bio-equivalence to an originator NCE drug which has lost exclusivity is roughly US \$1-2 Million and typically takes between one and two years⁷⁵.

Once the originator makes the decision to proceed to clinical trials the process is performed in several steps.

3.1.4 PATENTS

At some point prior to commencing the clinical trial process, a patent is applied for with specific claims for the medical effects of the molecule. A typical pharmaceutical patent application will have some one hundred pages and make twenty-five claims⁷⁶. The originator pharmaceutical company then makes a decision on whether or not to begin the clinical testing process required to obtain governmental authorization to sell a medically useful formulation of the molecule. The patent regimes in the EU and US are summarized below⁷⁷. Secondary patents, and Divisional, and Continuation⁷⁸ applications are separately described. They are usually filed during the clinical trial process as well as during the post medical authorization period.

3.1.4.1 Patents in the EU

The Commission has recently declared that:

Patents are a driving force for promoting innovation, growth and competitiveness. A recent Commission study on the value of patents... which was based upon a survey of 10,000 inventors in eight Member States... assessed inter alia the monetary value of patents... [T]he overall 'patent premium'... for the reviewed Member States amounts to 1% of national GDP for the period 1994-1996 and had reached 1.16% of GDP during the period 2000-2002⁷⁹.

⁷⁵ Henry Grabowski, *PATENTS, INNOVATION AND ACCESS TO NEW PHARMACEUTICALS*, at p. 5 Working Papers No. 02-28, Duke University, Department of Economics Found at <http://econpapers.repec.org/scripts/redir.pl?u=http%3A%2F%2Fwww.econ.duke.edu%2Fpapers%2FAbstracts02%2Fabstract.02.28.html;h=repec:duk:dukeec:02-28> (Last visited March 28, 2009.) (Citing U.S. Cong. Budget Office Report *How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry*, 1998) Also published in *J. Int. Econ. L.*, Vol. 5, No. 4, December 2002, pp. 849-860.

⁷⁶ See e.g. Robert Silverman, *PATENT FILING STRATEGIES FOR PHARMACEUTICAL PRODUCTS: A SIMPLE COST-BENEFIT ANALYSIS BASED ON FILING COSTS AND PHARMACEUTICAL SALES*, 33 *AIPLA Q.J.* 153, 157-158 (Spring 2005) ("Patent-Filing").

⁷⁷ While I will refer to the Patent Cooperation Treaty I will not describe its complete operation. See Patent Cooperation Treaty, done June 19, 1970, art. 39, 40 (as in effect in 1970) (amended to include a 30 month time limit on Apr. 1, 2002), 28 U.S.T. 7645, 7685-86, available at <http://www.wipo.int/pct/en/texts/pdf/pct.pdf> ("PCT".)

⁷⁸ "Continuation Patents" in the US are similar to Divisional Patents under the EPC.

⁷⁹ COM(2007) 165 final COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL- Enhancing the patent system in

In the EU most pharmaceutical patents have been granted pursuant to the European Patent Convention of 5 October 1973 (the “EPC 73”) as Revised⁸⁰. The EPC 73 will be superseded by the European Patent Convention of 2000 (the “EPC 2000”) which entered into force December 31, 2007 as its provisions become effective. A patent filed under EPC 73 may be requested for one or more of the contracting states⁸¹ and when granted is effective within those territories. Patents are filed with the European Patent Office⁸² and are granted for “any inventions which are susceptible of industrial application, which are new and which involve an inventive step.”⁸³ The patent term is 20 years from the date of filing⁸⁴. A European Patent grants the inventor the same rights as, and is the “equivalent to a regular national filing,”⁸⁵ in the contracting state applied for, and any infringement is dealt with by the courts of the Member State pursuant to that state’s law⁸⁶.

After the grant of a European Patent or a PCT patent must be validated in a Contracting State in order to be given effect⁸⁷. In the EU this will usually entail significant translation costs of roughly \$180,000 for validation in all EPC signatories⁸⁸. This makes it imperative for a pharmaceutical manufacturer to consider a patent filing strategy that takes the chances of an unsuccessful application for approval of the drug into account in its decisions of what, when and where to file for patent protection.

3.1.4.2 Changes in EPC 2000

EPC 2000 affected patents in a number of ways, some of which are specifically directed towards pharmaceutical patents. For example, Art.

Europe April 3, 2007 Celex No. 507DC0165. (“COM(2007) 165”) at Introduction para. 2 (Footnote omitted) (Footnote 3 of COM(2007) 165 states “The ‘patent premium’ is the value of the patented invention net of the value of the invention if the inventor had no patent on it.”)

⁸⁰ Patents may also be applied for in each individual Member State with recognition in other contracting states pursuant to the International Convention on the Protection of Industrial Property (the “Paris Convention”). Many international pharmaceutical companies initially file basic patents under the Patent Cooperation Treaty, which gives them up to 31 months to file a European Patent. *See* Patent-Filing at pp. 155-157. This has the effect of preserving patent priority until the prospects of the drug’s success become clearer. *Id* at 155.

⁸¹ EPC 73 Article 3.

⁸² EPC 73 Arts 10-25.

⁸³ EPC 73 Art. 52.

⁸⁴ EPC 73 Art. 63.

⁸⁵ EPC 73 Arts. 66 and 67.

⁸⁶ EPC 73 Arts. 64 and 74. *See also*, PROTOCOL ON JURISDICTION AND THE RECOGNITION OF DECISIONS IN RESPECT OF THE RIGHT TO THE GRANT OF A EUROPEAN PATENT of 5 October 1973 (“PROTOCOL ON RECOGNITION”) which gives the courts of Member States competence to decide claims under European Patents granted for that Member State.

⁸⁷ *See*, EPC 73 Art. 67, and Patent-Filing at pp.155-157 and 167-168.

⁸⁸ *See*, EPC 73 Art. 65 and Patent-Filing at pp. 157 and 168 (Translation costs for one Typical EPC pharmaceutical patent in all 35 EPC signatories cost an estimated \$180,000 in 2005 Dollars. Translation costs for the same patent in all 125 PCT signatories cost an estimated \$400,000 in 2005 Dollars.)

54(5) EPC 2000 (Novelty) with respect to pharmaceutical patents expressly permits granting patents for subsequent therapeutic applications of an already patented substance, (provided, however, that the applications are not comprised in the state of the art)⁸⁹. A protocol was added to Article 69 of EPC 2000 which (Art. 2) attempts to define the extent of protection accorded a European Patent when validated by a Member State although National courts will still differ on this “doctrine of equivalents.”⁹⁰ Importantly, Articles 105a and 105b introduce a limitation procedure wherein a European Patent holder may limit or withdraw claims.

Pursuant to Articles 105b and 105c of EPC 2000, the holder of a European patent is henceforth provided with a centralized administrative procedure, making it possible to limit or revoke his patent. This procedure will be in effect in all contracting states for which the European patent was granted. This procedure may, in particular, prove to be useful in fighting a nullity action, or avoid one, when an element of the state of the art of the technique is discovered after the granting of the patent.⁹¹

EPC 2000 also continues the effort to establish a European Patent Court begun in 1975, by amending the European Patent Litigation Agreement (EPLA). To date, over the past 34 years, none of the Conventions or Annexes relating to the establishment of a European Patent Court have been ratified.

3.1.5 Patent Disputes in the EU

Opposition proceedings may be brought by a third party before the Opposition Division of the EPO on the bases that the invention is not patentable under Articles 52-57 EPC 73, that it is not disclosed in a sufficiently clear manner, or that the subject matter extends beyond the application as filed.⁹² Appeals are decided by a Board of Appeal, with a further appeal of questions of fundamental importance to the Enlarged Board of Appeal⁹³. Decisions are circulated to the central industrial property offices of the contracting states⁹⁴. In addition to these procedures, Courts of contracting Member States have sole competence to hear questions of patent enforcement and validity of EPC patents validated in the EPC signatory, according to their own National laws⁹⁵.

⁸⁹ Xavier Buffet-Delmas, Laura Morelli, MODIFICATIONS TO THE EUROPEAN PATENT SYSTEM, 20 NO. 8 *Intell. Prop. & Tech. L.J.* 18, 18-19 (August 2008) (“Modifications to the EPC”).

⁹⁰ Modifications to the EPC at p. 19.

⁹¹ Modifications of the EPC at 20.

⁹² See Articles 99-105c EPC 73.

⁹³ See Articles 106-122a EPC 73.

⁹⁴ Art. 119 EPC 73.

⁹⁵ See, *Roche Nederland BV and Others v Frederick Primus and Milton Goldenberg*, Case C-539/03, ECR 2006 page I-06535 (“Roche Nederland”) at para. 30, *Gesellschaft für Antriebstechnik mbH & Co. KG v Lamellen und Kupplungsbau Beteiligungs KG*, Case C-

3.1.6 Patents in the US

In the US, patents are granted by the United States, Patents and Trademarks Office (“PTO”), an agency of the US Department of Commerce, pursuant to Title 35 of the U.S. Code and The Constitution of the United States Article I, Section 8, Clause 8⁹⁶. Patents may be granted by the PTO for “[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.⁹⁷” The grant of a US patent gives the holder the right to exclude others from making, using, offering to sell, or selling the patented invention⁹⁸. US patents are for a term of 20 years from the date the patent was filed⁹⁹. In the US patents are granted to the “first to invent”¹⁰⁰ as opposed to the European system of “first to file.”

3.1.6.1 Patent Disputes in the US

The PTO may review claims of invalidity *sua sponte* or in proceedings brought by third parties¹⁰¹. Appeals from PTO review are heard first by the Board of Patent appeals and then by the Federal Circuit Court of Appeals¹⁰². Federal District Courts have jurisdiction to hear all patent infringement claims as well as claims and counterclaims arising under Federal law or supplemental claims under State law¹⁰³.

4/03 ECR 2006 page I-06509 (Counterclaims and defenses), *Merck Genericos - Productos Farmaceuticos Ldª v Merck & Co. Inc. and Merck Sharp & Dohme Ldª* Case C-431/05. ECR 2007 page I-07001 (“Merck Genericos”) at para. 46. *See also*, Article 22 (4), Council Regulation (EC) No 44/2001 of 22 December 2000 on jurisdiction and the recognition and enforcement of judgments in civil and commercial matters (OJ 2001 L 12, p. 0001) (“Regulation 44/2001” or “Brussels I”).

⁹⁶ “Congress shall have power ... to promote the progress of science and useful arts by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries.”

⁹⁷ 35 U.S.C. § 101.

⁹⁸ 35 U.S.C. § 271(a).

⁹⁹ 35 U.S.C. § 154.

¹⁰⁰ 35 U.S.C. § 102(g).

A person shall be entitled to a patent unless -- during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

¹⁰¹ *See e.g.* 35 U.S.C. §§ 301-301 and 311-318. (Procedures governing requests by third parties for re-examination and inter partes re-examination procedures brought by the Director.)

¹⁰² 35 U.S.C. §§ 134 and 141.

¹⁰³ 28 U.S.C. §§ 1330-1369 (Section 1367 deals with supplemental jurisdiction.)

3.1.7 Clinical Trials

The pathway to obtaining marketing approval for a new medicinal product in the EU and the US is fairly similar¹⁰⁴. In many ways these procedures help prevent market failure by filling an asymmetrical information gap between the manufacturer, physicians and the public insofar as the latter may rely upon regulatory authorization as imprimaturs of their safety and efficacy¹⁰⁵. Clinical trials may be described (with differences noted) as follows:

3.1.7.1 PRE-CLINICAL TEST STAGE

Under Directive 2001/20/EC¹⁰⁶ no clinical trial may proceed without a request for written authorization of the Ethics Committee regarding the proposed conduct of the clinical trial¹⁰⁷. Clinical trials for biologicals, gene therapy and other specialized products without MA also require approval prior to initiating trials¹⁰⁸. In particular, the procedures in Annex I commence with the assignment of a Study Director who is in charge of the trials and a Principal Investigator who is assigned to investigate specific areas of the trials on behalf of the Study Director.¹⁰⁹ The originator agrees with the Study Director on a Study Plan that details the methods and procedures for conducting the various stages of clinical trials¹¹⁰. Annex I, Section II part 8 describes the conduct of the study plan which deals with the various clinical phases. Annex I Section II part 9 describes the procedures for the final report to be annexed to the dossier seeking marketing approval.

Finally, Regulation 2001/20 Article 11 provides for a database of extracts of all clinical trials which is available only to authorities of Member States. Regulation 726/2004 provides for the entry into a publicly available database of certain data from the ongoing clinical trials supervised by the EMEA¹¹¹.

¹⁰⁴ Annex I of Directive 2004/10 (“Annex I”) prescribes the protocols and procedures for pre-clinical and clinical studies used for the preparation of dossiers submitted for approval of Medicinal Products under the decentralized procedures under Directive 2001/83 and the centralized procedure under Regulation 726/2004.

¹⁰⁵ Ariel Katz, *Pharmaceutical Lemons: Innovation and Regulation in the Drug Industry*, 14 Mich. Telecomm. & Tech. L. Rev. 1, 7-10 (2007) (“Pharmaceutical Lemons”) (Discussion regarding Market failure) (Citing, *inter alia*, Henry G. Grabowski & John M. Vernon, *THE REGULATION OF PHARMACEUTICALS: BALANCING THE BENEFITS AND RISKS*, (1983).

¹⁰⁶ Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 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 OJ L 121, 01/05/2001 p. 34 (“Directive 2001/20”).

¹⁰⁷ Directive 2001/20 Articles 6 and 9(2).

¹⁰⁸ Directive 2001/20 Art. 9 (5)-(7).

¹⁰⁹ Annex I Section I.

¹¹⁰ Annex I Section II 8.1.

¹¹¹ Regulation 726/2004 Article 57 (2) (as provided by Communication from the Commission regarding the guideline on the data fields contained in the clinical trials

In the US, NDA approval from the US Food and Drug Administration (“FDA”) is as follows: In the preclinical stage an Investigatory New Drug Application (“IND”) is filed with regulatory authorities after an initial meeting with the FDA¹¹². Pre-clinical research is designed to determine if the drug is reasonably safe for initial small-scale testing on humans¹¹³. During this stage, the originator usually performs both laboratory tests and tests on animals.¹¹⁴

3.1.7.2 PHASE I CLINICAL TRIALS: Safety

The next stage, Phase 1, consists of tests on between 20-80 healthy humans in order to determine the safety and the mechanism of the drug’s action on human metabolism¹¹⁵.

3.1.7.3 PHASE II CLINICAL TRIALS: Side Effects and Efficacy

Phase II consists of tests performed on a larger group (typically several hundred) of humans who have the condition which the drug is supposed to affect. The activity of the drug is closely monitored for possible side effects¹¹⁶.

3.1.7.4 PHASE III CLINICAL TRIALS: Effectiveness on a large scale

A follow up meeting is then held with the FDA to determine whether or not to continue on to Phase III and to establish the details of the objectives and design of the trials¹¹⁷. Phase III trials are commenced after Phase II trials indicate that the drug is indeed effective. Phase III trials usually involve from several hundred to several thousand subjects and are designed to determine the probable effectiveness on the general population as well as the risk-benefits of the drug.¹¹⁸

One study found that in the U.S. the period from initiating Phase I tests through final FDA approval averages over 7 ½ years for a New Chemical Entity and 8.15 years for a Biological Entity¹¹⁹. The entire process takes

database provided for in Article 11 of Directive 2001/20/EC to be included in the database on medicinal products provided for in Article 57 of Regulation (EC) No 726/2004 OJ C 168, 03/07/2008 p. 3)

¹¹² *The New Drug Approval Process: Steps from test tube to New Drug Application Review, an interactive chart*. Found at <http://www.fda.gov/cder/handbook/develop.htm> (Last Visited March 1, 2009) (“NDA Process”). See also Christopher P. Adams, Van V. Brantner *Spending on New Drug Development* (March 14, 2008) Available at SSRN: <http://ssrn.com/abstract=869765> (Last visited March 9, 2009). (“Spending on New Drugs”).

¹¹³ *Id.* See also Sector Report at para. 118.

¹¹⁴ *Id.*

¹¹⁵ *Id.* See also Sector Report at para. 118 (1).

¹¹⁶ *Id.* See also Sector Report at para. 118(2).

¹¹⁷ *Id.*

¹¹⁸ *Id.* See also Sector Report at para. 118(3).

¹¹⁹ Henry Grabowski, *Data Exclusivity for New Biological Entities*, at p. 11. Working Paper June 2007. Found at

between 8.5 and 13.5 years to complete¹²⁰. Other studies show comparable results that vary according to sampling parameters such as selection of time frames, since regulatory authorities have required that clinical trials show more and more detailed information¹²¹.

There has been an increase in the cost and failure rates of clinical trials in recent years. A number of causes have been cited including stricter regulatory standards, shifts in the types of drugs being developed to drugs treating chronic diseases¹²².

According to the GAO Report, only 80.7% of NME's pass Phase I trials, 57.7% of those pass Phase II Trials and of those only 56.7% pass Phase III Trials.¹²³ Only between 1 in 5,000 to 10,000 compounds tested reach successfully reach the marketplace in the EU¹²⁴. In other words, approximately only one in four drugs in human clinical trials make it to market¹²⁵. Only three out of ten marketed drugs generate revenues that match or exceed average research and development costs¹²⁶.

3.1.8 Drug Approval in the EU

The pathway in the EU is similar to that in the US. According to the Sector Report, the process of obtaining approval of a drug is similar to that followed in the US consisting of a Pre-clinical stage followed by Phase I, II

<http://www.econ.duke.edu/Papers/PDF/DataExclusivityWorkingPaper.pdf>. (Last visited March 25, 2009.) (Grabowski Data Exclusivity".)

¹²⁰ See, e.g. Sauer, Robert M. and Sauer, Corinne, Is it Possible to have Cheaper Drugs and Preserve the Incentive to Innovate? The Benefits of Privatizing the Drug Approval Process.. Available at SSRN: <http://ssrn.com/abstract=875359> . at p. 17. (a later version was published in J. Tech. Trans., Vol. 32, No. 3, May 2007 ("Incentive to Innovate".) Last visited March 28, 2009.) See also Spending on New Drugs at p. 5 (Clinical trials take between six and twelve years for NCE's citing C. Adams and V. Brantner, *New Drug Development: Estimating Entry from Human Clinical Trials*, FTC Working Paper 262, (July 2003) Found at <http://ssrn.com/abstract=428040> Last visited April 2, 2009.)

¹²¹ See e.g. Grabowski Data Exclusivity at p. 11, Spending on New Drugs at 5. The Sector Report, on the basis of a sample of 20 top selling molecules between 1973 and 1998, found that the average time from first patent application to launch on the market was between six and ten years (para 120) and the average for 141 INN's between 1978-1998 was 8.6 years (paras 120-121). These measurement periods and sampling do not synchronize with the Sector Report. According to the Commission 16 January Press release the periods of decline in novel medicines initiating the Sector Report was from 1995-2004 and according to the Fourth Paragraph of the Report's Summary the focus of the Sector Report were the years from 2000-2007. These results appear to show short development times compared to other studies. Selection of 20 and 141 INN's respectively appear to be small samples. Since patents are usually not applied for until shortly before commencement of clinical trials (Sector Report paras 112-116), use of these parameters also omits considerable amounts of time spent in the pre-clinical period. This also omits consideration of those biologicals for which INN's are not always available and which have longer development time frames.

¹²² CBO Study at pp. 21-25.

¹²³ Incentive to Innovate at pp.17-18.

¹²⁴ Sector Report para. 139.

¹²⁵ *Id.*, See also Spending on New Drugs at p.5.

¹²⁶ Bruce N. Kuhlik *The Assault on Pharmaceutical Intellectual Property*, U. Chi. L. Rev. 93 (Winter 2004) ("Assault on Pharma") at p.94.

and III trials¹²⁷. A sample of the 20 best selling molecules listed in the Sector Report indicates an average time from patent to market of between six and ten years

3.1.9 MARKETING APPROVALS EU/US

3.1.9.1 Marketing Authority in the EU

In the EU a drug given marketing approval via an original application in a Member State under Directive 2001/83 may obtain “Mutual Recognition” in any other Member State (and EEA countries) by filing an abbreviated application in referencing the original Marketing Authorisation¹²⁸. An Originator may also file multiple applications in more than one Member States under the “Decentralised Procedure” with the choice of one Member State who reviews the application as the “Reference Member State.”¹²⁹,

In the EU, once the clinical trials are completed the results are put into a dossier and presented to either the National Authority or the EMEA along with other documents and a request for a grant of Marketing Authorization¹³⁰. The Marketing Authority or the EMEA have 210 Days to decide whether or not to grant the MA¹³¹.

Market Authorizations under Regulation 726/2004 requires no further medical review and are valid in all Member States¹³². Once an MA is granted by the EMEA it is valid throughout the Community and recorded in a register¹³³.

Member States, however, may delay the actual sale of the medicinal product, which may also be subject to pricing and reimbursement rulings.

Marketing Authorizations under Directive 2001/83 are valid in the Member State. Pursuant to Chapter 4 of Title III of Directive 2001/83 governs the procedure for mutual recognition of marketing authorizations in other Member States. An applicant may, pursuant to Directive 2001/83 Article 28 submit multiple applications for MA to any number of Member States with one Reference Member State (“RMS”) being responsible for examining the dossier. Under Chapter 4 an applicant seeking Mutual Recognition submits a dossier identical to the one submitted to the Member State where Marketing Authority was granted. Under Articles 28 and 29, once the RMS

¹²⁷ Sector Report at par. 118. and *Directive 2004/10 EC of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of applications for tests on chemical substances* OJ L 121, 1.5.2001 p.34-44 (“Directive 2004/10”)

¹²⁸ Directive 2001/83 Articles 27-39.

¹²⁹ Directive 2001/83 Article 28 (as amended by Directive 2004/27.)

¹³⁰ See, Directive 2001/83 Art. 6 and Regulation 726/2004 Art.6.

¹³¹ Regulation 726/2004 Art. 6(3) and Directive 2001/83 Art. 17.

¹³² Regulation 726/2004 Article 13.

¹³³ Regulation 726/2004 Article 13.

grants Marketing Authority the other Member States must grant Mutual Recognition except in the exceptional grounds specified in Article 29. The authorities have 90 days to verify the contents and may only object on the exceptional grounds specified in Article 29 (1) of the Directive¹³⁴.

Marketing of medicinal products is also subject to national regulations regarding pricing and/or reimbursement, which are quite complicated and vary according to National law¹³⁵. In the Member States of the EU medicinal products are subject to pricing and reimbursement decisions prior to the Member State permitting the sale of the product. The procedures are subject to each Member State's internal laws¹³⁶. These pricing and reimbursement issues are discussed in the Sector Report. The Sector Report gives an analysis with respect to what it views as inappropriate interventions by originators before the national bodies responsible. However, it eschews any recommendations with respect to these regulations themselves claiming that this would be outside the Commission's competence.¹³⁷

3.1.9.2 FDA Approval in the US

In the US, under HWA an originator, once clinical trials are successfully completed files a new drug application ("NDA") with the FDA¹³⁸ along with a list of all patents which "could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug,"¹³⁹. At this point the FDA determines whether or not to grant the NDA. Drugs approved by the FDA are known as "listed drugs."¹⁴⁰ Once granted the FDA publishes a list of these patents in the so-called "Orange Book"¹⁴¹ which is publicly available¹⁴². Marketing approvals for biologics follow a similar path, but are not included in the HWA system¹⁴³.

In the US once an NDA is approved the originator may market the new drug in any of the 50 States.

3.1.9.2.1 Post Approval Marketing- First Mover Expenses

Once a drug has received MA in the EU or its NDA has been approved in the US, the originator of a new drug as a "first mover" must establish a market for the new drug, create a brand identity, and sometimes build new

¹³⁴ *The Queen, a la demande de Synthron BV v Licensing Authority of the Department of Health*, Case C-452/06. ECR 2008 page 00000. ("Synthon").

¹³⁵ See Discussion of pricing and reimbursement in Sector Report paras. 279-311.

¹³⁶ See e.g. Discussion in paras 288-301 in the Sector Report.

¹³⁷ Sector Report para. 7.

¹³⁸ 21 U.S.C. § 355(b)(1), *Janssen Pharmaceutica N.V. v. Apotex, Inc.*, 540 F.3d 1353, 1355 (Fed. Cir. 2008) ("Janssen v. Apotek".)

¹³⁹ 21 U.S.C. § 355(b)(1), (c)(2), *Janssen v. Apotek* at 1355.

¹⁴⁰ 21 U.S.C. § 355 (j)(2)(A)(i).

¹⁴¹ 21 U.S.C. § 355(j)(7)(A) "Approved Drug Products with Therapeutic Equivalence."

¹⁴² *Janssen v. Apotek* at 1355.

¹⁴³ See e.g., Public Health Services Act. 42 U.S.C. §§ 201 et seq.,

production facilities¹⁴⁴. This usually consists of hiring a marketing force – which is essential in the EU where drug advertising is circumscribed¹⁴⁵. The Sector Report states that originator companies spent, on average, 23% of their Global Turnover on marketing and promotional activities, beginning at 52 Billion Euros in 2000 and rising to 57 Billion Euros in 2007 (with some variations)¹⁴⁶.

3.1.10 PATENT EXTENSIONS EU-SPC, and in the US

3.1.10.1 EU-SPC

Within six months of the initial grant of an MA in the EU an application may be made to the relevant Member State authorities for a Supplemental Protection Certificate (“SPC”) for an extension of its basic patent protection in that Member State¹⁴⁷. The SPC Certificate extends the effect of a valid basic patent for five years with the maximum “effective protection of 15 years¹⁴⁸. It should be pointed out that the extension provided under an SPC is not a patent extension but its legal effect is coextensive with the grant under applicable national law¹⁴⁹. An SPC Certificate may only relate to the basic patent of the first medicinal product to receive an MA in the Community and not to MA’s for additional therapeutic uses or to secondary patents¹⁵⁰. SPC’s granted by non EU, EEA Members such as Switzerland are treated on the same basis as those granted by Member States¹⁵¹. In addition, unlike Data Protection or Marketing Exclusivity an SPC will fail if the underlying patent is invalidated¹⁵².

¹⁴⁴ New Biological Entities at pp. 7-8 (Noting that after Phase III clinical testing of drugs to treat sepsis failure to obtain FDA approval caused extensive losses spent on building expensive manufacturing facilities and dismantling a large sales force hired specifically for the project.)

¹⁴⁵ Directive 2001/83, Art. 88 and Sector Report at para. 56.

¹⁴⁶ Sector Report para. 57.

¹⁴⁷ Council Regulation (EEC) No 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products OJ L 182, 02/07/1992 p. 1 Arts 2-7. (“Regulation 1768/92”)

¹⁴⁸ Regulation 1768/92 Art. 13.

¹⁴⁹ See e.g. Merck Genericos paras. 43-45.

¹⁵⁰ See e.g. *Yissum Research and Development Company of the Hebrew University of Jerusalem v Comptroller-General of Patents* Case C-202/05. ECR 2007 page I-02839, *Pharmacia Italia SpA, formerly Pharmacia & Upjohn SpA*. Case C-31/03, ECR 2004 page I-10001, and *Hassle AB v Ratiopharm GmbH* Case C-127/00, ECR 2003 page I-14781.

¹⁵¹ *Novartis AG, University College London and Institute of Microbiology and Epidemiology v Comptroller-General of Patents, Designs and Trade Marks for the United Kingdom* (C-207/03) and *Ministre de l’Economie v Millennium Pharmaceuticals Inc.* (C-252/03). Joined cases C-207/03 and C-252/03. ECR 2005 page I-03209.

¹⁵² See e.g. Regulation 1768/92 Art. 15 and *Generics (UK) Limited Claimant v. Daiichi Pharmaceutical Co. Ltd, Daiichi Sankyo Co. Ltd.* Case No: HC 07 COO988 [2008] EWHC 2413 (Pat) (Action by generic seeking to invalidate patent and the SPC certificate based upon patent.)

3.1.10.2 US-PATENT EXTENSIONS

In the US Patent extension is bit more complicated. Under the HWA's patent term extension provisions¹⁵³ an Innovator gets a patent term extension equal to one half of the IND period and the amount of time formal clinical trials take plus the time the FDA takes for its clinical review. But in no event for more than five years¹⁵⁴.

Thus, in the EU SPC equals remaining patent term plus Five years (but no more than 15) and in the US Patent Extension equals remaining time plus no more than five years¹⁵⁵. In the US because the preclinical and clinical trial periods normally greatly exceed five years this difference is functionally meaningless except for providing material to those who might wish to write law review articles on the subject.

3.1.10.3 Secondary and Continuation Patents and “Evergreening”

While “Basis Patents” on the original API or biological are normally filed prior to the commencement of Clinical trials other patents ancillary to the basic patent are filed for different reasons and at different points in the life cycle of a medicinal product. In the preclinical phase patenting focuses on three main phases. As pointed out in Patent Life-Cycle¹⁵⁶; First, a synthesis is made of the API, that can easily provide many compounds of similar structure in quantities sufficient to perform assays on targets. The basic patents developed here are often the subject of broad claims (due to the uncertainty of which claims will prove out in clinical testing). Second, as candidates are narrowed down process chemists develop processes that can produce the larger quantities necessary to produce the API on the scale needed for clinical studies. These are the subject of process patents. Once a compound shows clinical promise, process chemists shift to developing processes that can produce large quantities cheaply and efficiently. This results in the patent portfolio containing multiple methods of “making” claims that incorporate many updates and tweaks to the process. In addition, when a biological hypothesis indicates a particular mechanism of activity on a variety of molecular pathways patents are filed for all known medical uses and as long as claims are not wholly speculative they satisfy the “utility” requirement for patentability¹⁵⁷.

¹⁵³ Codified at 35 U.S.C. §§ 155-156. (Section 155 applies to biologics subject to FDA review and 155 and 156 to HWA applications.)

¹⁵⁴ *Id.*, John Gladstone Mills III, Donald C. Reiley III, and Robert C. Highley, 1 Pat. L. Fundamentals § 1:22 (2d ed. A.L.R. 2009), Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, Vol. 54 Food & Drug L.J. 187-194 at p. 190.

¹⁵⁵ Japan also provides for a five-year pharmaceutical patent extension. Pharmaceutical Lemons at p. 6, citing Patent Law, Japan Law No. 121 of 1959 art. 67(2) (amended by Law No. 220 (1999)).

¹⁵⁶ Patent Life-Cycle at p. 298 (2008).

¹⁵⁷ Patent Life-Cycle at p. 298.

Sometimes it is only it is determined in the clinical testing stage that another formulation will make a better product and the secondary patent actually becomes the valuable innovation¹⁵⁸.

Another example of late-stage patents example concerns crystals and polymorphs- or ways in which compounds pack together in solid forms. Compounds may pack together in a disordered forms (“amorphous”) or ordered forms (“crystalline”) and there may be multiple forms of crystalline forms (“polymorphs”)¹⁵⁹. Different polymorphs of an API often interact differently within the human body and these differences are often not discovered until late in the process.¹⁶⁰ The process of discovering new polymorphs is the result of either trial and error or chance and this will often dictate the timing of later stage patents¹⁶¹.

Thus a typical patent estate¹⁶² for an NCE will include two basic applications covering composition of matter-the first regarding the chemical structure generically and the second specifically. The method of use claims may or may not be separated from the claims in the basic patents. There may be applications directed to particular polymorphs, manufacturing processes, “picket-fence chemistry”¹⁶³, combination therapy, formulation, or new use.

Arguments regarding “anti-commons” problem of “evergreening” or the attempt to extend patent monopoly by filing “patent thickets” tend to ignore that fact that any other drug firm may compete, simply by being the first to patent a follow-on advance¹⁶⁴. In the case of secondary patents and generic versions of the basic patent generics remain free to use the chemical formulation of the expired basic patent but are not free to market copies of late stage advances¹⁶⁵.

¹⁵⁸ See, e.g., *Pfizer Inc., v. Apotex, Inc.* 480 F.3d 1348 (Fed. Cir. 2007, cert. denied -U.S.-, 128 S. Ct. 110 (2007)(“Pfizer v. Apotex”) (After commencing clinical trials with one salt of amlodipine the originator encountered manufacturing problems. The originator then found that a different salt was easier to handle, patented it and changed to that salt in order to finish its clinical trials. Later, after being upheld by three District Courts, the Federal Circuit Court of Appeals invalidated the patent on the second salt on grounds of obviousness. As a result of the invalidation a generic version was launched five months prior to patent expiration. The originator potentially lost \$1 Billion in sales. See, Eric E. Williams *PATENT REFORM: THE PHARMACEUTICAL INDUSTRY PRESCRIPTION FOR POST-GRANT OPPOSITION AND REMEDIES*, 90 J. Pat. & Trademark Off. Soc’y 354, 370 (May 2008) (“Post-Grant Opposition”). Amlodipine is listed as one of the 219 INN’s of the Sector Report.)

¹⁵⁹ Patent Life-Cycle at p. 293.

¹⁶⁰ Patent Life-Cycle at p. 294.

¹⁶¹ Patent Life-Cycle at p. 294.

¹⁶² This description of a typical patent estate is taken from Patent-Filing at p. 185.

¹⁶³ A laboratory procedure designed to imitate a natural chemical process.

¹⁶⁴ Patent Life-Cycle at p. 299 FN.108 (citing Thomas H. Lee, *Me-Too Products--Friend or Foe?* 360 NEW ENG. J. MED. 211, (January 15, 2004) (“Me-too products reflect and create competition among drug and device manufacturers, and that competition is also a powerful driver of better quality and lower cost.”).

¹⁶⁵ See e.g. Diane Christine Renbarger, *PUTTING THE BRAKES ON DRUGS: THE IMPACT OF KSR V. TELEFLEX ON PHARMACEUTICAL PATENTING STRATEGIES*,

3.1.11 DATA PROTECTION AND MARKETING EXCLUSIVITY

Data Protection and Marketing Exclusivity are exclusive grants of rights given in recognition that time spent satisfying regulatory requirements of safety and efficacy uses up a significant amount of the Patent grant. Due to the problem of others “free riding” on the results of clinical studies Data Protection has been given specific protection in TRIPS¹⁶⁶. It is especially important to note that Data Protection and Marketing Exclusivity are not dependent upon continued patent protection but rather, upon the grant of Marketing Authorisation.

3.1.11.1 EU Data Protection and Marketing Exclusivity

Data Protection and Marketing Exclusivity in the EU are accorded to the products as authorized in a Member State¹⁶⁷. Originally, there was no Data Protection in Directive 65/65¹⁶⁸. Directive 65/65 was amended in December 1986 by Directive 87/21 EEC¹⁶⁹ providing for the so-called “abridged procedure” as well as for six years of data protection (unless the Member State opted for either 10 year data protection or opted for no data protection after patent expiration.) Directive 87/21 extended 10 year Data Protection to biotechnology and other high tech medicines approved under Directive 87/22¹⁷⁰.

42 Ga. L. Rev. 905, 927 (Spring 2008) (“Putting the brakes on”) (Noting example of late stage patenting of Wyeth Pharmaceutical drug Effexor XR as an extended release capsule which only barred generic from packaging it in the same time-release form.)

¹⁶⁶ Agreement on Trade-Related Aspects of Intellectual Property Rights, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, 15 April 1994, in World Trade Organization, *The Legal Texts: The Results of The Uruguay Round of Multilateral Trade Negotiations* 321 (1999) Article 39.3.

¹⁶⁷ In a recent Opinion delivered on 26 March 2009 (1) in Case C-527/07 ECR 2009 page 00000 *Generics (UK) Ltd, Regina v Licensing Authority* Case C-527/07 OJ C 22, 26/01/2008 p. 36 (“Generics (UK) Ltd. v. Licensing Authority”) AG Mazak pointed out that the purpose of Marketing Authority and Data Exclusivity was to provide mutual trust in the Mutual Recognition procedures for Abbreviated Applications and thus, the quality and integrity of the information in an original dossier must comply with Community requirements before it may be relied upon for Mutual Recognition procedures.

¹⁶⁸ Council Directive 65/65 EEC of January 26, 1965 on the approximation of provisions laid down by law, regulation, or administrative action relating to proprietary medicinal products, Official Journal (no. 22) 368, reprinted in 1965-1966 O.J. Sec. Ed. 20 (1972) (“Directive 65/65”).

¹⁶⁹ Council Directive 87/21 EEC of 22 December 1986 amending Directive 65/65 EEC on the approximation of provisions laid down by law, regulation, or administrative action relating to proprietary medicinal products. 1987 Official Journal (L 15) 38. (Directive 87/21”).

¹⁷⁰ Council Directive 87/22 EEC of 22 December 1986 on the approximation of national measures relating to the placing on the market of high-technology medicinal products, particularly those derived from biotechnology. 1987 Official Journal (L 15) 38. (“Directive 87/22”).

3.1.11.2 Regulation 2309/93 Art 13 (4)

Regulation 2309/93¹⁷¹ (replaced by Regulation 726/2004) created a centralized approval system (administered through the EMEA¹⁷²) for biotechnology and high-technology medicinal products. Article 13(4) of Regulation 2309/93 provided the same 10-year Data Protection and Marketing Exclusivity found in Article 4 of Directive 65/65 (for certain enumerated types of biologicals.) Regulation 141/2000¹⁷³ provided a special approval regime for so-called “Orphan Drugs” or medicinal products, which treated extremely rare diseases or would otherwise be economically infeasible to develop without incentives.¹⁷⁴

According to the Commission’s Notice to Applicants¹⁷⁵ as of 1998 the Data Protection periods provided under Directive 65/65 Article 4.8a(iii) (Abridged Procedure) were as follows:

- Ten years in all member states for products approved under the centralized procedure.
- Ten years in all member states for products approved under the old concertation procedure established by Directive 87/22.
- Ten years for all other products in Belgium, France, Germany, Italy, The Netherlands, Sweden, and the United Kingdom.
- Six years for all other products in Austria, Denmark, Finland, Ireland, and Luxembourg.
- Six years for all other products in Greece, Spain, and Portugal, but this period will not be applied beyond the expiry of a patent protecting the original product.¹⁷⁶

3.1.11.3 Directive 2001/83

Article 10 (1) of Directive 2001/83 provided for 6 years of Data Protection and Marketing Exclusivity (10 years for high technology medicinal products) which could be extended to 10 years by the Member State. Directive 2001/83 was amended by Directive 2004/27 to provide for 8 years of Data Exclusivity, and 10 years of Marketing Exclusivity (which could be extended by one year when (within the first 8 years) the authorization holder

¹⁷¹ Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products Official Journal L 214, 24/08/1993 p. 1 (“Regulation 2309/93”)

¹⁷² European Agency for Evaluation of Medicinal Products (“EMA”).

¹⁷³ Regulation (EC) 141/2000 of the European Parliament and of the Council on Orphan Medicinal Products. 2000 Official Journal (L 18) 1. (“Regulation 141/2000”).

¹⁷⁴ Regulation 141/2000 Art. 1.

¹⁷⁵ European Commission, The Rules Governing Medicinal Products in the European Union, Notice to Applicants-Medicinal Products for Human Use, Procedures for Marketing Authorization, Vol. 2A at 6 (Office for Official Publications of the European Communities 1998).

¹⁷⁶ Richard F. Kingham Grant H. Castle DATA AND MARKETING EXCLUSIVITY FOR PHARMACEUTICALS IN THE EUROPEAN COMMUNITY, 55 Food & Drug L.J. 209, 214 (2000) (A useful reference for information regarding pre- 2001 Data Protection.)

obtains authorization for a new indication along with an extra year of data protection for any further clinical trials.) (The “8+2+1 rule”).

3.1.11.4 Transitional Periods for New Members Under the Treaty of Accession 23 September 2003

On 23 September 2003 a number of new Member States were admitted to membership in the Community. As a condition of membership the new states were required to accede to the *acquis communautaire* including implementation of all community directives and regulations (including those regarding Data Protection and Marketing Exclusivity). Some new members were granted so-called “transition periods” in the annexes to their Documents of Accession which govern the renewal of already existing marketing authorizations. In addition, Directives were issued which required the reassessment of the safety and efficacy of medicinal products that had been authorized prior to accession under Community Regulations¹⁷⁷. These have been a bit problematic in practice¹⁷⁸.

3.1.11.5 Regulation 726/2004

Article 14(11) of Regulation 726/2004¹⁷⁹ governing the Centralized Procedure for Marketing Approvals, provides for eight-years of data protection and a ten-years of marketing protection. These may be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications.

3.1.11.6 Reg 1394/2007 BIOLOGICS

Regulation 1394/27 supplements Directive 2001/83 and Regulation 726/2004 with regard to medical authorization for certain advanced therapy products such as tissue therapy and other biopharmaceuticals. Biological

¹⁷⁷ See e.g. Second Council Directive 75/319 of 20 May 1975 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1975 L 147, p. 13), as amended most recently by Commission Directive 2000/38/EC of 5 June 2000 (OJ 2000 L 139, p. 28) ('Directive 75/319'), and Regulation of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ 2004 L 136, p. 1), Article 88 of which provided for the repeal of Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products (OJ 1993 L 214, p. 1).

¹⁷⁸ Compare, Action brought on 2 September 2008 - *Commission v Republic of Poland*, Case C-385/08, OJ C 313, 06/12/2008 p. 12 (Commission alleges that the marketing of medicinal products that are generics of the reference product Plavix was not be covered by the transitional period), Action brought on 29 July 2008 *Commission v. Lithuania*, Case C-350/08 OJ C 247, 27/09/2008 p. 9 (Marketing of biologic “Grasalva” for which there was no pre-clinical or clinical information prior to accession) and Judgement in *Commission v. Czech Republic* Case C-115/07 OJ C 95, 28.4.2007 (Failure to implement Directive 2004/27.)

¹⁷⁹ Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Text with EEA relevance) OJ L 136, 30/04/2004 p. 1 (“Regulation 726/2004”).

medicinal products authorized under this procedure obtain the same 8+2+1 data and marketing protections granted under the Directive and the Regulation.

One can see that the situation is far from harmonious, quite capable of being gamed, or just plain misunderstood. There is wide divergence within the Community regarding applicable exclusionary periods, especially with regard to MA's granted prior to 2005 and in respect of the Accession countries. Questions regarding abbreviated procedures relying upon reference products in accession states, or where originator exclusivity are shorter, are also confusing. This breeds litigation.

3.1.11.7 DATA PROTECTION IN THE US

In the US, data from clinical trials for previously unapproved new chemical entities acquires five years of data exclusivity even if the underlying product was unpatented or off-patent¹⁸⁰. The five year bar against generic applications is shortened to four years if a generic company files a Paragraph IV application claiming patent invalidity or non-infringement, however, this registration will not be effective until passage of the full five year exclusivity term¹⁸¹. A shorter, three-year period of data exclusivity is granted when an NDA has been filed for a new indication of an existing medicine, for a new formulation or delivery system, or for a new combination provided, the applicant also submits at least one new clinical investigation essential to regulatory approval¹⁸². A further six-month period exclusive period may be granted provided pediatric clinical trials have been conducted¹⁸³. The FDA also grants "Orphan drugs" (drugs for treating rare diseases) seven years of Marketing Exclusivity as well as granting them "fast track" clinical trial and NDA approval procedures¹⁸⁴.

3.1.12 GENERIC ENTRY

After an originator's medicinal product loses patent protection and Marketing Exclusivity ("LoE") any other manufacturer may apply for Marketing authorization for the product. In the EU and in the US, procedures exist for market authorization of generic copies of the drug by rely upon clinical trial reports and other data previously submitted by the originator.

¹⁸⁰ 21 U.S.C. § 355(c)(3)(E)(ii). *See also*, Brook K. Baker, *ENDING DRUG REGISTRATION APARTHEID: TAMING DATA EXCLUSIVITY AND PATENT/REGISTRATION LINKAGE*, 34 Am. J.L. & Med. 303, 306-307 (2008) (Discussion of HWA data exclusivity.)

¹⁸¹ 21 U.S.C. §355 (j)(5)(F)(ii).

¹⁸² 21 U.S.C. §355 (j)(5)(F)(iii).

¹⁸³ 21 U.S.C. § 355a(b).

¹⁸⁴ *See*, 21 U.S.C. §360bb(a)(2) and 21 U.S.C. §360cc(a).

3.1.13 EU CENTRALIZED AND MEMBER STATE ABBREVIATED PROCEDURES

In the EU a number of Directives and Regulations permit Generic manufacturers to use data and clinical studies supplied by originators after LoE, in order to obtain Marketing Approval using an “abbreviated procedure”.

Directive 2001/83 Article 10(1) contemplates the submission of “abbreviated applications” for MA which refer to the clinical results of the originators drug.

(a) The applicant shall not be required to provide the results of toxicological and pharmacological tests or the results of clinical trials if he can demonstrate:

...
(iii) ... that the medicinal product is essentially similar to a medicinal product which has been authorised [(the “reference product’)] within the Community, in accordance with Community provisions in force, for not less than six years and is marketed in the Member State for which the application is made¹⁸⁵.

Similarly, Regulation 726/2004 Article 3(3) governs the grant of MA for a generic medicinal product on the same basis as Directive 2001/83 with the proviso that:

b) the summary of the product characteristics is in all relevant respects consistent with that of the medicinal product authorised by the Community except for those parts of the summary of product characteristics referring to indications or dosage forms which were still covered by patent law at the time when the generic medicine was marketed¹⁸⁶;

Subparagraph (c) provides for such similarity being recognized where the substance has the same INN. For small molecule NME’s the procedure should be similar to that of Directive 2001/83 but in the case of biologicals where the biosimilar may not have the same INN and in the case of other advanced drugs, the EMEA, under Article 4, may require further clinical trials.

During the period reviewed in the Sector Report the EMEA granted MA for some biosimilars under both the Directive and the Regulation¹⁸⁷.

¹⁸⁵ Directive 2001/83 Article 10(1).

¹⁸⁶ Regulation 726/2004 Article 3(3)(b).

¹⁸⁷ Lincoln Tsang & Daniel Kracov, *Biosimilars, developments in the EU and US*, PLC Life Sciences Handbook 2008/09 pp. 17-21 at p. 20 (Somatropin epoetin alpha, generic Omnitrop.) *See also*, ORDER OF THE PRESIDENT OF THE SIXTH CHAMBER OF THE COURT OF FIRST INSTANCE 12 December 2007 In Case T-105/04 ECR 2007 page 00000 (Removing *Sandoz GmbH v. Commission* from register on consent.)

3.1.13.1 Parallel Imports and Data Exclusivity in the EU

In the case of MA's centrally granted pursuant to Regulation 726/2004 no further marketing authorizations are required and parallel importers may not be required to obtain such additional authorization¹⁸⁸. In addition, under principles established by the ECJ in the *Kohlpharma* case¹⁸⁹, a parallel importer of a drug may file an abbreviated application under Directive 2001/83 Article 10 and use any other medicinal product authorized in another Member State as the reference product for purposes of bioequivalence. For example, where the reference product has been authorized in another Member State with a shorter period of exclusivity this may result in grant of MA for a generic product as a parallel import. In such case, generic MA could not be obtained directly by using an originator reference product registered in the same Member State. (Provided that the reference product is a generic sold in the state with the shorter period of exclusivity that has used a reference product with MA in that Member State¹⁹⁰.)

The ECJ will shortly be deciding a question with great relevance to generic manufacturers' ability to use as reference products, medicinal products with MA grants by accession states, which have not complied with Community standards. In *Generics (UK) Ltd. v. The Licensing Authority*, Austrian authorities had, in the pre-accession period, authorized the medicinal product galantamine, under brand name 'Nivalin'. Data Exclusivity had expired (or had never been in effect) in Austria (although Data Exclusivity for Nivalin has not expired in accession country Sweden.) Subsequently, in the post-accession period, the Austrian MA was extended although the medical dossier had not been updated. *Generics (UK) Ltd.* applied to the U.K authorities to market a generic version using the Austrian MA for Nivalin as the reference product. The question raised by the reference is whether the U.K licensing authority is required by Directive 2001/83 to grant an abbreviated application using the Austrian MA for Nivalin or if it may question the fact that the Austrian dossier was not updated pursuant to Community law governing accession¹⁹¹. Note that in *Synthon* the ECJ held that Member States had little discretion in denying recognition when the

¹⁸⁸ See e.g., Regulation 726/2004 Article 13 and Commission Communication on the Community Marketing authorisation procedures for medicinal products. OJ C 229 22/7/1998 pp 4-17 at p. 8 "PARALLEL DISTRIBUTION OF COMMUNITY AUTHORISED MEDICINES."

¹⁸⁹ *Kohlpharma GmbH v. Germany*, Case C-112/02. ECR 2004 page I-03369 ("Kohlpharma").

¹⁹⁰ See, Communication from the Commission - Commission Communication on parallel imports of proprietary medicinal products for which marketing authorisations have already been granted. EU: COM(2003) 839 Celex No. 503DC0839 30 December 2003 at p. 16 ANNEX Questions and Answers.

¹⁹¹ This also brings into question the Sector Report's bald assertion that Regulation 726/2004 and Directive 2001/83 contain the exclusive means for refusal to grant Marketing Authority and bar Member States from requiring applicants to certify that they are not infringing a patent. See, Sector Report at p. 15, and paras 278, 714, 716 incl. table 22 patent Linkage Issues, 749, 755, 758-759 incl. Case Study, Patent Linkage in Portugal, 895, 1119, 1132, 1157 incl. table 36.

dossier submitted for Mutual Recognition was the same as the dossier in the Member State. It did not address the question in this case of what happens if there is no documentation fitting the definition of dossier on file in the Member State. The AG submitted his Opinion on March 26, 2009 and an ECJ decision is expected shortly.

3.1.14 HATCH WAXMAN

In the US until the 1980's generic pharmaceutical manufacturers were required to submit the same expensive clinical studies as originators in order to obtain approval from the FDA. This contributed to scandals in the US where generic manufacturers cut corners and attempted to bribe FDA officials¹⁹². Congress in response and in an attempt to create a balance between encouraging innovation and encouraging post exclusivity competition between originators and generics passed the Drug Price Competition and Patent Term Restoration Act of 1984¹⁹³.

3.1.14.1 LITIGATION AND PATENT CHALLENGES UNDER HATCH-WAXMAN

The structure and operation of laws governing the pharmaceutical market have been approached by attempting to combine their interaction in a holistic model. The Hatch-Waxman statutory scheme governs the approval of new and generic drugs¹⁹⁴. The HWA was devised with the aim of striking a "balance between two competing policy interests: (1) inducing pioneering research and development of new drugs and (2) enabling competitors to bring low-cost, generic copies of those drugs to market." ¹⁹⁵

Under the HWA, an originator drug manufacturer that has had its drug approved by the FDA must notify the FDA of all patents it owns "with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug".¹⁹⁶ These patents are listed in an FDA publication commonly referred to as the "Orange Book." Those seeking to manufacture a generic version may submit to the FDA an abbreviated new drug application ("ANDA"). The ANDA rather than relying on independent clinical studies, may rely on those submitted by the originator. The generic manufacturer need only submit information showing the generic version's bioequivalence to the pioneer product¹⁹⁷. The generic manufacturer must further include one of four certifications regarding each of the patents listed

¹⁹² See, Generic Pharma. Reg. at p. 169.

¹⁹³ Pub. L. 98-417, 98 Stat. 1585, codified at 21 U.S.C. §355 and 35 U.S.C. §271(e) (the "Hatch- Waxman Act" or "HWA").

¹⁹⁴ See 21 U.S.C. § 355; 35 U.S.C. §§ 156, 271(e). (The description of the HWA that follows substantially summarizes the excellent explanation by U.S. District Judge Farnan in *DEY, L.P., v. SEPRACOR, INC.*, 595 F.Supp.2d 355, 355-359 (D. Del. 2009.) (There seems to be no need to completely re-invent the wheel, so long as appropriate credit is paid to the source.)

¹⁹⁵ *Andrx Pharms., Inc. v. Biovail Corp.*, 276 F.3d 1368, 1371 (Fed.Cir.2002).

¹⁹⁶ 21 U.S.C. § 355(b)(1).

¹⁹⁷ See 21 U.S.C. § 355(j)(2)(A).

in the Orange Book for the originator's drug¹⁹⁸. One of the most common certifications is the so-called "Paragraph IV" certification, a statement that the Orange Book patent for the pioneer drug is invalid and/or not infringed by the proposed generic drug.

The patent holder, after receiving notice of a Paragraph IV certification, has 45 days to sue the ANDA applicant for infringement. If the patent holder does not bring suit within this period, the FDA may approve the ANDA¹⁹⁹. If the patent holder sues, the FDA may not approve the ANDA until entry of a final judgement that each such Orange Book patent is either not infringed or is invalid, the patents expire, or thirty months have passed, whichever is earlier²⁰⁰.

To incentivize the filing of ANDAs with Paragraph IV certifications and challenge questionable Orange Book patents, (although possibly subjecting the generic manufacturer to suit,) the HWA grants the first generic manufacturer to file an ANDA with a Paragraph IV certification 180 days of market exclusivity. During this 180-day exclusivity period, the FDA may not approve later filed ANDAs based on the originator's NDA²⁰¹.

The original version of the HWA created some problems regarding collusive settlements of claims²⁰². Under the pre-2003 version of the HWA, the 180-day exclusivity period could be "triggered" by either the first Paragraph IV ANDA filer's commercial marketing of its generic drug product, or a court decision of non-infringement or invalidity of the Orange Book patents. Significantly, only the first Paragraph IV ANDA filer could begin the 180-day exclusivity period via the commercial-marketing trigger. In these circumstances, should an originator convince the first-filer to delay going to market, perhaps via a favorable settlement agreement, then subsequent ANDA filers would be blocked from going to market while they waited for the first filer to complete its exclusivity period. This situation is commonly referred to as "parking" the exclusivity period²⁰³.

Under the earlier version of the HWA the only recourse subsequent ANDA filers had was to trigger the first filer's exclusivity period via a successful court judgment. However, if the pioneer successfully refused to litigate with the subsequent ANDA filer and instead offered a covenant not to sue, the subsequent ANDA filer remained locked out of the market until after the primary filer completed its exclusivity period. (This is not an available feature in the EU where generic first filers do not obtain exclusivity.)

Recognizing that such a situation obstructed the policy objectives of the HWA, in December 2003 Congress passed Title XI of the Medicare

¹⁹⁸ See 21 U.S.C. § 355(j)(2)(A)(vii) (I-IV).

¹⁹⁹ See 21 U.S.C § 355(j)(5)(B)(iii).

²⁰⁰ *Id.*

²⁰¹ See 21 U.S.C § 355(j)(5)(B)(iv).

²⁰² See also Sector Report paras 573, 659-660 and Annex to Chapter C.2.4 at pp. 425-426.

²⁰³ See, e.g., *Apotex, Inc. v. Pfizer Inc.*, 385 F.Supp.2d 187, 189-90 (S.D.N.Y.2004).

Modernization Act of 2003 (the "MMA"). The MMA replaced the exclusivity period triggering provisions with new "forfeiture" provisions. These provisions are designed to, *inter alia*, curb "parking" of the exclusivity period. Under the amended version of the statute, the 180-day exclusivity period is triggered only when the first ANDA filer takes its generic to market. However, the MMA sets forth a number of "forfeiture events" that result in the total elimination of the exclusivity period²⁰⁴.

Thus, under both the pre-2003 and current versions of the HWA, a subsequent ANDA filer could hasten market entry by establishing the invalidity or non-infringement of the NDA holder's Orange Book patents²⁰⁵.

The MMA also extended the relevant federal court declaratory judgment jurisdiction under 28 U.S.C. § 2201²⁰⁶ regarding patents in order to further facilitate the ability of subsequent ANDA filers to obtain a court judgment of non-infringement or invalidity of the NDA holder's Orange Book patents²⁰⁷.

Accordingly, the HWA provides a system simplifying market authorization for generic drugs as well as providing an efficient, centralized procedure where a generic manufacturer may assert any and all claims testing the strength of patent protection. The HWA system cuts transaction costs for all parties and eliminates the cost to the Government of obtaining information sufficient to determine whether or not a pharmaceutical patent is weak, or if it has been obtained by misuse, inequitable conduct, fraud, or any other inappropriate means. In addition, any antitrust claims are heard at the same time as the main claim. The parties with the most at stake and the best access to information are the ones who conduct the litigation. This eliminates the necessity of amending the patent system to provide for these functions.

3.1.15 Conclusion

The process of commercializing a medicinal product is long, uncertain, expensive, and extremely complicated. Business decisions are complicated

²⁰⁴ See 21 U.S.C. § 355(j)(5)(D)(i). (For example, a primary ANDA filer that, for some reason, is not sued by the NDA holder, will lose its exclusivity period if it fails to go to market within 75 days after its ANDA is approved. 21 U.S.C. § 355(j)(5)(D)(i)(I)(aa)(AA). Likewise, a primary ANDA filer will lose its exclusivity period if it fails to take its generic to market within 75 days after a court judgment of invalidity or non-infringement. 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(AA).)

²⁰⁵ See *e.g.* *Caraco Pharm. Labs., Ltd. v. Forest Labs., Ltd.*, 527 F.3d 1278, 1286 (Fed.Cir.2008.)

²⁰⁶ 35 U.S.C. § 271(e)(5) ("to the extent consistent with the Constitution.")

²⁰⁷ See also, *Janssen Pharmaceutica N.V. v. Apotex, Inc.*, 540 F.3d 1353, 1357 (Fed. Cir. 2008) ("Prior to the MMA, NDA holders employed several different methods of delaying the early resolution of patent disputes.") (citing *Teva Pharm. USA, Inc. v. Novartis Pharm. Corp.*, 482 F.3d 1330, 1342 & Fn. 7 (Fed.Cir.2007))

and involve considerations evaluating the effects of complex scientific, legal and regulatory systems on a global scale.

4 THE PHARMACEUTICAL SECTOR REPORT “Is there no balm in Gilead?”²⁰⁸

The Sector Inquiry began by questioning the reason why fewer NME’s were being approved and reaching the market in the EU. The Sector Report issued November 28, 2008 contains the preliminary results of the Commission investigation.

4.1.1 THE REPORT

The Sector Report comprises 426 pages including 22 pages of Annexes. It is divided into an Executive Summary, a Glossary and five lettered Sections along with their subsections. The Executive Summary contains a general description of each Section and Subsection along with conclusions with respect to each. There are 21 separate summaries of the materials in the Sector Report which repeat relevant portions of the Executive Summary nearly verbatim. The summaries do not present a great deal of detail regarding methodology. They are also organized such that issues are discussed and reintroduced in a somewhat fragmented manner. Accordingly, I present an edited version consolidating points from the Executive Summary and the Introduction²⁰⁹. I also present a somewhat more detailed summary of four areas of the Sector Report, and their methodology in the analyses contained in section Five.

4.1.2 The EXECUTIVE SUMMARY

4.1.2.1 INTRODUCTION To Summary

The Executive Summary²¹⁰ begins by detailing how important the pharmaceutical sector is to Europe and the need for access to safe, innovative and affordable medicines. It then details the genesis of the Sector Inquiry under EC competition rules as the result of information which suggested that competition might be restricted or distorted as indicated by a decline in innovation (as measured by the number of novel medicines reaching the market.) The Report also refers to instances of delayed generic market entry compare to what might be expected. The Sector Report confirms the decline in new chemical entities and generic products reaching the market.

The Sector Inquiry relates to the period from 2000-2007 and involved investigation of a sample of 219 INN’s. The main findings are:

²⁰⁸ Jeremiah 8.22.

²⁰⁹ Sector Inquiry pp. 21-25.

²¹⁰ Sector Report pp. 5-16.

1. Patents are key to the pharmaceutical sector, permitting companies to recoup their investment and as a reward for their innovative efforts.
2. Originator companies have designed and implemented strategies (a “tool-box” of instruments) aimed at ensuring continued revenue streams. Although there may be other reasons for delays to generic entry the Report found that originator strategies may have the effect of delaying or blocking such entry. These strategies include filing of patent clusters of up to 1,300 EU-wide patents for a single medicine, engaging in disputes with generic companies resulting in nearly 700 cases of patent litigation, concluding settlement agreements with generic companies which may delay generic entry and intervening in approval procedures for generic marketing authority.
3. The Report confirms that generic entry occurs later than might be expected with average time for generic entry after LoE of seven months and four months for the most valuable medicines. Based upon average drops in price levels upon generic entry the Sector Report estimates that savings from generic entry, without any delay is about 3 Billion Euros annually.
4. Preliminary findings suggest that originator companies develop and practice defensive patenting strategies primarily to block development of new competing products. This can lead to obstacles to innovation in the form of higher costs for competing pharmaceuticals (e.g. for royalties) or in delays.
5. Generic and originator companies agree for the need for a Community Patent and for a unified and specialized patent judiciary. Various stakeholders reported bottlenecks in marketing approval and pricing procedures that may contribute to delays in bringing products to market.

4.1.2.2 Main Market Features

The Report concludes that the Pharmaceutical Sector is R&D driven and highly regulated. It identifies originator and generic companies as the two main supply side companies. Originator companies are active in R&D and the development, manufacturing, marketing and supply of innovative medicines which are usually subject to patent protection as a reward and incentive for innovation. When patent protection expires, originator companies lose their exclusive rights to manufacture and market these medicines. At this point generic manufacturers can enter the market with copies of originator medicines or their equivalent, typically at lower prices. This helps contain public budgets, contributes to increases in consumer welfare, and creates incentives for further innovation.

During the 2000-2007 period under study originator companies spent an average of 17% of their turnover on R&D, on a worldwide basis, with 1.5% spent on basic research to identify potential NME's and the balance spent on pre-clinical and clinical trials. Worldwide marketing and promotional expenditures accounted for 23% of turnover. A few “Blockbuster” medicines (annual global turnover exceeding US \$ 1 Billion) account for a substantial part of originator sales and profits. A number of Blockbuster medicines have lost patent protection and more will do so in future. This

inter alia has created incentives for originator companies to extend the period during which they enjoy blockbuster revenues.

Generic companies are generally smaller than originator companies, often regional in nature, and with limited R&D activity. Their main source of income comes from the sale of medicines equivalent to blockbuster products whose exclusivity has expired.

The Demand Side of the market is unusual in that purchasing decisions for prescription medicine by the ultimate consumer are made by others, (generally the prescribing physician and/or the pharmacist.) In addition, consumers generally do not bear the full cost which is met by national health schemes. This results in limited price sensitivity.

4.1.2.3 Product Life Cycle

The Report identifies three phases of the life cycle of a new medicine: (1) R&D up to market launch. Companies identify potential new medicines and take them through pre-clinical and clinical trials. Originator companies rely heavily on innovations acquired from third parties; (2) the period between launch and loss of exclusivity (e.g. patent expiry.) Here, the originator companies market the medicines with a view to recouping up-front investments and making a profit. Effective patent protection is vital to this business model and provides incentive for further innovation.; and (3) the period following LoE when generic companies can enter the market. The market share of generic medicines varies significantly between Member States. The generic share is highest in Poland (56%, Portugal and Hungary (both 32%) and lowest in Ireland (13%), France (15%) and Finland (16%).

The Report found that originators launched second generation/follow-on medicines for 40% of the sample INN's which lost exclusivity. Launch of these medicines occurred on average, one year and 5 months prior to LoE and in some cases, the first generation medicine was withdrawn. Originators promote the follow-on medicines intensively. If successful, this decreases the probability that generics will be able to gain significant market share. The launch of follow-on products is often carefully prepared from a patent point of view. This requires new patent filings. Nearly 60% of the patent related litigation cases concern medicines for which follow-on medicines were launched. While it is generally accepted that incremental innovation is achieved by such patenting, such secondary patents are criticized by other stakeholders as weak.

4.1.2.4 Impact of Generic Entry

Half of the 219 INN's losing LoE (representing about 74% of sales), faced generic entry within the first year. Generic companies market generics on average, 25% lower than the originator in the first year and 40% below that two years later. Generic companies achieve about 30% of market share in the first year and 45% after two years. Where generic medicines become available average-weighted-savings to the health system is 20% one year after entry and 25% after two years.

4.1.2.5 The Regulatory Framework

Patent, Marketing Authority and Rules on Pricing/Reimbursement are particularly relevant to the Sector.

Patent protection in the EU is for a term of 20 years. SPC's for the Sector extend patent protection for a maximum of five years. Despite significant efforts there is no Community patent nor Community patent judiciary. While the EPO handles centralized application, opposition, and appeal procedures, once validated patents turn into a bundle of national patent rights, which must be challenged at the national level. This can lead to conflicting decisions and is costly and time-consuming.

4.1.2.6 Marketing Authorization

The Report noted reporting constituencies' complaints of bottlenecks in marketing authorization procedures leading to obstacles/delays and administrative burdens²¹¹. These complaints ranged from allegations of lack of resources and obstacles for generic companies in the form of discrepancies in assessment criteria, patent linkage and agencies' consideration of disclosure of information to competitors²¹². Originators supported more international harmonization of marketing authorization procedures citing significant differences between the EU and US.

4.1.2.7 Pricing and Reimbursement

The Report noted originator complaints regarding delays and uncertainty created by national pricing and reimbursement procedures arguing that these shortened exclusivity periods. Generic companies made similar complaints about delays in pricing and reimbursement decisions as well as complaints about additional requirements regarding patent status or equivalence to reference products arguing that this gave originator companies opportunities to intervene and prolong their de-facto exclusivity²¹³.

4.1.2.8 The Introduction to the Sector Report

The Introduction states that with respect to its first issue (generic entry) the Commission examined all patent and product life cycle strategies of originators which are listed²¹⁴ as:

- (a) **patenting activities of originators.** This includes strategies of filing patent clusters or patent thickets for the same medicine and divisional patent applications, often late in the life cycle of the product²¹⁵,
- (b) **contacts, disputes and litigation between originator and generic companies.** The Commission found approximately 1,300 patent related contacts and disputes, the majority of which were initiated by originators²¹⁶. The Commission found 700 litigation cases of which 149

²¹¹ Sector Report p. 15.

²¹² *Id.*

²¹³ Sector Report at pp.15-16.

²¹⁴ Sector Report para. (9).

²¹⁵ Sector Report p. 9-10.

²¹⁶ Sector Report p. 10.

reached final judgement²¹⁷. The average duration was 2.8 years. Injunctions were sought in 225 cases and granted in 112. The total cost of litigation from 2000-2007 was estimated to exceed 420 million Euros.

- (c) **opposition procedures and appeals before patent offices.** The Commission found that oppositions before the EPO were brought by generic companies against originator companies more frequently than oppositions in all other sectors and that they prevailed in achieving revocation or restriction of scope approximately 75% of the time²¹⁸. The Commission found that generic companies opposed secondary patents almost exclusively.
- (d) **patent settlements and other agreements between originator and generic companies.** The Commission found that originator and generic companies resolved claims in litigations, patent disputes and opposition procedures by means of settlement agreements in 200 settlement agreements between 2000 and June 2008 covering 49 medicines. Of these, 67% were best selling medicines losing exclusivity between 2000 and 2007²¹⁹.
- (e) **interventions of originator companies before national authorities deciding on marketing authorization, pricing and reimbursement of generic products.** The Commission found that originator companies intervened a significant number of times before national authorities other than patent offices when generic companies applied for marketing authority and pricing/reimbursement status²²⁰. These interventions concerned claims that generic products were less safe or of inferior quality, or that grants of marketing authority or pricing or reimbursement status could infringe patent rights²²¹. These interventions often focused on a few high-turnover products. The Commission also found that when patent related interventions were litigated 2% of the claims of originator companies were upheld. The Commission found that such interventions resulted in on average, marketing authorization delays of four months²²².
- (f) **promotional activities, including follow-on products,** The Commission found that originators spent on average 23% of their turnover on promotion and marketing activities and found indications that these included practices intended to question the quality of generic medicines²²³. The Commission found that where originator companies launched second-generation products they undertook extensive marketing efforts designed to switch users to the new medicine prior to generic market entry, which would decrease generic market share. The Commission also found that where second-generation products came on the market after generic entry originators had difficulty in convincing doctors to prescribe them or to obtain a high price for the product²²⁴;

²¹⁷ Sector Report p. 10.

²¹⁸ Sector Report pp. 10-11.

²¹⁹ Sector Report p. 11.

²²⁰ Sector Report pp.11-12.

²²¹ *Id.*

²²² Sector Report p. 12.

²²³ Sector Report p. 12.

²²⁴ Sector Report p. 13.

and

(g) **second generation products.** The Commission found that while there were incremental advantages to second-generation products, circumstances typically associated with their introduction of follow-on products suggest that they often form part of originators' larger life-cycle strategy attempting to delay or prevent generic erosion due to loss of exclusivity²²⁵. Generic companies complained that such products are part of originators' "evergreening" strategies designed, because they show little innovation and serve primarily to retain revenue streams from first generation products²²⁶.

As regards the second issue investigated (relationships between originator companies), the Introduction states²²⁷ that the Inquiry investigated the patent strategies of originators, contacts, disputes and litigation between them, opposition procedures before patent offices and settlement agreements between them.

4.1.2.9 Sector Report's Conclusion

The Sector Report's Conclusion²²⁸ determined that while patents are key to originator companies recouping their investment and are a reward for innovation, originator companies have designed and implemented a "tool-box" of instruments aimed at ensuring continued revenue streams. It further finds that although there may be other reasons for delays to generic entry, successful implementation of the tool-box may have the effect of delaying or blocking such entry. The Commission refers to filing patent clusters of up to 1,300 patents for a single medicine and engaging in disputes with generic companies leading to nearly 700 cases of patent litigation, settlements which may delay generic entry and intervention in national procedures for generic approval. The additional costs caused by delays to generic entry can be very significant for health budgets and ultimately the consumer. The Inquiry confirmed delays to generic entry over the period 2000-2007 which, had they not occurred would have lead to savings of about 3 Billion Euros over the period.

The Conclusion preliminarily found that originator defensive patenting strategies were practiced primarily to block development of competing products leading to obstacles to innovation in the form of higher costs for competing pharmaceutical companies, or in delays.

The Conclusion preliminarily found support for stakeholders' views that there was a need for a single Community Patent and the creation of a unified and specialized Patent Judiciary. The Conclusion refers to stakeholders' perception of bottlenecks in marketing approval and pricing and reimbursement decisions, which may contribute to delays in bringing products to market.

²²⁵ Sector Report paras 831-836.

²²⁶ Sector Report para. 830.

²²⁷ Sector Report para. (11).

²²⁸ Sector Report pp.401-403.

4.1.3 THE FOUR AREAS OF THE REPORT ANALYZED

In the next section I analyze four areas of the Sector Report. 1. The Report's failure to address the Sector Inquiry's original mandate to determine why fewer NME's were coming onto the market; 2. Litigation between originator and generic manufacturers; 3. The Report's failure to examine generic manufacturers' "Tool Boxes"; and 4. The Report's recommendations.

5 ANALYSIS AND CRITICISM OF FOUR KEY ISSUES IN THE SECTOR REPORT

The thesis' analyses of the Report's failure to explain why fewer NME's were coming to market is addressed in six points: 1. The absence of any predicted findings of Astrazeneca type, misuse of public procedures. 2. The examination of originator/originator competition. 4. Examination of Divisional patent applications in relation to originator/originator competition. 5. Diversion from the goal by possible institutional bias. 6. The absence of an examination of prior Commission findings regarding competition and innovation in the Pharmaceutical Sector.

The Thesis' analyses of how the Report treats originator/generic litigation is addressed in nine points. 1. The Report expressly ignores the effect of the ECJ's holding in Roche Nederland in its statistical analysis of litigation in 27 Member States. 2. The Report's analysis of originator/generic litigation regarding secondary patents and divisional patent applications is not relevant to generics' ability to utilize a basic drug patent and clinical information to market a generic drug. 3. The Report makes the assumption that generic manufacturers are entitled to originators' subsequently filed, valid IPR for secondary patents and claims in their divisional applications. 4. The Report's assertion that originator/generic litigation and other "tool box" devices delays generic entry is contradicted by the Report's own findings. 5. The Report's statistics fail to distinguish between Data from fundamentally different Data sets. 6. The Report makes conclusions based upon very small samples. 7. The Report treats Data collected after the fact as if it were from ex ante designed double blind statistical tests. 8. The Report assumes that IPR cases lost by originators were interposed solely for purposes of tactical delay. 9. The Report makes inappropriate inferences against originators from the Data.

The Thesis' analysis of the Report's failure to examine generic companies' commercial behavior is divided into two parts. 1. An introduction to the issue including reports of additional "Dawn Raids" conducted by DG Competition based upon information gained in the Sector Inquiry and 2. Indications of the existence of generic uses of commercial practices similar to the originator "tool boxes" found in the Report and evidence of such commercial practices taken from other sources including public filings.

The Thesis' analysis of the Report's Recommendations is divided into 3 sections. 1. The Recommendation for a Unified Patent System and Patent Judiciary is not new and is not likely to be enacted in the near future. 2. Strengthening patenting requirements is an inefficient way to solve competition problems would have significant transaction costs and would

create many negative externalities. 3. Competition law is a poor tool to fix patent-based originator “tool boxes.

5.1.1 The Sector Report’s poor organization, contradictory statements and errors make it difficult to analyze

It must be noted initially that the Preliminary Sector Report appears to have been assembled from numerous sources acting independently without harmonizing them. It is characterized by poor organization, extensive repetition, and contradictory statements²²⁹. For example, patents and the patent system are described *ab initio* numerous times in various places rather than as one unitary issue with sub parts applicable to relevant issues. More significantly, while the Sector Report analyzes some 698 cases of patent litigation against all classes of defendants²³⁰ the Report’s Conclusion claims that originator companies engaged “in disputes with generic companies leading to nearly 700 cases of reported patent litigation²³¹.” Some statements (an example is quoted in the footnote²³²) belabor the obvious and demonstrate either DG Competition’s complete naivete regarding business practices or willful ignorance of how an exclusionary legal regime operates. Important citations are completely erroneous²³³,

²²⁹ Sector Report para. (13). (Paragraph 13 states that the exclusivity period for the entire sample expired during the 2000-2007 period examined. This is wrong as it is clear that the 219 INN’s selected include, for example the T50 list of INN’s for which originator products were launched during the 2000-2007 period. *See, e.g.*, Para. 323 and Figure 37 and Annex at p. 410, paras. 15-18 (Selection of 219 INN’s.)

²³⁰ Sector Report paras. 461-480. “More specifically, originator and generic companies were asked to report on all patent-related litigation to which they were a party, and which was launched in the EU in the period 2000-2007.”(Para. 461.)

²³¹ Sector Report p. 401 “Competition between Originator Companies and Generic Companies.”

²³²

3.1.2.6. Detecting Potential Infringement Issues by Patent Owners

(979) Mirroring patent clearance studies, once a patent has been granted, the patent holder will in many cases ensure that his patents are not infringed. The analysis of material submitted indicates that many originator companies are concerned to defend their intellectual property rights and that many carry out a continuous and thorough review of their own patent portfolio with the intention of detecting potential infringements by other originator companies. As, for example, one company stated: “Our company is continually reviewing its patent portfolio to ensure that our IP is properly respected [...]”

²³³ *N.B.* The Sector Report made a significant error when citing the applicable Directives and Regulations in Section 2.2 “Regulatory Framework” (Sector Report para. 251 Fn 133) concerning procedures for obtaining Marketing Authority. Directive 2001/83 (which the Sector Report had earlier cited correctly several different times. *See*, Sector Report at paras. 56 Fn 19, 89 Fn 32, 100 Fn 43, 137 Fn 57, 212 Fn 90, 246 Fn 129.). Section 2.2 of the Sector Report cites Directive 2001/83 “(as last amended by Directive 2008/27/EC OJ L 81, 20.3.2008, p. 45)”. This is painfully wrong. Directive 2008/27 (including the incorrect OJ citation) refers to the deliberate release of genetically modified organisms into the environment. It does not refer to Directive 2001/83 or indeed, to medicinal products at all. This is quite sloppy, as anyone who actually looked at that Directive’s title should have seen the problem. The correct citation, of the Directive

requiring readers to employ their own “Guide for the Perplexed”²³⁴ in order to know which statutory measure is being referred to. Rather than proceeding from first principles with further elucidation, the same idea springs several times from several places, like twenty Athena’s from the brows of twenty Zeus’²³⁵. Even the Report’s premise that innovation is slowing as measured by fewer NME’s coming to market is suspect. The CBO Study for instance, questions using the number of NME’s approved per year as an accurate measure of innovative output²³⁶. In addition, areas of inquiry are organized differently in different sections where same or similar issues are examined.

These factors unduly complicate the process of critically analyzing the Sector Report’s contents.

5.2 Failure to address the primary reason for the Sector Inquiry-Why are fewer new medicines are coming into the market.

“Patent protection has never been stronger, but the number of new pharmaceuticals coming to market is declining.”²³⁷

...

“[I]f innovative products are not being produced...then we need to find out why and, if necessary take action.”²³⁸”

The Sector Inquiry was initially concerned with a slowdown in marketing authorizations for NME’s²³⁹. One of the chief stated concerns was that cases of competition law violations such as found in the Commission Decision of

2001/83’s last amendment is “Directive 2008/29/EC of the European Parliament and of the Council of 11 March 2008 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the implementing powers conferred on the Commission, OJ L 81, 20/03/2008 p. 51.”

²³⁴ See Moses Maimonides, *THE GUIDE FOR THE PERPLEXED*, 12th Century A.D.

Translated from the original Arabic Text by M. Friedländer (2d Ed. Routledge & Kegan Paul Ltd. London 1904).

²³⁵ See, Hesiod’s Epic Poem, *Theogony* (c. 700 BC).

²³⁶ CBO Study at pp. 35-36 (Noting that failure to include innovations stemming from modifications to existing drugs which benefit consumers does not measure important results from R&D.)

²³⁷ January 16 Speech p.2.

²³⁸ Closing sentence of January 16 Speech.

²³⁹ COM(2008) 666 Celex No. 508DC0666 Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions - Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector, Brussels, 10/12/2008. (“COM (2008) 666”) Improving Competition and Market Access (“The inquiry concerns ‘the introduction of innovative and generic medicines for human consumption onto the market’.”)

15 June 2005 in Case COMP/A. 37.507/F3AstraZeneca, might be impeding the introduction of NME's²⁴⁰. When it was issued, the Sector Report addressed a number of secondary issues such as delays in generic entry and competition between originators for non-innovative improvements to existing drugs. The Sector Report curiously, never addressed the Sector Inquiry's *raison d'être*, why were fewer NME's coming to market? I would like to explore why the Sector Report did not "find out why". It is always difficult to discern reasons for a negative. However, in view of the importance of the question and the amount of effort expended by the Commission and stakeholders on finding answers I wish to explore some possible rationales for this mission failure.

5.2.1 The Report Did Not Find More AstraZeneca Type Abuses of Public Processes

Initially, it appeared that the Commission had information regarding substantial abuses of public procedures such as it found in the AstraZeneca case relating to bringing new medicinal products to market. The January 16 Speech by Neelie Kroes, the Press Release, and FAQ either cited AstraZeneca or intimated that there were more such cases. In contrast, the Sector Report, cited AstraZeneca several times²⁴¹ (inferring that the Report's originator "tool boxes" were functionally similar to those described in pre 2000AstraZeneca strategy documents²⁴².) However, unlike AstraZeneca, the Sector Report gives no example of false statements or sham legal actions brought by originators in furtherance of any marketing strategy. Nor are any examples cited of false statements made in order to obtain marketing authority, grants of SPC certificates, or false statements before any court or national authority. The abuses of a dominant position found in the AstraZeneca Decision did not consist of having a business strategy but rather, of the abuse of public procedures in order to accomplish them. The actions described in AstraZeneca, misrepresentations to Courts and public authorities, were illegal acts that on their own were punishable as such under National Law. The Sector Report discloses no such behavior.

Most importantly however, regardless of the existence of originator business strategies, the Report makes no finding that basic patents for new medicinal products (the measure cited for commencing the Inquiry) are

²⁴⁰ *Id.* ("The main focus of the inquiry is the commercial behaviour of market participants affecting market entry of competing novel or generic medicines.")

²⁴¹ See paras. 248 (re originator misleading statements to national authorities), 870-872 (citing AstraZeneca as a clear case of originator resort to tool boxes) 871-872 (citing to and quoting from AstraZeneca strategy documents from the 2005 Commission Decision before describing the originator tool box examples it describes in the Report) and p. 407 Annex describing case as an example of an abuse of a dominant position under Article 82 EC.)

²⁴² See Sector Report at paras 870-872 (which quotes from paragraphs 532 and 299 of the AstraZeneca Decision. Para. 532 are the Commission's assessment of documents dating from 1998-199 period cited in paras. 298-293 of the Decision and para 299 of the Decision quotes a November 1998 strategy document.

being delayed by reason of any anticompetitive action²⁴³. It seems likely therefor, that the Commission's inferences that AstraZeneca type abuses were widespread, were based upon the documents it found in its AstraZeneca investigation, but that it failed to find any other such evidence in the Sector Inquiry²⁴⁴. If the Commission has found other evidence indicating similar behavior when it commenced the Sector Inquiry, that evidence does not appear in the Sector Report. If it existed at all.

The AstraZeneca case itself did not deal with blocking innovative drugs but rather, with denying or delaying generic entry through misuse of public proceedings. The activities complained of in the AstraZeneca Decision occurred prior to the 2000-2007 period of the Sector Inquiry and were widely publicized. The European basic patent for Omeprazole expired April 3, 1999²⁴⁵ and various basic patents filed at the national level expired between April 10, 1999 and August 8, 1999²⁴⁶. The first abuses complained of by AstraZeneca, began with misrepresentations made from June, 1993 through December 1994 and the second set of abuses, by reason of misrepresentations made between March and November 1998²⁴⁷. The initial complaint was made by Generics (UK) Limited and Scandinavian Pharmaceuticals Generics AB on May 12, 1999²⁴⁸. The abuses complained of dealt with statements in connection with obtaining SPC certificates from national authorities and the assertion of SPC certificates obtained essentially by false pretences against generic companies from national authorities and in national courts. The most significant legal questions concerning the conditions for filing for SPC certificates were settled by the ECJ in 2003 in *Hässle AB v Ratiopharm GmbH*²⁴⁹. It is fair to infer that, even if other pharmaceutical companies had been practicing the same sort of misrepresentations found in AstraZeneca they had probably ceased to do by 2000, or that evidence of past misuse no longer existed by 2008. One would expect that the Sector Report would have listed any anticompetitive activities directed at developing new medicines discovered by the Inquiry. If such anticompetitive practices did exist at one time in the Sector, the AstraZeneca Decision may have achieved one of its primary goals by discouraging other undertakings from engaging in such abuses.

If, however, the Sector Inquiry did not find the type of information regarding such practices where it expected to it should have discharged its mandate to give an accurate picture of the sector as a whole and sought elsewhere for answers to its primary question. It appears that DG

²⁴³ Commission statements regarding the second set of "Dawn Raids" made two days prior to release of the Sector Report referred to possible abuses of a dominant position but specifically denied that they were related to the Sector Inquiry.

²⁴⁴ Despite having free access to all corporate records of the undertakings it inspected and copying more than 20,000 pages of them during the January 15, 2008 Dawn Raids and sending out more than 200 questionnaires. *See*, Sector Report, paras. 17 and 18.

²⁴⁵ AstraZeneca Decision para. 20.

²⁴⁶ AstraZeneca Decision para. 21.

²⁴⁷ AstraZeneca Decision paras 916 and 917.

²⁴⁸ AstraZeneca Decision p. 1 Recitals.

²⁴⁹ Case C-127/00 European Court Reports 2003 page I-14781

Competition did not. If this was the result of discovering that there was no competition law related causation it should have made that finding.

5.2.2 The Report's Investigation of Originator c. Originator Practices did not address the Inquiry's Mandate

The Sector Report made a study of patenting and disputes between originators²⁵⁰. It found that originators performed patent searches before committing itself to research and commercialization of new drugs. It further found that nine originators filed patents defensively in order to protect themselves from competition in the R&D and Commercialization stages of drug development²⁵¹. It found that defensive patenting strategies consisted of filing patents to protect its original products from competing products²⁵², and from other originators blocking their commercialization of an original product²⁵³. The Report also found that basic patents often contained broad claims and that they attempted to file them early²⁵⁴. The Report inferred that broad claims and early filing were somehow connected to “smokescreen” patent protection which it claims is a strategy of filing patents with broad claims in order to disguise which subjects are of real importance to the originator²⁵⁵. This is a fundamental misreading of the normal processes of drug discovery and marketing approval. Readers are referred to the thesis’ description of the R&D and patenting phases of drug discovery and marketing. No pharmaceutical company would wish to commit itself to a huge investment in R&D and bringing a drug to market without attempting to find out if the investment was subject to IPR protection. Broad basic patent claims are the norm, especially when, at the time, the operation of the NCE in the human body is not known without information from clinical trials. This is not “smokescreen design”. As the process moves forward problems arise in clinical trials and in manufacture which must be solved. Business and clinical processes must be properly understood before they can be identified as market abuses. Divisional Applications for the basic patent will have been ruled upon the latest, some time during the Clinical trial stage and would not be a factor some 10 or 12 years later when MA is granted, nor later, near the expiration of LoE when generics usually commence opposition proceedings. The Sector Report fails in this area.

5.2.3 Claims that Divisional Patent Applications

²⁵⁰ Sector Report paras. 926-1081.

²⁵¹ Sector Report para. 962.

²⁵² Sector Report para. 961.

²⁵³ Sector Report paras. 946-948.

²⁵⁴ Sector Report paras. 952-956.

²⁵⁵ Sector Report paras. 953-954. (“The patent application will then usually claim a whole class of compounds that have a similar molecular structure and are believed to show similar effects. Later on the company may be able to split the application into divisional applications covering individual claims made in the first applications and/or file applications for secondary patents relating to e.g. the formulation, dosage or new indications of the compound.”)

have blocked basic innovation are overblown

The Report stated that six of 43 originators found that competitor's divisional patent applications had interfered with their R&D efforts²⁵⁶. The originator behavior reported appears to be normal commercial behavior in the pharmaceutical sector where capital investment decisions hinge on the originator's ability to protect an investment. Since a divisional application deals with the claims of a patent application it would appear that the effects on innovation would be minimal since the claims would either have already been contained in the original grant or the new claims would be relatively close to them²⁵⁷. Claims relating to secondary process and manufacturing patents likewise have little relevance to the innovation issues of the basic patent.

The Report identified 1,100 instances in 27 EU States from 2000-2007 where patents may have been infringed²⁵⁸. The Report listed 200 patent related contacts over the seven-year period²⁵⁹. The Report singles out 99 instances of originator requests for licenses of which 77 were resolved amicably, 4 were the subject of ongoing negotiations and 16 cases where the patent holder indicated that it planned to use them in order to introduce a novel medicine²⁶⁰. In five of the cases of refusal to license, the patent was designed around²⁶¹. The Report makes conclusions about patent hold up based upon a tiny universe of approximately 14 instances a year spread over the EU. In addition, despite such a sterling record of licensing cooperation the Report concludes that while in many cases originator companies tried to settle potential disputes, “[h]owever, in approximately 20% of the cases where a licence was requested the patent holder refused.²⁶²” This is an extraordinary attempt to misdirect attention from the 80% of requests (80 cases) over a period of seven years, which were resolved by a license grant. In 16% of the remaining cases (16 cases) the patent holder intended to use its exclusionary right to develop innovative medicines. This leaves 4 cases of refusal to license, in 27 Members, over a seven year period which, even leaving out consideration of the small sample, isn't even statistically significant on a percentage basis. This would be so, even if the 4 cases solely related to innovative R&D. (A fact which is not even suggested by the Report.) This also contradicts the Commission's widely promulgated view of technological licensing as broadly procompetitive²⁶³. In light of the

²⁵⁶ Sector Report paras. 974-976.

²⁵⁷ EPC 73 Art. 76, EPC 2000 Art. 76.

²⁵⁸ Sector Report para. 986.

²⁵⁹ Sector Report para. 989.

²⁶⁰ Sector Report para. 996.

²⁶¹ Sector Report para. 998.

²⁶² Sector Report Section Summary at p. 350.

²⁶³ See Commission Regulation (EC) No 772/2004 of 27 April 2004 on the application of Article 81(3) of the Treaty to categories of technology transfer agreements (Text with EEA relevance) OJ L 123, 27/04/2004 p. 11 Recital 5:

Technology transfer agreements concern the licensing of technology.

Such agreements will usually improve economic efficiency and be pro-

Sector Report's inappropriate examples of anticompetitive patent licensing²⁶⁴ the mere fact of their limited appearance in patent disputes is not sufficient to create an inference that anticompetitive abuses exist.

Likewise in respect of litigation between originators, the Report lists 66 litigations between originators over seven years and 27 Member States²⁶⁵. Of these, 62% (41 cases²⁶⁶) involved 5 INN's of which 43 cases were concentrated in just three countries²⁶⁷. These average out to 9.43 litigation cases a year, spread unevenly over all 27 Member States. From this tiny sample the Report proceeds to use percentage figures (along with elaborate charts and graphs) in order to make conclusions based upon a (better sounding) 64% settlement rate and a loss rate for patent holders coming to final judgment of 77%.

To put this in its proper perspective the Commission elsewhere reports that in the years 2000-2006, between 1,500 and 2,000 patent infringement actions were brought in the EU yearly, of which 60-70% concerned European Patents²⁶⁸. At the rate of 1,500 per year, that would come to 105,000 patent infringement actions. One should consider the motivation of the Sector Report's putting so much effort into analyzing just 66 cases. And their relevance.

competitive as they can reduce duplication of research and development, strengthen the incentive for the initial research and development, spur incremental innovation, facilitate diffusion and generate product market competition.

See also, Commission Notice - Guidelines on the application of Article 81 of the EC Treaty to technology transfer agreements (Text with EEA relevance) OJ C 101, 27/04/2004 p. 2 Section II arts. 8 and 17. (While the TTBER exemptions do not apply where the market share is exceeded the Commission's views regarding the procompetitive effects of licensing and its views on the application of Art 81(3) defenses should also be taken into account.)

²⁶⁴ *See* Sector Report at para. 628 where provisions in settlement agreements acknowledging that the generic was infringing a patent and refrain from entering the market as well as clauses where generics may enter markets under license agreement are considered to limit generic entry. In the former case a generic which has infringed a patent would have no right to enter and in the latter case the Commission's position is questionable in light of *Bayer AG and Maschinenfabrik Hennecke GmbH v Heinz Sullhofer*, Case 65/86. ECR 1988 page 5249. (No challenge clause in settlement of pharmaceutical patent litigation did not violate competition law where no royalties were paid and where the licensed process was outdated. The ECJ specifically held in para. 19 that in the event a National Court were to determine that a no challenge clause where royalties were paid restricted competition the Court would still have to verify whether, given the positions held by the undertakings concerned on the market for the products in question, the clause is of such a nature as to restrict competition to an appreciable extent.)

²⁶⁵ Sector Report para. 1006.

²⁶⁶ Sector Report para. 1007 states "namely 40 of the 66 cases" pointed to the chart in Figure 135 which clearly identifies 62% or 40.91. I won't quibble but this is just one example of the Sector Report's "New Math" approach to statistics.

²⁶⁷ Sector Report para. 1012.

²⁶⁸ COM (2007) 165 Communication from the Commission to the European Parliament and the Council - Enhancing the patent system in Europe, Brussels, 3.4.2007, Celex No. 507DC0165 ("COM (2007) 165") at 2.2.2. "National patent litigation systems in the EU: facts, figures and costs".

The Report states that 75.8% (50 cases) of originator/originator litigation concerned substances in the same ATC3 class and indicated that the parties were actual or potential competitors²⁶⁹. This comes to 7.14 cases a year. According to the World Health Organization, ATC3 indicates a therapeutic/pharmacological subgroup that works on a particular system²⁷⁰. ATC3 is a broad classification covering several disease areas. DG Competition's decision in AstraZeneca, held that ATC3 is not an appropriate indicator of whether or not parties are in actual or potential competition which requires market analysis at the ATC-4 level²⁷¹.

Accordingly, the Sector Report's examination of originator/originator patenting and disputes makes no relevant contribution responsive to the question of whether or not there is a distortion of the competitive environment which delays or prevents innovative medicines coming to market.

5.2.4 Possible Institutional Bias

DG Competition may have felt constrained to look only for violations of Articles 81 and 82 EC. The Sector Report focused upon post-basic patent grant events such as originator/generic conflicts. The Report only examined originators' decisions to patent or to commercialize patents in its general description of the market environment.²⁷² There was no examination of whether or not fewer basic patents were being filed or medicines based upon those basic patents being developed and brought to market²⁷³.

5.2.5 Leaving Inquiry into Market Conditions for Biologicals out of the Inquiry Because Competition there was limited to Originator/Originator Competition

While the Sector Report acknowledged the importance of biologicals to the future of pharmaceuticals it chose not to examine the effects of such change on pharmaceutical innovation in the EU because existing patents would be valid for a long time and because "competition is confined to the originator-originator segment²⁷⁴". Biological pharmaceuticals are one of the fastest

²⁶⁹ Sector Report para. 1030.

²⁷⁰ See e.g. WHO website "About the ATC/DDD System" Found at <http://www.whocc.no/atcddd/atcssystem.html> Last visited April 18, 2009. (An example would be "A10B Blood glucose lowering drugs, excl. insulins". This is a very broad category. In the AstraZeneca case the Commission defined the relevant market for medicinal products for competition law purposes as the 4th ATC level. See AstraZeneca Decision at para. 502.)

²⁷¹ See AstraZeneca Decision para. 372.

²⁷² See e.g., Sector Report pp. 6-7 Main Market Features.

²⁷³ Compare with CBO Report at pp. 35-41 (detailing measurement of innovative performance.)

²⁷⁴ Sector Report para. 37.

growing areas for new medicines²⁷⁵. One would have expected that all major aspects of innovative behavior would be examined in an inquiry seeking answers to a supposed lack of innovation and not just originator/generic competition regarding NME's. Originator/originator competition would appear to be most relevant to considerations of the number of NME's being brought to market as originators not generics are the only market segment performing significant R&D in that area. The conscious decision not to examine an important part of the sector provides more evidence of institutional bias.

5.2.6 The Sector Report Failed to acknowledge Prior Commission Communications making findings why the EU Pharmaceutical Sector has been falling behind in innovation

Oddly enough, the Sector Report, which examines innovative medicines only made a minor reference²⁷⁶ to key Community initiatives which have previously examined the “whys’ and wherefores” of slowdowns in the introduction of innovative medicines in the EU such as the European 7th Framework Programme, The Innovative Medicines Initiative (“IMI”)²⁷⁷ is a public/private effort to counter fifteen years of lagging pharmaceutical R&D in the EU. Basic research performed under the IMI is designed to support industry efforts to develop innovative medicines and make the EU more attractive to globalized originators.

5.2.7 The European Competitiveness Report-COM(2006) 697

The Commission previously made some rather specific conclusions as to why innovation is lagging in the EU pharmaceutical sector. Its conclusion was that the form of intense competition in the US created a “Schumpeterian²⁷⁸” dynamic, conducive to innovation which was lacking in

²⁷⁵ New Biological Entities at p. 16 (4% of US Market in 1982-1992 growing to 16% in 1993-2000 period.)

²⁷⁶ Sector Report para. 129. (Mentioning that the IMI would contribute 1 Billion Euros to the public private partnership and that the other 1 Billion Euros would be contributed by the European Federation of Pharmaceuticals Industries and Associations (“EFPIA”) The fact that an organization which represents originators (Sector Report para. 18) was contributing 1 Billion Euros for R&D for innovative medicines could have received more prominence in a Sector Inquiry looking into rates of innovation in the EU.

²⁷⁷ See, e.g Council Regulation 73/2008 of 20 December 2007 setting up the Joint Undertaking for the implementation of the Joint Technology Initiative on Innovative Medicines, OJ L 30, 04/02/2008 p. 38 (“Regulation 73/2008”), See also Innovative Medicines Initiative home page <http://www.imi-europe.org/Pages/default.aspx> Last visited April 16, 2009.

²⁷⁸ See, Joseph A. Schumpeter, *Capitalism, Socialism, and Democracy*, (New York: Harper, 1975) [orig. pub. 1942]. See also, Herbert J. Hovenkamp, *Schumpeterian Competition and*

the EU.

Since 2000, the US has consolidated its central role as a locus of innovation in pharmaceuticals. US firms hold the majority of biopharmaceutical patents, and this dominance continues to expand. Also, US firms play a pivotal role in the global division of innovative labour in pharmaceuticals, as shown by their shares of co-invented patents at international level. These trends are confirmed by data on patent citations. The internal structure of the US national innovation system is a powerful source of competitive advantage and industrial leadership. In particular, the biotech sector plays a vital role in integrating explorations of new research opportunities with clinical and market development.

The US market for pharmaceuticals is both more concentrated and more volatile than markets in Europe. In other words, the higher concentration of the US market does not mean that it is less competitive. On the contrary, the US market is highly contestable; product turnover is much more frequent than in the EU and Japan; and competition from generic producers is substantial. US market behaviour is consistent with that of a market characterized by Schumpeterian competition, where innovators can gain temporary quasi-monopoly profits, which in turn spur innovation efforts by competitors that quickly leads to more innovative products and a high turnover of market shares. Dynamic competition is less evident in the EU as a whole, and especially in certain continental European countries.

Europe is lagging behind the US in its ability to generate, organise, and sustain innovation processes and productivity growth in pharmaceuticals. Moreover, a disproportionate share of pharmaceutical R&D is performed in the US, with negative consequences in terms of both high value-added employment and complementary investments in clinical research²⁷⁹.

The Sector Report made no reference to the Commission's view that innovation in the EU pharmaceutical sector is lagging because there is less dynamic competition in the EU than in the US. COM(2006) 697 speaks directly to the Sector Report's mandate to discover the state of competition

Antitrust, U. Iowa Legal Studies Research Paper No. 08-43 (October 2008) Found at <http://ssrn.com/abstract=1275986> Last visited April 20, 2009. (Concluding, *inter alia*, that positive innovative effects from antitrust practices even if defined in Schumpeter's broad and non mathematical terms are difficult to foresee.)

²⁷⁹ Communication from the Commission - Economic reforms and competitiveness: key messages from the European Competitiveness Report COM(2006) 697, Section 4 COMPETITIVENESS IN SECTORS. Celex No. 506DC0697. ("COM(2006) 697") (Emphasis added.)

in the sector. This may have been a simple case of “Target fixation²⁸⁰” wherein DG Competition was only looking for, and expecting to find anticompetitive behavior in originators’ patent monopoly. This is strongly indicated by the Sector Report’s fixation on “Dead weight Loss²⁸¹” and “Rent-seeking” based upon patent holding originators’ ability to obtain higher monopoly prices for drugs and the lower prices charged by generic manufacturers²⁸². This elides the entire point of having an IPR system. “By definition, therefore, the intellectual property system permits owners to raise price above marginal cost, creating deadweight losses by raising the price to consumers. If it doesn't do that, it isn't working.²⁸³” Deadweight loss issues concerning originator/generic competition have nothing to do with the entrepreneurial risk taking process. These values were created by the underlying grant of the legal monopoly whose deadweight loss is under the Report’s microscope.

After all, a central drawback of intellectual property rights is that they increase deadweight loss, as higher prices mean that some who value goods over marginal cost nonetheless will not purchase them...Accounting for the negative effect of market power on social benefit, however, does not diminish the point that there will be a gap between the private and social incentives for experimentation²⁸⁴

Certainly, the model of Schumpeterian competition advocated by the full Commission appears to be at odds with DG Competition’s recommendations for tighter competition bounds on the sector to the extent they relate to innovative behavior such as patent filings.

DG Competition may well have been exhibiting a “static competition bias” and ignoring the dynamic nature of the innovation industry. This is illustrated by a popular joke economists tell about themselves: the man who drops his keys at night and looks for them under the street lamp because the

²⁸⁰ A phrase describing some fighter pilot’s tendency to fix their attention so intently on a target that they are no longer conscious of their surroundings and crash into the ground or another obstacle.

²⁸¹ See, Richard A. Posner, *ECONOMIC ANALYSIS OF LAW*, (7th Ed. Aspen Publishers 2007) (“Economic Analysis,”) at Section 9.3 *Efficiency Consequences of Monopoly: Deadweight Loss and Rent-Seeking*. (Deadweight loss is the consequence of a monopolist’s ability to transfer wealth from consumers by the ability to increase pricing from competitive to monopoly levels. Rent-seeking is an entity’s desire to achieve the transfer of wealth to it via competitive or anti-competitive means.)

²⁸² Sector Report paras. 913-925 “Possible Economic Effects of Life Cycle Tools.”

²⁸³ Mark A. Lemley, *PROPERTY, INTELLECTUAL PROPERTY, AND FREE-RIDING*, 83 *Tex. L. Rev.* 1031, 1059 (March 2005) (“Free Riding”) (emphasis added) (The Report seems to ignore the fact that incentives to innovate come from expectation that the innovator will be able to profit from the deadweight loss during its period of exclusivity.)

²⁸⁴ Michael Abramowicz & John F. Duffy, *INTELLECTUAL PROPERTY FOR MARKET EXPERIMENTATION*, 83 *N.Y.U. L. Rev.* 337, 361-362 (May 2008) (“Market Experimentation”).

light is better there²⁸⁵.

The Sector Report, while acknowledging that pharmaceutical R&D is global²⁸⁶ failed to note even the existence of other important investigations under different legal regimes asking why the rate of pharmaceutical innovation is similarly slowing in other countries²⁸⁷. The CBO Study posits the question of whether rising failure rates in clinical trials are the result of depletion of the stock of NME's which are easily discoverable or perhaps from originator investment decisions focusing on developing drugs with the highest expected return²⁸⁸. This global slowdown in the development of innovative drugs has not escaped the notice of the press²⁸⁹. The authors of Grim Prognosis make it clear that this is a global problem and point to the fact that while worldwide R&D spending more than doubled from 2002-2006, 43% fewer new chemical based drugs were introduced. The article points to the "debate being over debate about whether the cause is government regulation, corporate structure or an excessive scientific reliance on chemicals rather than biology." There is also a question of whether or not the industry is relying on a structure based upon its origins in the European chemical industry of the 1800's. One looks in vain for discussion of these topics in the Report, especially in its discussion of market structure, a prerequisite to any determination regarding whether the market structure is being distorted.

One report pointed out the need for taking a longer-range view of the problem stating that up and down trends in innovation were to be expected.

[T]he supply of not-yet discovered innovation ebbs and flows...Because science does not advance at a steady pace, the pool of undeveloped discoveries will at times be smaller and more expensive to exploit. At those times real research productivity will be lower²⁹⁰.

For whatever reason, the Section Report fails to address its primary goal.

²⁸⁵ See, David S. Evans, Keith N. Hylton, *THE LAWFUL ACQUISITION AND EXERCISE OF MONOPOLY POWER AND ITS IMPLICATIONS FOR THE OBJECTIVES OF ANTITRUST*, (September 26, 2008) at pp.37-38. Available at <http://ssrn.com/abstract=1275431> (Last visited March 14, 2009) ("Objectives of Antitrust") (A later version of this paper was published in GCP, The Online Magazine for Global Competition Policy, Vol. 4 No. 2 November 1, 2008.)

²⁸⁶ Sector Report para. 53 (R&D is an international activity.)

²⁸⁷ See e.g. The GAO Report and the CBO Study.

²⁸⁸ CBO Study at p. 23.

²⁸⁹ See e.g. Barbara Martinez & Jacob Goldstein, *Big Pharma Faces Grim Prognosis*, Wall Street Journal, December 6, 2007 Found at

<http://online.wsj.com/article/SB119689933952615133.html> Last visited April 24, 2009 ("Grim Prognosis")

²⁹⁰ CBO Study at p. 37.

5.3 LITIGATION BY ORIGINATORS

[A]lthough the fact that an undertaking is in a dominant position cannot deprive it of its right to protect its own commercial interests if they are attacked, and that such an undertaking must be conceded the right to take such reasonable steps as it deems appropriate to protect those interests,...²⁹¹

The Sector Report's examination of litigation by originators is characterized by small samples, incorrect assumptions, and unsupported inferences. Its uncontrolled observational studies and after-the-fact data analyses are presented as statistical facts. They are not reliable enough to be translated into legal causation. Most telling of all is that by an innocent or deliberate misunderstanding of the market and IPR in general, originator defensive actions are treated as anti-competitive oppressive litigation. The most obvious example being the Sector Reports' characterization of patent infringement actions as active rather than reactive. It is beyond cavil that under an exclusionary property regime such as patent law, an action for patent infringement is a reaction to an infringement or perceived infringement of that right. Infringement triggers infringement actions which "cannot of itself fall under... [Article 82EC] in the absence of an abuse of a dominant position"²⁹². The Sector Report's switch diverts attention away from an examination of abuses of dominant position, creating the inference that bringing an infringement action is the anticompetitive abuse to be condemned. As the above statement by the ECJ in *Glaxo II* points out, competition law does not prevent a dominant commercial undertaking from acting in self-defense, it only condemns actions that go beyond self-defense and distort competition.

5.3.1 The Report Expressly Ignores the Holding of the ECJ in *Roche Nederland* in Comparing Litigation Results From 27 Member States

The Sector Report asserts that there is a danger of inconsistent judgements being entered with respect to the validity of patents granted by the EPO when the courts of different member states adjudicate the "same patent granted by the EPO"²⁹³. The Report elides the ECJ's holding in *Roche Nederland* that "[a]ny diverging decisions could not, therefore, be treated as

²⁹¹ *Sot. Lelos kai Sia EE v. GlaxoSmithKline AVEE Farmakeftikon Proionton, formerly Glaxowellcome AVEE*, Joined Cases C-468/06 to C-478/06 ECR 2008 page 00000 par. 50 ("Glaxo II") citing, *United Brands and United Brands Continentaal v Commission* Case 27/76 [1978] ECR 207, par. 189.

²⁹² Judgment of the Court of 29 February 1968. *Parke, Davis and Co. v Probel, Reese, Beintema-Interpharm and Centrafarm*. Case 24-67, ECR 1968 Page 00055 (at p. 72.)

²⁹³ See Sector Report at paras 241-243.

contradictory²⁹⁴”. Footnote 133 of the Sector Report boldly asserts “Even if the Court of Justice held in Case C-593/03 that there is no risk of contradictory decisions for the formal reason..., nevertheless,, on substance, the different national courts will all deal with the same question of whether the patent is valid or not.” (Emphasis added.) However, Roche Nederland also holds that an EPO patent when validated in a Member State is to all intents and purposes a Member State Patent because it “shall... confer on its proprietor from the date of publication of the mention of its grant, in each Contracting State in respect of which it is granted, the same rights as would be conferred by a national patent granted in that State.”²⁹⁵ The Sector Report also conveniently ignores Article 66 EPC 73 which states that an EPC patent “shall, in the designated Contracting States, *be equivalent to a regular national filing...*”, and Section II²⁹⁶ of the Protocol On Recognition. Articles 9-11 of the Protocol on Recognition, provide for contracting states to recognize decisions in other contracting states which invalidate European Patents.

The Report’s erroneous position that all European Patents are precisely alike enables it to compare patent decisions from 27 Member States without explaining differences between their substantive patent law or how that might affect the results.

While it is crucial to the Commission’s patent law “parade of horrors” to turn a blind eye to the ECJ’s holding in Roche Nederland, the EPC, and the Protocol on Recognition, these are not inconsequential matters to be lightly dispensed with in a footnote²⁹⁷.

5.3.2 Problems with the analysis of Secondary Patents and Divisional Patent Applications

The first problem with the Sector Report’s litigation analysis lies in the assumptions it makes regarding secondary patents and divisional patent applications in the Report’s Sections 2.1 “Patent Filing and Patent Enforcement Strategies²⁹⁸”. The first great assumption regarding “patent thickets” is that the vast majority of patents filed concern only the top 20 selling INN’s²⁹⁹. In fact, the top ten selling INN’s have among them more than 5,000 granted patents and pending applications³⁰⁰. The Sector Report

²⁹⁴ Roche Nederland at para. 32.

²⁹⁵ Roche Nederland at para. 12 (quoting Article 64(1) of EPC 73.)

²⁹⁶ PROTOCOL ON JURISDICTION AND THE RECOGNITION OF DECISIONS IN RESPECT OF THE RIGHT TO THE GRANT OF A EUROPEAN PATENT (PROTOCOL ON RECOGNITION) of 5 October 1973.

²⁹⁷ This puts me in mind of a trial I was involved in where counsel, having been overruled by the Court on a point of law, ignored the ruling and continued to argue “Even if you are right, your Honor...”

²⁹⁸ Sector Report paras. 370-432.

²⁹⁹ Sector Report para. 385. See also Sector Report at paras 349-352 for statistics.

³⁰⁰ Sector Report para 352.

concludes from this both the existence of “patent clusters” or “patent thickets” and that:

Patent clusters can lead to uncertainty for generic as to whether or when they can start to develop a generic medicine without infringing one of the many (new) patents, even though patent holders admit internally that some of these patents might not be strong³⁰¹.

The Report blames the existence of these Patent Clusters and other “tool box” items for significant delays in post LoE generic market entry. Secondary patents result in most cases from discoveries made at the clinical testing stage. Divisional patent applications refer to claims made in the basic patent, often as subsequently suggested by further testing. Claims are refined in divisional patent applications, sometimes in response to objections made by examiners or objectants. In any event, Secondary, patents by their nature do not block new, innovative NCE’s but only derivative developments of them. Divisional claims regarding basic patents would have been resolved in the 8 to 12 years prior to any grant of marketing authority. Divisional claims made with respect to secondary patents would not relate to the patents referred to in the SPC and would not block a generic’s use of the basic claim. Moreover, the distinction between “basic” and “secondary” patents is not made in either EPC but reflects, in this case the judgement of DG Competition as to which is the primary patent³⁰². The terms actually relate to the relation of the patent to the issuance of SPC certificates rather than on any official patent class or intrinsic value judgement. The Report’s focus on the “up to 1,300 patents and applications EU wide”³⁰³ on one blockbuster medicine concern mainly secondary patents on “formulations, processes and non-formulation products (excluding NCE’s), such as salts, polymorphic forms, particles, solvates and hydrates”, and NOT basic patents on innovative new drugs. As such, they have absolutely no bearing on delays to the introduction of innovative NME’s nor on the basic substances upon which generic drugs are based.

The Sector Report did not examine the effects of Regulatory Regimes on patenting or the introduction of innovative medicines. If it had it might have found that one of the reasons for secondary patenting relates to how some government health insurance rebates schemes operate³⁰⁴. For example, in one such situation in the US the Medicaid program requires originators to rebate a portion of the price they receive on certain private-sector sales of a drug. In the case of a brand-name drug, the originator is required to pay a larger rebate if price increases exceed a cost of living index. However, this provision does not apply if the drug is modified and the resulting price is higher. Responding to regulatory pricing is outside the scope of competition

³⁰¹ Sector Report Summary at p.166.

³⁰² See, European Commission Pharmaceutical Sector Preliminary Report – 28 November 2008 COMMENTS FROM THE EPO 10.03.2009 (Final) (“EPO Comments”) at p. 3.

³⁰³ Sector Report para. 285.

³⁰⁴ See, CBO Report at pp. 16-17.

law since Community pricing regulations have not been harmonized but such considerations are as much or more likely to affect originator decisions regarding secondary patenting than the erection of secondary patent thickets³⁰⁵.

Another problem with the Sector Report's is its mischaracterization of the terms "Patent Clusters" or "Patent Thickets". According to the Report Patent Clusters are a technique which originators use, of filing numerous secondary patents designed (according to the Report) to block generic entry into the market³⁰⁶. However, as defined by COM(2007)165 a "patent thicket refers to the potential problem that in view of the high number of patents necessary to produce a product, innovation in the sector is slowed down because of fear of hold-up and patent infringement litigation."³⁰⁷ The Report misuses a term describing an innovation delaying practice and applies it to secondary patents and non-innovative market entry by generics. In other words, the Report uses the transfer of deadweight loss from originator to generic as a proxy for innovation.

5.3.3 The Report Assumes that Generics are entitled to Subsequently acquired Originator IPR

Another improper assumption used by the Report regarding secondary patenting is that generic companies somehow have a right to use *valid* later filed IPR regarding product improvements or process patents. The Report stresses that generic companies cannot produce bioequivalents to the late stage medicinal product³⁰⁸. As previously pointed out nothing keeps the generic company from utilizing the basic expired patent to create a generic version³⁰⁹. The generic process envisions the ability of a generic manufacturer to use the IP from an expired basic patent. This does not constitute a free riding right to exploit later filed valid IPR's. If the later filed patent represents incremental innovation why on earth does anyone

³⁰⁵ See Glaxo II paras 60-62 and 69.

³⁰⁶ Sector Report Section 2.1 p.9, Summary at p. 166, paras. 397, 845.891, and Conclusion at p. 401.

³⁰⁷ COM(2007) 165 FN 30, COM(2008) 465/3 COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, AND THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE, An Industrial Property Rights Strategy for Europe. ("COM(2008)465/3") at FN 16. Found at http://ec.europa.eu/trade/issues/sectoral/intell_property/survey2006_en.htm ... http://ec.europa.eu/internal_market/indprop/docs/rights/communication_en.pdf Last visited April 27, 2009.

³⁰⁸ Sector Report paras. 382-397. ("In such a situation any attempt to develop a generic version of the medicine in the form of a salt, a crystalline or amorphous form would inevitably infringe a patent (for example a patent for the relevant salt, crystalline or amorphous form of the medicine." para 387.)

³⁰⁹ Putting the Brakes on at p. 957.

else have a right to that IPR?³¹⁰ If it does not represent incremental innovation, either the generic has no need of it or it may challenge the IPR's validity. To the extent that the EPO has determined that a secondary patent has met the criteria of the EPC it is not within the capacity or the purview of Competition law to sift through them to determine whether or not they are incremental advances or obstructions to competition or to reallocate the value of such property to generics. Such concerns would appear to be more in the province of patent reform than Articles 81 and 82 EC. Indeed, a generic would not be viewed as a competitor under the SSNIP test since, by definition, a generic does not invest in the R&D underlying the patents³¹¹. In dynamic competition the fact is often overlooked that originators are not in competition with generics over R&D³¹².

The argument that generics cannot market a product which infringes even a weak secondary patent and therefore they are entitled to use the infringed IP is an argument against attempting pharmaceutical innovation. Every time new functionality or a new process achieves incremental innovation it will be deemed anticompetitive and must be shared. That would be a prescription for pharmaceutical entropy.

However, Generic undertakings have several options regarding the use of originators' secondary patents. 1. They can invent around the problem (if it is a problem) whether it is a manufacturing, process etc. (in a case of expensive innovation, not a likely prospect for the generic business model) 2. They can (and often do) challenge secondary patent validity (with a fair degree of success³¹³.) 3. To the extent that a process invented by an originator is the only technical option, a generic can obtain a license from the originator, and, if it is refused has a good chance of obtaining one on FRAND terms³¹⁴. The Sector Report does not review such patents on a refusal to license basis but rather on the basis of some form of IPR property entitlement for generics. The Report would create a new "SSNIP" test for competitive Generic market entry ("Small but Significant Number of

³¹⁰ The CBO Study notes that nearly one third of all R&D spending is on product improvements which are of significant incremental value to consumers. See CBO Study at pp.35-37.

³¹¹ Small but Significant Non-transitory Increase in Price. See, Commission Notice - Guidelines on the application of Article 81 of the EC Treaty to technology transfer agreements OJ C 101, 27/04/2004 p. 2 at 29.

The parties are considered to be potential competitors on the product market if in the absence of the agreement and without infringing the intellectual property rights of the other party it is likely that they would have undertaken the necessary additional investment to enter the relevant market in response to a small but permanent increase in product prices.

³¹² Dean V. Williamson, *Antitrust, Innovation and Uncertain Property Rights: Some Practical Considerations*, at 1.3. (January 2008) Found at <http://ssrn.com/abstract=1124223> Last visited April 30, 2009.

³¹³ Sector Report para. 514.

³¹⁴ See, e.g. *NDC Health GmbH & Co. KG and NDC Health Corporation v Commission*, Case C-481/01 P (R) ECR 2002 page I-03401 and *Radio Telefis Eireann (RTE) and Independent Television Publications Ltd (ITP) v Commission*, Joined cases C-241/91 P and C-242/91 P. ECR 1995 page I-00743.

Invalidated Patents”). It therefore analyzes secondary patent litigation in the same sample tranche as it analyzes divisional patent applications (which may relate either to the basic patent grant or to a secondary patent).

While there are problems with the methodology used regarding its review of divisional patent applications (as pointed out below) the Sector Report provides some indications that there may be cause for competition concerns. However, as the Report hopelessly muddles disparate sets of data, a proper investigation of those concerns awaits another day.

5.3.4 The Report’s Conclusions about the effect of Patent Clusters is Contradicted by its Conclusion Regarding Delays to Generic Entry

The Sector Report itself exposes the irrelevance of “patent clusters” to its causation theories for delay to generic entry. The Report states that generic entry for the top selling 20% of top selling products takes, on average, 4 months from LoE, with progressively longer and longer delays until generic entry ascribed to classes of progressively less well selling INN’s which have fewer and fewer secondary patents³¹⁵. If patent clusters were effective in barring generic entry the delay for generic entry for the top selling INN’s (with more such patents clusters) should be longer rather than shorter. Thus the Report’s focus on originator/generic secondary patent litigation creating delay in generic entry is misplaced and irrelevant to any “tool box” analysis. It is as legitimate to infer from the Report’s statistics that patent thickets promote faster generic entry, as it is to infer that they impede them.

5.3.5 The Report Fails to Separate Fundamentally Different Data Sets Regarding Patent Filings

The Sector Report’s suspicion that originators have manipulated applications for patents may well have a point. There is economic literature heavily criticizing the structure of patent continuations and divisional patent applications from an antitrust perspective³¹⁶. The Sector Report provides troubling allegations by three generic manufacturers to the effect that

³¹⁵ Sector Report paras. 165-167 and Figure 13.) “[I]t takes less time for high value products to be faced with generic entry. This finding is not surprising considering that top selling INN’s are normally the most attractive to enter.”)

³¹⁶ See, e.g. Herbert J. Hovenkamp, *Patent continuations, Patent Deceptions, as Standard Setting: the Rambus and Broadcom decisions*. U. Iowa Legal Studies Paper No. 08-25 (June 2008) Found at <http://ssrn.com/abstract=1138002> Last visited April 20, 2009. (Noting that while the use of continuation or divisional patents and their relation back feature to write updated claims on competitor’s existing products is largely exempt from antitrust laws such use can create violations of Section 2 of the Sherman Act.) See also, Mark A. Lemley & Kimberly A. Moore, *Ending Abuse of Patent Continuations*, 84 B. U. L. Rev. 63 (2004).

originators file identical or nearly identical divisional applications that have either been found invalid or were just filed to extend the length of opposition proceedings³¹⁷. The possibility of anticompetitive gaming of divisional patent applications merits a closer look. However, the Report's methodology does not provide clear or useful information to illuminate the problem. Since divisional patent applications relate back in time to the filing of a patent, both claim splitting and lack of transparency in the application process provide possibilities for gaming the system. The fact remains, however, that a patent from a divisional patent application of a basic patent would expire at the same time as the basic patent. It could not extend the temporal protection of claims derived from the original application. Divisional patent applications relating to secondary patents do likewise but generic's entitlement to that IPR can only be based upon invalidating granted patents or to opposition to their grant. Generics' primary complaint seems to be, therefore, that claim manipulation of divisional claims makes it more difficult to object to basic patent claims or have them declared invalid in opposition proceedings³¹⁸. Assignment of relative litigation advantage in opposition proceedings (which are primarily brought by generics) does not appear to be a competition problem. Without a factual examination of the cases in question one cannot determine if the divisional applications were intended to create confusion, are legitimate attempts to refine or narrow claims rejected by the EPO or are merely "sour grapes" complaints by frustrated patent opponents. This is highlighted by the fact that while the Sector Report finds that generic companies also engage in patenting strategies including patenting processes, products and formulations³¹⁹ these practices are condemned by the Report only when used by originators. (It would appear that the authors of the Report never heard of another "goose" saying: "What is good for the goose is good for the gander"³²⁰.)

In addition, by lumping patent application which relate to basic patent claims with those relating to follow-on inventions in the litigation data the Sector Report has confused the issues and made it impossible to rely upon data which cannot be unscrambled.

5.3.6 The Data Regarding Originator/Generic

³¹⁷ Sector Report paras 418-420. This entry in the Report appears to have been taken almost verbatim from *Patent-related Barriers to Generic Medicines in the European Union A Review of the Weaknesses in the Current European Patent System and their impact on the Market Access of Generic Medicines*, European Generic Medicines Association (May 2008) at section 2.2 "Multiple divisional patent applications which are entirely identical to the parent. Found at http://www.egagenerics.com/ega-barriers_rpt.htm Last visited May 3, 2009.

³¹⁸ Sector Report para. 539 ("The opposition proceeding is a way for generic companies to obtain verification of the validity and scope of an originator company's patent, which may be invoked in litigation...This may then allow the generic company to enter the market without the risk of infringing that patent.") and Figure 81 showing that the vast majority of opposition proceedings are brought by generics.

³¹⁹ Sector Report para. (78). The Sector Report only mentions this without drawing the same inferences against generics it draws against originators.

³²⁰ See Introduction *infra*.

Litigation is Insufficient and Inconclusive

The Sector Report provides information regarding 698 cases of patent litigation in 7 years of which 149 had reached final judgment³²¹. The Sector Report divides these up further into 84 cases initiated by a generic and 65 by an originator and divides them up into classes denominated as “GEN’s success” and “ORI’s success³²²”. The Report lists the 20 most litigated INN’s³²³ and compares litigation rates for the 50 best selling INN’s (the “T50 Group”) to litigation concerning the 75 top-selling INN’s facing LoE from 2000-2007³²⁴ (the “E-75 Group”). The Report then divides the cases into classes of patents (product, process, second medical use, and first medical use³²⁵). The Report then combines classes and tracks litigation between “primary” and “secondary” patents³²⁶ and then analyzes primary and secondary patents by generic and originator’s relative success³²⁷.

The Report then analyzes 255 cases where interim injunctions were applied for and 112 where they were granted³²⁸. The Report lists those Member States where interim injunctions are granted more frequently and those where they were not³²⁹. The Report does not examine the factual bases for any of the requests or any differing requirements of law. Significantly, while citing Directive 2004/83 for legal requirements for granting an injunction³³⁰. The Report fails to note that the Directive itself has not been implemented in certain Member States including one in which the majority of patent litigation is brought (Germany, Portugal, Sweden and Luxembourg)³³¹. Even where the Directive has been implemented “there are still important differences in national procedures and practices due to non-harmonised issues such as collecting factual evidence, cross-examinations, hearings, the role of experts, etc.”³³² This is strong evidence demonstrating that the enforcement of IPR is not well harmonized in the EU. The Report itself shows wide variations in the success or failure rates of litigation³³³ and the results of requests for interim relief among Members. These variations undermine inferences taken from the small sampling of cases distributed

³²¹ Sector Report paras 468 and 500.

³²² Sector Report paras. 500-501.

³²³ Sector Report paras.481-485.

³²⁴ Sector Report paras 486-487.

³²⁵ Sector Report paras 488-489 incl. Figure 69.

³²⁶ Sector Report paras 490- 493.

³²⁷ Sector Report paras 506-515.

³²⁸ Sector Report para. 521.

³²⁹ Sector Report para. 522.

³³⁰ Sector Report para. 520 and FN 272.

³³¹ Minutes of February 29, 2008 Meeting between European Communities Trademark Association and DG Internal Market-European Commission, Item 6. Found at www.ecta.eu/position_papers/2008-02-Commission.pdf Last visited April 20, 2009.

³³² COM (2007) 165 Communication from the Commission to the European Parliament and the Council - Enhancing the patent system in Europe, Brussels, 3.4.2007, Celex No. 507DC0165, Section 2.2.1. The deficiencies of patent litigation in Europe.

³³³ See Sector Report at paras. 521, 522 (percentages of interim injunctions granted by Member State), para. 515 (Duration of litigation ending in final judgements in Member States).

among 27 Members.

In its introduction to its analysis of originator/generic litigation the Sector Report states, in rather conclusory fashion:

Patent litigation can have an impact on market entry by generic companies. In particular, the threat of lengthy and costly patent litigation across EU Member States can dissuade smaller generic companies from launching a competing product before patent expiry, even if they consider the patent to be invalid or not to be infringed. Most importantly, interim injunctions can have a very serious effect on generic companies whose product is taken off the market and all further production and commercialisation are forbidden until the main action is decided....³³⁴

This is an extraordinary statement. It demonstrates either an extreme bias, or misunderstanding of the fact that patents are *supposed* to permit IPR holders to try and prevent market entrance prior to expiration. Likewise it ignores the fact that interim injunctions require a showing to “a sufficient degree of certainty” that a right is being infringed and, where appropriate, that the party seeking relief post sureties³³⁵. This attitude, echoed in Report’s economic analysis of “life cycle tools”,³³⁶ questions the basic legitimacy of IPR rights notwithstanding the Report’s bromides to the contrary³³⁷.

5.3.7 The Sector Report Makes Unscientific use of its Statistical information

The Sector Report uses the above referenced originator/generic patent litigation statistics comprising partial results from 149 cases to make findings about the Sector and the patent system in general. However, there is more in what the facts do not say than in what they do. The Report is not a true statistical study of litigation results. It is an attempt to infer conclusions from after the fact observations. Most litigation studies are based upon a 50/50 won/lost rate based upon the following assumptions:

First, the model is an “all or nothing” model where damages are stipulated and only liability is in issue. ...
Moreover, the model assumes equal stakes, ... symmetrical

³³⁴ Sector Report para. 466 (emphasis added.)

³³⁵ See e.g. Article 9, Directive 2004/48.

³³⁶ Sector Report paras. 915 (entry delay for fear of interim injunction), para. 916 (generic entry on reduced scale to reduce risk of “potential damages”), paras 916-917 (interim injunction proving unfounded may not be compensable and delays price reductions.)

³³⁷ Sector Report para. 433 (enforcing patent rights as such is not objectionable.) Note that the Report’s analysis of dangers to generic companies from failed attempts to assert IP rights does not balance them with consideration of the effects of generics’ IP infringement on originators.

information, ... risk neutrality, ... and lack of strategic behavior. ... To the extent that one or more of these assumptions does not hold true for a given set of disputes, the outcomes may not approximate 50%³³⁸.

In patent litigation, one of the greatest assumptional differences is that risk to the infringer is far less than it is to the patent holder³³⁹. “When you got nothing, you got nothing to lose.³⁴⁰” This risk asymmetry is extreme when a pharmaceutical patent holder which has invested hundreds of millions of Euros and years of clinical studies faces a generic opponent who typically invests one or two million and one or two years in development (plus, of course legal fees). This may translate into risk aversion in which the patent holder will likely settle more cases it perceives as close³⁴¹. In another empirical study of patent litigation the authors were of the opinion that patent holders’ assumptions may have been affected by their assigning an unrealistic scope to the language of the patent claims³⁴². The same study also observed that “[a]nother possible reason for the low number of patentee victories is that in order to win a judgment a patent owner must not only prove infringement of at least one claim of the involved patent, but must also defeat every validity attack on that patent claim and every charge of inequitable conduct.³⁴³”

The Sector Report does not consider the effects on its statistics the fact that a generic plaintiff will usually choose to test patents it feels are vulnerable to attack, leaving the stronger patents alone. In such a case one would intuitively expect generics’ win/lose ratio to be more favorable. Where the litigation is begun by generic infringement or potential infringement or where the generic commences a declaratory action seeking to invalidate a patent they would be expected to have a higher success rate. This is the model chosen for examination by the Sector Report. However, p-Values (probability that the evidence contradicts a null hypothesis) are skewed when the evaluator “cherry picks” results which suit her³⁴⁴.

For example, there is a disconnect between the Report’s analysis of patent litigation and its analysis of litigation going to judgement. 80% of all

³³⁸ Kimberly A. Moore, *JUDGES, JURIES, AND PATENT CASES--AN EMPIRICAL PEEK INSIDE THE BLACK BOX*, 99 Mich. L. Rev. 365, 376-377 (November 2000) (“Inside the Black Box”) (footnotes omitted.)

³³⁹ Inside the Black Box at pp.377-378.

³⁴⁰ Bob Dylan “Like a Rolling Stone” Copyright ©1965; renewed 1993 Special Rider Music.

³⁴¹ Inside the Black Box at p. 378.

³⁴² Paul M. Janicke & LiLan Ren, *Who Wins Patent Infringement Cases?*, 34 AIPLA Q.J. 1, 40 (Winter 2006) (“Who Wins?”.)

³⁴³ *Id.*

³⁴⁴ David W. Peterson & John M. Conley, *OF CHERRIES, FUDGE AND ONIONS: SCIENCE AND ITS COURTROOM PERVERSION*, 64 AUT Law & Contemp. Probs. 213, 227-230 (Autumn 2001) (Discussion of problem of litigants choosing statistical reports leaving out data tending to undercut their argument.) (“Cherries, Fudge and Onions”) (Citing Richard A. Posner, *The Law and Economics of the Economic Expert Witness*, 13 J. Econ. Persp. 91, 98 (1999).

litigation involved only 20 INN's of which 6 represented 49% of all litigation and with one (INN1) representing over 100 cases or roughly 15% of the total³⁴⁵. Not all of the top 20 litigated INN's faced LoE³⁴⁶. Moreover, more than half of all cases were initiated in just 5 Member States³⁴⁷. The Report's analysis of the outcome of litigation does not take these anomalies into account and lists the 149 cases by generic or originator's success and whether related to basic or secondary patent. Clearly one or two big wins or losses for any of the top 6 INN's or any differences in National Law or procedure³⁴⁸ would, and may well have had, profound effects on the results as reported by the Sector Report³⁴⁹.

The Sector Report's conclusions about originator's use of life cycle toolboxes lists five "blocks"³⁵⁰. Four of the five relate to originator uses of patents. The Report's evaluation of these tools³⁵¹ minimizes their legitimate use³⁵². The Report's manipulation of the figures this way has clearly given at least one expert in the field the impression that the Report found that originators in the EU are engaging in "Repetitive Meritless Patent Challenges"³⁵³. However, the Report's statistical methods are a bruised reed³⁵⁴ upon which to support conclusions concerning all originators, all patents, and all INN's.

³⁴⁵ Sector Report paras, 481-483.

³⁴⁶ Sector Report para. 484 and 487 (77% of the top litigated INN's faced LoE while 23% did not.

³⁴⁷ Sector Report para 474. See also COM(2007) 165 at 2.2.2. (90% of current patent litigation takes place before the tribunals of four Member States, Germany, France, UK and the Netherlands.)

³⁴⁸ In Germany, for example patent cases regarding infringement and patent cases regarding invalidity are initiated and tried in separate courts. See Sector Report para. 240 Fn 117. The Federal Patent Court (Bundespatentgericht) tries invalidity proceedings. The nullity panels of this court consist of four technical judges and one judge with a law degree. Infringement suits are tried before any one of ten specialized District Courts of First Instance (Landgerichte in first degree, and Oberlandesgerichte in appeal).

³⁴⁹ Sector Report para. 502 (generic companies won 62% of all patent litigation), para. 503 (generic companies won 71% of patent cases they initiated), para 504 (originator companies won 51% of cases they initiated, along with gratuitous remark that they lost 49%), para. 505 (generic companies won 60% of all patent litigations), paras 507-508 originators won 57% of all basic patent litigation and generics won 74% of all secondary patent litigation.)

³⁵⁰ Sector Report para. 901. A more extensive list appears at para. 144 where patenting activities are separated from litigation activities. However, since the litigation activities there are posited upon patent positions they are essentially the same.

³⁵¹ Sector Report paras 905-912 (Effect of the Combined Use of Practices) and 913-925 (Possible Economic Effects of Life Cycle Tools).

³⁵² Sector Report paras. 906-908, and 909 ("Having said this, the basic effect of multiple actions can however be that entry will tend to occur later...")

³⁵³ Wading into the Thicket at p. 10. Commissioner Rosch, assuming that this was a Commission finding then spoke about patentee's immunity from suit in the US under *Eastern Railroad President's Conference v. Noerr Motor Freight, Inc*, 365 U.S. 127 (1961) and *United Mine Workers v. Pennington*, 381 U.S. 657 (1965) (collectively the "Noerr Pennington Doctrine") and their exception for "sham" litigation and patents obtained by fraud under *Professional Real Estate Investors v. Columbia Pictures Industries*, 508 U.S. 49 (1993) and *Walker Process Equipment v. Food Mach. & Chem. Corp.*, 382 U.S. 172 (1965) (collectively referred to as "Walker Process Fraud".)

³⁵⁴ See e.g. 2 Kings 18:21 "Now, behold, thou trustest upon the staff of this bruised reed,..., on which if a man lean, it will go into his hand, and pierce it..."

The greatest problem with the data in the Sector Report is that the samples are so small, and the information subject to so many variables, that inferences taken from it are not very reliable. In respect of litigation going to judgement, a sample size of 149 cases spread over 27 Member States would not appear to be viable. By way of contrast, the sample size in Inside the Black Box included 1,411 US patent infringement cases of all types reaching trial over a 17-year period. It concluded that in infringement cases the patentee won 58% of the time³⁵⁵. It also found of those cases tried to a jury patent holders had a 68% chance of winning and if tried before a judge they had a 50% chance of winning.³⁵⁶ A similar study using different sample sizes (239 cases) over a 7-year period, for which there were written opinions, found that patents were found valid in 54% of the time³⁵⁷. In another study of 262 cases reaching the Federal Circuit Court of Appeals in the US found that only 25% of appeals were won by patent holders³⁵⁸. A more ambitious study including 6,300 cases over a three year period found that only 5% of all patent disputes were resolved at trial of which there were 277 findings of infringement and 236 cases where patents were invalidated³⁵⁹.

Statistical variations in even these large sample cases leads one to exhibit caution in how far one may rely upon after-the-fact analysis of complicated factual scenarios and how far one may take inferences from 149 cases in 27 countries where key information is either absent or its selection manipulated³⁶⁰.

One important difference between the sample in the Sector Report and the larger samples in the above-referenced studies is that the larger studies relate to one unified National legal system with one set of patent laws. Differences found in the Sector Report are as likely attributable to differences in national substantive law or, in cases where Directive 2004/48 has not been implemented to differences in substantive law. Without

³⁵⁵ Inside the Black Box at p. 385.

³⁵⁶ Inside the Black Box at p. 408.

³⁵⁷ John A. Allison & Mark A. Lemley, *Empirical Evidence on the Validity of Litigated Patents*, 26 AIPLA Q. J. 185 (1998).

³⁵⁸ Who Wins? at p.5.

³⁵⁹ Jay P. Kesan & Gwendolyn G. Ball, *How are Patent Cases Resolved? An Empirical Examination of the Adjudication and Settlement of Patent Disputes* 84, No. 2 Wash. U. L. Rev. 237 (2006) (“Kesan & Ball”).

³⁶⁰ Cherries, Fudge and Onions at p. 220-221.

Consider the analogy of an onion. A scientific inquiry can be likened to peeling away the layers of an onion. At the center of the onion lies the truth being sought. Depending on where we are in the peeling process, we can examine and comprehend only some outer layers of the onion. Our knowledge of what lies further inside is merely inferential. With more investigation, we can peel away layers and progress toward the center. Realistically, however, there is little hope of ever clearly laying bare the very center. Our inferences about what lies there are based on what can be learned from some intermediate layer, and the closer that layer is to the center, the more reliable the inferences.

knowing more about each case, and the applicable legal rules it is impossible to assume that they are all based upon similar enough conditions to constitute a legitimate data set.

5.3.8 The Sector Report Makes “Lose/Lose” Inferences against Originators

In the end, the most troubling use the Sector Report makes of these statistics is the inference that somehow higher win rates for generics means that these patents were indefensible or that the infringement actions were somehow part of the originator tool box designed to thwart generic entry. There is no evidence in the Report that patents granted by the EPO were “shams”³⁶¹. There is no evidence that because originators lost patent infringement suits in some proportion the patent holders have engaged in bad faith litigation. It is entirely inappropriate, as the Sector Report does, to draw the inference that because a party lost a pharmaceutical patent case it must have brought it solely for anticompetitive reasons³⁶². If that were true than the roughly 50% won/lost rate for all patents mean that all patent holders who lose likewise have violated competition law. It also ignores any presumption of patent validity under member State law or the right to access to the courts. Here DG Competition turns its blind eye to the ECJ’s holding in *Parke Davis v. Probel* that the holder of an IPR granted by the state has the right to assert it before the state’s courts. In any litigation coming to judgement there has to be a winner and there has to be a loser. To conclude that all losers cannot have believed that their case was viable and therefor must be punished is more than a bit Draconian³⁶³. The most that can be gleaned from the data presented is the Report’s conclusion that secondary patents in general may be somewhat weaker than basic patents perhaps has some validity.

³⁶¹ See *ITT Promedia NV v Commission*, Case T-111/96 ECR 1998 page II-02937 para. 55 (Commission requirement that it is necessary “that the action (i) cannot reasonably be considered as an attempt to establish the rights of the undertaking concerned and can therefore only serve to harass the opposite party and (ii) it is conceived in the framework of a plan whose goal is to eliminate competition” before abuse may be found) and para. 117 (Finding “Consideration of that question could not have shown that Belgacom’s second action did not aim to assert what Belgacom could reasonably consider, at the time when it brought that action, to be its rights, and that the action therefore served only to harass the applicant.”)

³⁶² Sector Report at para. 917. “As the sector inquiry shows, the above-mentioned limitations [para. 916 Possible Economic Effects of Life Cycle Tools] ...can be judged ex-post to be unfounded. this takes place whenever patent litigation proceedings end with (a) a judgment allowing generic entry, (b) a settlement [in which] an originator company agrees to earlier generic entry and/or transfers ..value to the generic...in order to compensate for delayed entry.. or (c) withdrawal of a case...” These time periods were added to the alleged delay in generic entry caused by originator “tool boxes”. See, Sector Report, figure 133 page 321.

³⁶³ From Draco, an Athenian legislator who, in the 39th Olympiad (621 or 622 BC to us folks) established the first set of Athenian laws contained in a Constitution. See Aristotle, *The Athenian Constitution* at iv. Under Draco’s Code the death penalty was used for even minor offenses. He reportedly was accidentally killed in an Aeginetan theater when admirers threw so many hats, shirts, and cloaks on him (in lieu of applause) that he smothered. (No Draconian punishment is recorded for participating audience members but the incident may well have given rise to the invention of coat checking.)

However, that secondary patents may be weaker than basic ones is a *non sequitur* with respect to abuses of competition law or their effect on basic innovation.

5.4 FAILURE TO ADDRESS GENERIC TOOL BOXES

On November 24, 2008, four days before issuance of the Sector Report, the Commission launched “Dawn Raids” on a number of pharmaceutical companies “believed to be engaged in “restrictive business practices and/or the abuse of a dominant market position”³⁶⁴. EurActive reported that one of the companies in question was Teva Pharmaceuticals Industries, Ltd. Teva is the largest generic company, with 2007 turnover of over three Billion Euros³⁶⁵. According to EurActiv, the Commission stated that while information acquired during the Sector Inquiry “allowed the Commission to draw conclusions on where Commission action based on competition law could be appropriate and effective”, the raids were not part of the Sector Inquiry.³⁶⁶ This highlights the one-sidedness of the Sector Report. Its failure to balance an examination of what it termed aggressive tactics by originators with a comparison of generic companies’ use of their “toolboxes” against originators.

5.4.1 Indications of Aggressive Generic Commercial Behavior Gleaned from the Report

The Sector Report contains evidence of generics’ use of commercial behaviors similar to those cited in its originator toolbox but fails to consider their effects on either originator behavior or upon the market. Some examples are:

- (a) Generic entry focuses on high-turnover blockbuster products³⁶⁷.
- (b) Litigation costs are a small proportion of gain (10%) which indicates that patent litigation by either originators or generics can be a profitable activity³⁶⁸.
- (c) The basic business model of generic companies is to develop an

³⁶⁴ *Raids leave pharma sector baffled*, EurActiv.com, Nov. 26, 2008. Found at <http://www.euractiv.com/en/health/raids-leave-pharma-sector-baffled/article-177516> Last visited April 11, 2009. (“EurActive”). See also, Darren Ennis & Ben Hirschler, *EU raids drugmakers ahead of tough sector report* Reuters, November 25, 2008. Found at http://mobile.reuters.com/mobile/m/FullArticle/CHLT/nhealthNews_uUSTRE4AP0WZ20081126?src=RSS-HLT Last visited April 11, 2009.

³⁶⁵ Sector Report Table 5 at p. 40.

³⁶⁶ EurActiv.

³⁶⁷ Sector Report para. 10.

³⁶⁸ Sector Report para. 922. (While the Report asserts this only as a benefit to originators the principle is equally applicable to a generic which stands to gain by invalidating an originator’s patent or coming to a settlement including a licensing agreement prior to LoE.)

identical/ equivalent product to a successful originator product after LoE. However, “Occasionally they may even enter the market earlier, most notably in cases where patent(s) of originator companies are not (considered to be) valid...patent settlement agreements between originator and generic companies...can also lead to early generic entry.”³⁶⁹

- (d) Large generic companies typically concentrate on those originator products generating the highest revenues³⁷⁰.
- (e) Generic companies typically have higher revenues in the EU than in the US³⁷¹.
- (f) Generic companies typically enter the market for the most commonly sold originator product version³⁷².
- (h) Generic companies pursue their own patent strategies to protect their products including patenting processes, products, and formulations³⁷³.
- (i) Generics do not bear the same costs as originators for R&D because they are able to use originators’ clinical results after LoE³⁷⁴.
- (j) The highest share of generics’ expenditure is for their marketing costs³⁷⁵.
- (k) The Sector Report lists various forms of originator litigation against generics as “life cycle strategies” such as litigation against and settlements with generics but does say the same about the converse: generic litigation, actual infringement or opposition proceedings against originators³⁷⁶.
- (l) Generic entry was greatest and occurred sooner for those INN’s with LoE which were the most valuable in terms of revenue³⁷⁷.
- (m) The pace of generic entry increased from 2000 to 2007³⁷⁸.
- (n) Generics concentrate on entry for the most commercially attractive versions of originator products³⁷⁹.
- (o) Generic companies file the majority of oppositions and appeals against originators before the EPO³⁸⁰.
- (p) Generics commenced oppositions before the EPO concentrating primarily on just six INN’s, and in all, one third of the most opposed INN’s concerned the top 20 selling INN’s facing LoE³⁸¹.
- (q) Of 207 patent settlement agreements between generics and originators

³⁶⁹ Sector Report para. 69.

³⁷⁰ Sector Report para. 70.

³⁷¹ Sector Report para. 74. The Report’s explanation is that many generics are not multinational and are EU based. The Report does not consider other reasons such as the existence of pricing regulations in Member States, which mandate higher prices for generics than in the US where there is no price regulation and heavy generic v. generic price competition.

³⁷² Sector Report para. 77.

³⁷³ Sector Report para. 78.

³⁷⁴ Sector Report para. 79.

³⁷⁵ Sector Report para. 81.

³⁷⁶ Sector Report para. 144.

³⁷⁷ Sector Report paras. 159, 160 and 166. (Despite the fact that these INN’s were protected by the greatest number of basic and secondary patents.)

³⁷⁸ Sector Report para. 163.

³⁷⁹ Sector Report para. 176.

³⁸⁰ Sector Report para. 544.

³⁸¹ Sector Report paras. 549 and 550.

63 (30%) concerned just two INN's and of the 49 INN's involved 31 (63%) concerned the best selling and of the 15 highest settlement rates 11 (73%) concerned INN's facing LoE³⁸².

The above evidence, taken from the Report tends to prove that generic companies' business model is to "cherry pick" INN's with the highest economic value, whether protected by IPR or not, and to litigate what is viewed as weak patent protection or file oppositions before the EPO to obtain LoE. They also engage, on occasion, in deliberate patent infringement where they feel that the risk/reward equation favors them and engage in their own patenting strategies. This is sufficient information for DG Competition to have inquired into whether or not originator behavior was a legitimate response to such generic activities or whether or not such behavior constituted a generic "toolbox" of commercial activities designed to obtain LoE or settlements earlier than they legitimately should have expected. A balanced approach would have then determined whether or not generics were "free riding" on IPR's, Data, and market building by originators or whether or not originators' commercial activities were legitimate responses or attempts to misuse their IPR's.

Other publicly available information indicates that generics typically engage in aggressive marketing and litigation tactics and infringe on originator IPR's fairly frequently, often on a global level. In many ways this represents a reasonably efficient mechanism to test the strength of IPR's. Indeed, that is a central premise of the HWA in the US. However, it seems rather inappropriate for the Commission to inveigh against the commercial behavior of one side of a sector without a proper examination of and comparison with similar behavior in another.

Patent infringement is a key business strategy of Teva Pharmaceutical Industries Ltd, the largest generic manufacturer in Europe³⁸³. Teva's own SEC Form 20-F for 2004 states that it pursues a business strategy, which includes marketing generic versions of products before expiration of patents by originators and lists some examples:

At times we or our partners seek approval to market generic products before the expiration of patents for those products, based upon our belief that such patents are invalid, unenforceable, or would not be infringed by our products. As a result, we face significant patent litigation...[W]e may...elect to market a generic product even though litigation is still pending...To the extent that we elect to proceed in this manner, we could face substantial liability for patent infringement...For example, in 2004 we launched oxycodone and generic versions of Neurontine© tablets and capsules despite the fact that litigation with the branded company was still pending. Our ability to introduce new

³⁸² Sector Report para. 586.

³⁸³ Sector Report para. 73.

products may depend upon our ability to successfully challenge patent rights held by branded companies³⁸⁴.

In November 2006 Teva withdrew the above mentioned patent challenges before the EPO and settled its patent infringement case before the Netherlands District court with regard to Perdue Pharma L.P. and Mundipharma International Ltd.'s patents on OxyContin. This followed the reversal by the Federal Circuit Court of Appeals of a judgement invalidating the Oxycontin patent in a suit brought by Teva³⁸⁵.

Teva's strategy is also recounted in an article in Bloomberg.com, captioned "Teva Grabs Billions Gambling on Copies of Brand-Name Drugs"³⁸⁶:

Teva "risks paying billions of dollars in legal damages by taking a calculated gamble: It begins selling copies while patents on a drug are still being disputed in court. Teva bets it will win the court case, allowing it to avoid triple damages for violating valid patents on brand-name drugs.

The article goes on to state that Teva which has "pulled off the maneuver 13 times since 2004..." often targets patents which it believes to be obvious and has yet to pay damages. The article also pointed to two recent settlements with originators AstraZeneca Plc. (despite AstraZeneca obtaining an interim injunction against Teva) and Sanofi-Aventis SA. An analyst's opinion was quoted to the effect that Sanofi's settlement with Teva may have resulted from the threat that Teva would not wait for a court decision before commencing marketing in the US.

Teva was not the only generic company asserting the invalidity of patents before the EPO or in litigation before EU and US courts during the 2000-2007 period covered by the Sector Report. In December 2006, German generic ratiopharm GmbH won an appeal in the EPO against AstraZeneca's patent on blockbuster drug Nexium (INN Esomeprazole) the follow-on drug to Omeprazole. Nexium represented \$1.1 Billion Dollars in 2003 EU sales³⁸⁷. The trend of generics using increasingly more aggressive commercial practices has not escaped treatment in the press³⁸⁸. A Wall

³⁸⁴ Teva Pharmaceutical Industries Limited, SEC Form 20-F (Annual Report) Fiscal Year ended December 31, 2004 at p. 10. (Emphasis added.)

³⁸⁵ Mundipharma International Ltd Press Release, November 6, 2006 Found at <http://www.prnewswire.co.uk/cgi/news/release?id=183302> Last visited April 23, 2009.

³⁸⁶ Catherine Larkin and Susan Decker, *Teva Grabs Billions Gambling on Copies of Brand-Name Drugs*, Bloomberg.com, (December 1, 2008) ("Copies of Brand Name Drugs") Found at <http://www.bloomberg.com/apps/news?pid=20601109&sid=av00ORVykaus&refer=home#> Last visited December 1, 2008 .

³⁸⁷ Christopher Elser, *AstraZeneca Says Nexium Patent Rejected in Europe (Update2)* Bloomberg.com December 19, 2006 Found at <http://www.bloomberg.com/apps/news?pid=20601085&sid=aFJqHDXvydHI&refer=europ> e Last visited April 23, 2009.

³⁸⁸ Thomas Gryta, *Generic-Drug Firms Get Bolder*, Wall Street Journal, February 6, 2008. ("Generics get Bolder"). Originally posted at

Street Journal article noted that generic companies "'at-risk launches,' are expected to increase in the wake of recent court cases that seem to mitigate the hazards of doing so as competition forces generic drug makers to find new routes of increasing sales and extending market exclusivity.³⁸⁹"

The growing number of patent challenges brought in the US affects patents for the same INN's in the EU. For example, a number of high profile cases, primarily brought by generics under the HWA concerned high value INN's on the Report's 219 INN list³⁹⁰. While the Report does not reveal the names of the INN's facing LoE in its E75 list, (making it difficult to make comparisons with these INN's) one should note that US litigation or settlements with generics often involves the settlement of litigation or disputes in the EU³⁹¹. The Report should have noted the existence of such litigation pressures brought by generics in other countries, rather than confine its assessment of the effects of the HWA to a tepid two sentence statement on page 426³⁹².

In Teva's case its patent infringement strategy was plainly stated in an annual report, filed with the US Securities and Exchange Commission.

The Sector Report itself contains sufficient evidence on its own to show the use of aggressive commercial tactics by generics. There is abundant evidence elsewhere that they affect patenting and litigation decisions by originators. In order to find misuse of these procedures the fact must first be assessed in a balanced evaluation of market behavior in the sector as a whole³⁹³.

Accordingly the Report's failure to balance the effects of generic tool boxes against the effects of originator toolboxes displays bias or, at best is incomprehensible.

<http://online.wsj.com/article/SB120227504432347199.html> Found at <http://www.forums.pharma-mkting.com/archive/index.php?t-1836.html> Last visited April 24, 2009.

³⁸⁹ Generics get Bolder para. 2.

³⁹⁰ See e.g. *Esai Co. Ltd. v. Dr. Reddy's Laboratories Ltd.*, 533 F.3d 1353 (Fed. Cir. 2008) *reh. and reh. en banc* denied, (Rabeprazole), *Pfizer v. Apotex* (Amlodipine 2007), *Eli Lilly & Co. v. Zenith Goldline Pharmaceuticals, Inc.* 471 F.3d 1369 (Fed. Cir. 2006) (Olanzapine), *Sanofi-Synthelabo v. Apotex, Inc.* 470 F.3d 1368 (Fed. Cir. 2006) (Clopiogrel/Plavix-see *Commission v. Poland* Case C-385/08), *Forrest Laboratories, Inc. v. Ivax Pharmaceuticals, Inc.*, 501 F.3d 1263 (Fed. Cir. 2007) ((+) enantiomer of Citalopram), *Aventis Pharma Deutschland GmbH v. Lupin Ltd.*, 499 F.3d 1293 (Fed. Cir. 2007) ((steriosomer of Ramipril), and *Takeda Chemical Industries Ltd. v. Alphapharm Pty Ltd.*, 493 F.3d 1350 (Fed. Cir. 2007) (Pioglitazine).

³⁹¹ See Copies of Brand Name Drugs (Noting that, settlement of the dispute between Teva and AstraZeneca included worldwide sales of Pulmicort, and Generics Get Bolder (Worldwide at-risk launch by Barr and Teva of generic version of Allegra.)

³⁹² Sector Report Annex to Chapter C. 2.4. Overview of the USA Regulatory Environment on Patent Settlement Agreements" para. 5 "Commentators have considered that the processes implemented through the Hatch-Waxman Act give specific incentives to generic companies to challenge originator companies' patents with less risk. This incentive might well influence the dynamics of litigation." (Emphasis added.)

³⁹³ Glaxo II paras. 69 and 71.

5.5 The Sector Report's Recommendations are Inefficient and would incur substantial Transaction Costs

The Report lists a number of actions that should be taken. They include establishing a unitary European Patent and dedicated patent judiciary, the strengthening of patenting requirements for both basic and secondary patents, and competition law interventions against originator companies' use of tool boxes including measures taken against litigating "weak" patent claims and settlements of disputes and litigation which include value transfers. These proposed actions, with one exception, would impose significant transaction costs on originators, stifling, rather than promoting the growth of innovation and would increase the agency costs of enforcing them. This is in seeming apposition to the teachings of the Coase Theorem regarding consideration of the transaction costs of enforcing rights or creating liabilities³⁹⁴.

5.5.1 A Unitary European Patent has been a Good Idea-For 34 Years

Establishing a Community Patent and Community Patent Court are laudable goals. They would harmonize and simplify the process of obtaining and objecting to patents in the EU. However, "muscae morientes perdunt suavitatem unguenti pretiosior", there is just a small fly in this ointment³⁹⁵. A European Patent regime has been a Community goal for 34 years³⁹⁶. The 1975 Community Patent Convention, the 1989 Agreement, and the Protocol on Litigation have not been ratified. While the Commission has placed the enactment of a European Patent Convention on the front burner³⁹⁷ it

³⁹⁴ See, Economic Analysis of Law at pp. 54-55 and 586-590 (redefining property rights as a solution to distribution problems may also discourage investment and imposes uncertainty on risk averse. Legislative solutions with broad standards increase agency costs of enforcement.)

³⁹⁵ "Dying flies spoil the sweetness of the ointment". From a Latin version of Ecclesiastes: Chapter 10.1. See also Directive 2001/20 on the application of good clinical practice on the conduct of clinical trials on medicinal products for human use.

³⁹⁶ Compare, 76/76/EEC: Convention for the European patent for the common market (Community Patent Convention) OJ L 17, 26/01/1976 p. 1, with 89/695/EEC: Agreement relating to Community patents - Done at Luxembourg on 15 December 1989, OJ L 401, 30/12/1989 p. 1, and Protocol on the settlement of litigation concerning the infringement and validity of Community Patents (Protocol on litigation) OJ L 401, 30/12/1989 p. 34. See also, Revised Proposal for a Council Regulation on a Community Patent, 9465/08 Brussels, 23 May 2008, Interinst. File No. 2000/0177 (CNS) ("Proposal 965/08") and Draft Agreement on the establishment of a European patent litigation system 16.2.2004 Working Party on Litigation Found at <http://www.epo.org/patents/law/legislative-initiatives/community-patent.html> Last visited April 24, 2009.

³⁹⁷ See, Proposal 9465/08 and COM (2009) 330 Recommendation from the Commission to the Council To authorise the Commission to open negotiations for the adoption of an agreement Creating a Unified Patent Litigation System. Brussels 20 March 2009.

acknowledges that the matter is very difficult and that many stakeholders have voiced objections to various pathways to establishing Community Patents and a common patent judiciary³⁹⁸. Given the history of the last 34 years it would appear that this solution is not a near-term one.

Enactment of a Community patent system would probably have a positive effect on new drug investment decisions. However, even if these changes were to be enacted tomorrow, their effect on generic entry would have to wait 20 years until their LoE and because existing patents would continue to be governed and challenged as at present.

5.5.2 Strengthening Patent Requirements is an inefficient solution to competition problems and would discourage innovation

Preliminarily it should be observed that the Report's recommendations regarding "Patent Clusters" are based upon a finding that originators file numerous secondary patents late in a blockbuster's life cycle and an inference, based on successful challenges, that their intended function is to block generic entry³⁹⁹. However, EPC 2000 Article 54(4) and (5) which came into effect December 31, 2007 express agreement among Member States that secondary method patents should not be subject to the stricter novelty standards of EPC 73. None of the secondary patent litigations examined in the Report were governed by Article 54(5)EPC 2000. This would indicate the Report's conclusions about patent standards and secondary patents may be premature and actually be contrary in some instances to the views of Patent Convention Members.

Moreover, as pointed out in a recent study by the European Generic Medicines Association⁴⁰⁰ it is difficult for patent examiners to raise novelty and non-obviousness objections to Secondary patents such as for follow-on medicines so it would be difficult to incorporate more stringent standards into patenting requirements.

Unfortunately, the patent system is largely incapable of distinguishing unimportant me-too drugs from drugs of significant medicinal value, and there is little reason to trust that the drugs deemed "obvious" under current law would not provide great benefit to society⁴⁰¹.

³⁹⁸ See generally, COM (2007) 165 COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL-Enhancing the patent system in Europe -. Celex No. 507DC0165

³⁹⁹ See Sector Report paras. 410 and 508-515.

⁴⁰⁰ *Patent-Related Barriers to Market Entry for Generic Medicines in the European Union- A Review of Weaknesses in the Current European Patent System and their impact on the Market Access of Generic Medicines*, May 2008. ("Patent-Related Barriers") at pp.12-15. Found at <http://www.egagenerics.com/index.htm> Last visited April 30, 2009.

⁴⁰¹ Unpatentable Drugs at p. 538,

Making standards tighter for patent grants would require large increases in agency costs in relation to potential benefits that might be conferred. Most patents are not commercially viable, less than 1.5% of all patents are litigated, and of those only .01% are litigated to trial⁴⁰². The vast bulk of the time it takes to obtain a patent is expended in waiting for the examiner to get through the backlog of applications for an examination that may take only a few hours⁴⁰³. Moreover, the relative value of patents is skewed, as the most valuable are more than 1,000 times more valuable than the median⁴⁰⁴. Of the 98.5% of patents that are never litigated some are commercially successful, while many (between 55% and 67% in the US⁴⁰⁵) lapse for failure to pay maintenance fees. Stricter standards might weed these out of the system, however that would require expenditure of higher transaction costs to do it.

Heightened patent standards would also introduce two important negative externalities, increased application backlogs, and the societal costs of discouraging public disclosure of ideas which may be of value to others even if they do not ultimately merit patent protection. (After all, these are the ideas that generics seek to use when they invalidate a patent in order to market medicines based upon the unprotected idea.) Patent Thickets will be exchanged for Regulatory Thickets when patent offices apply stricter scrutiny to applications⁴⁰⁶. Moreover, many factors point to the difficulties patent examiners have in predicting patent strength at the outset⁴⁰⁷. Focusing on changes to regulatory systems which deal with innovation without considering other related regulatory systems may not supply an optimal solution⁴⁰⁸. Changes to the patent laws affect patents in all areas of commerce, not just pharmaceuticals. Even a small change in patenting requirements, beneficial in one aspect, may have unintended or negative consequences in another⁴⁰⁹. For example, in the US, the Supreme Court changed the standard for determining “obviousness” in *KSR International*

⁴⁰² Mark A. Lemley, & Carl Shapiro, *Probabilistic Patents*, 19 No. 2 J. Econ. Perspectives 75 (Spring 2005) at p.75. (“Probabilistic Patents”.)

⁴⁰³ For example, in 2000 there was a three-year application backlog in the PTO while patent examiners took an average of 18 hours to complete their examination. *Probabilistic Patents* at p. 79.

⁴⁰⁴ *Probabilistic Patents* at p. 80.

⁴⁰⁵ *Id.*

⁴⁰⁶ COM(2007) 165 Section 3.1 recognizes the application backlog and the failure to meet a goal, established in 1999, of bringing the average time to grant or refuse a European Patent to three years and welcoming various initiatives in place, designed to improve patent quality.

⁴⁰⁷ Unpatentable Drugs at 521-530 (Describing three scenarios where changes to Novelty requirements become problematic for pharmaceutical patents at the filing stage.)

⁴⁰⁸ See Arti K. Rai, *BUILDING A BETTER INNOVATION SYSTEM: COMBINING FACIALLY NEUTRAL PATENT STANDARDS WITH THERAPEUTICS REGULATION*, 45 Hous. L. Rev. 1037 (2008) (“Better Innovation”) (Arguing that “crude line drawing” patent law determinations may not achieve economic policy goals in the biopharmaceutical sector as well as “tweaks” to drug marketing regulations or insurance regulation.)

⁴⁰⁹ See, Paul J. Heald, *TRANSACTION COSTS AND PATENT REFORM*, 23 Santa Clara Computer & High Tech. L.J. 447, (March 2007) (Arguing that proposals for patent law reform should be evaluated by whether or not they increase or lower transaction costs.)

Co. v. Teleflex, Inc.,⁴¹⁰ KSR, (cited in published Federal Court decisions 259 times from April 2007-April 2009), disapproved of a formulaic application of the Federal Circuits “TSM”⁴¹¹ test previously used to reduce “hindsight bias” in determinations of whether a patent claim was “obvious” to a hypothetical “person having ordinary skill in the art to which said subject matter pertains”⁴¹². KSR, which concerned whether or not attaching an electronic speed control mechanism to a gas pedal was “obvious” and not patentable, has been extremely problematical for pharmaceutical patents in the US⁴¹³. It is uncontroverted that more and more pharmaceutical patents, both primary and secondary have been subjected to invalidity attack on the basis of the “obviousness” test enunciated by KSR⁴¹⁴. KSR makes secondary patents modifying existing drugs more vulnerable to generic challenge, may make settlement of secondary patent litigation more expensive, and may encourage more “at-risk” generic launches⁴¹⁵. The results have been analyzed in the academic literature⁴¹⁶, which notes the effects of the case not only on patent validity determinations but also in deterring originators from making decisions to proceed with clinical trials and applying for marketing authority⁴¹⁷. The ultimate effect of such decisions on innovation has not yet played out but they caution against “quick fixes” to anti-commons problems by manipulating the patent laws.

5.5.3 Competition law is a poor tool to control patent based originator “tool boxes”

The Report makes it fairly clear that DG Competition wants to prosecute originator use of patenting strategies as competition law abuses. The Report, however, has not identified illegal uses of decisions to patent or to commence infringement litigation by originators. Unlike the AstraZenca

⁴¹⁰ 550 U.S. 398, 127 S. Ct. 1727, 167 L.Ed.2d 705 (2007) (“KSR”).

⁴¹¹ “Teaching, Suggestion, or Motivation” to combine elements from prior art.

⁴¹² 35 U.S.C. § 103(a). This is also known as the “PHOSITA” test.

⁴¹³ See e.g., Unpatentable Drugs at pp. 544-545 (Finding that the PTO, post KSR has denied patent protection to drugs for cancer, HIV, Hypertension, Stroke, Diabetes, and Tuberculosis.)

⁴¹⁴ See e.g. *In re Sullivan*, 498 F.3d 1345 (Fed. Cir 2007) (Antivenom composition for treating snakebites using Fab fragment of whole antibody found obvious.) References in the literature to Mithradatium could have made the invention obvious under pre-KSR standards.

⁴¹⁵ Putting the Brakes On at pp. 936-937, and Patent Life-Cycle at pp.308-309 (KSR in giving examiners and judges more freedom to find obviousness without documentary evidence granted the patent bar more opportunities to challenge non-obviousness findings on appeal.)

⁴¹⁶ A non-exclusive list includes many articles cited *infra* such as, Better Innovation, Putting the Brakes On, Patent Life-Cycle, Unpatentable Drugs, and Pharma’s Nonobviousness Problem

⁴¹⁷ See Unpatentable Drugs at pp. 545-553 (discussing originator decisions not to proceed with drug development where patentability is an issue.) Pharma’s Nonobviousness Problem at pp. 429-430 (KSR truncated the point in the process of non-obviousness determinations, which “is a complex task to do right” and substituted a greater range of types of evidence ultimately taking longer to adjudicate.)

case the Report cites no use of fraud or mis-statements by originators to obtain IPR, nor of the assertion of unlawfully acquired IPR to deter competition. Thus, analogies to US antitrust doctrines like Walker Process fraud on the Patent Office are inapposite. Nor has the Report established that the assertions of legally obtained rights to exclude competition such as patent infringement actions are violations of Article 82 EC. The gravamen of the argument then, is that the presence of “too many” weak secondary patents or, that the assertion of these exclusionary rights “deters” generics from bringing products onto the market while patent protection is valid.

The Report reasons that, because AstraZeneca made IPR related misrepresentations⁴¹⁸ as part of an IP “strategy” with the object of excluding generics⁴¹⁹, any originator with a patent strategy which contemplates exclusion of generics violates competition rules⁴²⁰ (regardless of whether or not the exclusionary IPR was obtained pursuant to law.) The Report’s logic leapfrogs from one inference tree to another. In other words, if a company violates competition rules by obtaining IPR’s by misrepresentation and those IPR’s are utilized in a strategy to exclude competition, it follows that other companies which obtain IPR’s legally may not use them to exclude competition⁴²¹. Not exactly QED. This expands the realm of anticompetitive behavior into the realm of “good” and “bad” IPR’s and makes any undertaking with a patent strategy suspect. Since nearly every undertaking holding IPR’s has an IP strategy (and, any public company with billions of dollars worth of IPR’s which doesn’t would probably be subject to shareholder suits, or worse, go bankrupt.) DG Competition will have a huge job ahead of itself when it “rounds up the usual suspects.”⁴²² The concept should not be viewed in isolation, as similar principles will have to be applied wherever the right to exclude competitors granted by IPR is asserted. Standards organizations, patent pools, and industries using high numbers of patents in integrated circuits would all be subjected to the same high levels of regulatory scrutiny. Such a shift in applicable legal rules creates an “at their worst” IP property right system and interferes with the

⁴¹⁸ See Sector Report para, 248 FN 131.

⁴¹⁹ Sector Report para. 870.

⁴²⁰ Sector Report paras. 872-873.

[T]he sector inquiry sought to establish whether originator companies involved in the practice of such life cycle strategies simultaneously used other strategies to delay generic entry...This would be of particular interest if the companies apply a so-called “bridging strategy”, as in the Astrazeneca case,...

As outlined below in Chapter C.2.3, there is a high correlation between strategies and practices as originator companies combine the use of different instruments in their “tool-box” for the same product.

⁴²¹ This is the sort of mock-scholastic reasoning made famous by the movie Monty Python and the Holy Grail (Sony Pictures 1975). In Scene V Sir Bedevere reasons that, because one burns witches and because wood also burns and, because wood also floats, if one throws an accused witch into water and she floats she is therefor proved to be a witch.

⁴²² Casablanca (Warner Brothers 1942) (Captain Renault to gendarmes.)

commercial use of IPR⁴²³. In effect, violations of Articles 81 and 82 of the Treaty will be reduced to a possessory offence like illegal drug possession.

Leaving out considerations regarding the validity of the argument, enforcing competition rules in such case would require DG Competition to establish rules permitting or forbidding certain patent filings or certain patent litigation. It would require sifting through existing patents and suing patentees holding patents which DG Competition views as being anticompetitive or distorting competition. The same analysis applies to a great extent to assessments of patent settlement activities. The insertion of DG Competition into assessing the value of property rights and the motivation behind obtaining IPR grants goes far beyond its competence⁴²⁴. It would violate the basic right of free access to the Courts⁴²⁵. It should be remembered that IPR is a property right protected under the European Convention on Human Rights⁴²⁶. More to the point, it also would involve huge agency costs far exceeding any theoretical gains. The investment of time and energy into determining if a patent was “strong” or “weak” or valid or invalid would be prohibitive, especially when one stops to consider that the 219 INN’s discussed in the Report were subject to nearly 40,000 patents or pending applications. As noted in the EPO’s Comments to the Report⁴²⁷, the methodology used by the Report minimizes the complexity of determining which is the primary and which is the secondary patent for the purposes envisioned by the Report. Indeed, as the EPO Comments point out there are no separate standards for granting basic and secondary patents.

⁴²³ Stephen H. Haber, F. Scott Kieff, & Troy A. Paredes, *ON THE IMPORTANCE TO ECONOMIC SUCCESS OF PROPERTY RIGHTS IN FINANCE AND INNOVATION*, 26 Wash. U. J. & Pol’y 215, 231 ((2008).

⁴²⁴ Article 295 Treaty of Amsterdam Amending the Treaty on European Union, the Treaties Establishing the European Communities and Certain Related Acts, Oct. 2, 1997, 1997 OJ (C. 340) 1. “This Treaty shall in no way prejudice the rules in Member States governing the system of property ownership.” *Etablissements Consten S.a.R.L. and Grundig-Verkaufs-GmbH v Commission*, Joined cases 56 and 58-64, ER 1966 Page 00299. (Competition law may affect the exercise of IP rights but not their original grant.)

⁴²⁵ See, *ITT Promedia NV v Commission*, Case T-111/96 ECR 1998 page II-02937 para. 60: Before considering those various pleas, three points should be made. First, as the Commission has rightly emphasised, the ability to assert one’s rights through the courts and the judicial control which that entails constitute the expression of a general principle of law which underlies the constitutional traditions common to the Member States and which is also laid down in Articles 6 and 13 of the European Convention for the Protection of Human Rights and Fundamental Freedoms of 4 November 1950 ...As access to the Court is a fundamental right and a general principle ensuring the rule of law, it is only in wholly exceptional circumstances that the fact that legal proceedings are brought is capable of constituting an abuse of an dominant position within the meaning of Article 86 of the Treaty.

⁴²⁶ See, Convention for the Protection of Human Rights and Fundamental Freedoms, Nov. 4, 1950, 230 U.N.T.S.222. See also, *Anheuser-Busch Inc. v. Portugal*, App. No. 73049/01, 45 Eur. H.R. Rep. 36 [830] (Grand Chamber 2007) (Corporate ownership of IP rights is protected by the Convention.) and Laurence R. Helfer, *THE NEW INNOVATION FRONTIER? INTELLECTUAL PROPERTY AND THE EUROPEAN COURT OF HUMAN RIGHTS*, 49 Harv. Int’l L.J. 1 (Winter 2008).

⁴²⁷ See, EPO Comments at pp. 2-3.

The costs of DG Competition acting as a sort of IPR traffic cop, in addition to agency costs, would rely solely upon its business judgement as to whether or not, and how IPR's are to be used. Likewise, Directives or Regulations specifying the types and purpose of patent filings can not filter out "good" from "bad" patenting practices. The chill on innovation would be incalculable. DG Competition should not be in the business of telling originators which inventions merit IP protection and which do not and, therefor must be intended to hinder competition. Likewise, regulatory actions such as guidelines or litigation under Articles 81 and 82 would create similar costs and uncertainties. In 2005 there were almost 193,000 patent filings and in 2006, 145,000 applications were received under the Patent Cooperation Treaty⁴²⁸. All would have to comply with competition guidelines and be subject to a competition law review. Broad categories defining competition law violations by type of intellectual property grant, would create boundless uncertainty and a chilling effect on innovation and investment decisions. The doubtful wisdom of such an approach is reinforced by the fact that despite its recommendations, the Report's own data demonstrates that patent "tool boxes" have had less effect on INN's where they are more heavily practiced than where they are less heavily practiced.

The potential consequences of false positives caused by DG Competition determinations is not trifling. An example may be found in *Bundesverband der Arzneimittel-Importeure eV and Commission of the European Communities v Bayer AG*⁴²⁹. In 1996 the Commission found that voluntary restrictions of the supply of Bayer AG's second best selling drug Adalat to suppliers in Spain and France violated Article 81 EC, fined Bayer and ordered it to resume supplying it to parallel traders (who were selling it in the UK at 40% below the price set for Bayer.) The ECJ reversed the Commission's decision in January 2004 eight years later. However, in the interim, Bayer's worldwide sales of Adalat⁴³⁰, which had been growing, fell by 4%. What is less well known is that as a consequence of the Commission decision, Bayer cut its European R&D spending by 1% in 1998 and by 14% in 1999 while increasing its US R&D spending by 8% in 1998 and 31% in 1999⁴³¹. It is quite possible that actions by the Commission aimed at perceived effects of originator Tool Boxes could open a Pandora's Box⁴³² of unanticipated effects on EU R&D.

Intervention by DG Competition in IPR matters should be limited to misuse in obtaining them or misuse of asserting such rights beyond their grant so as to distort competition, or to agreements which have as their object the prevention, restriction or the distortion of competition. Involvement in the initial IPR grants on a grand scale by DG Competition and changes in IP

⁴²⁸ COM(2007)165 at 3.1.

⁴²⁹ Joined cases C-2/01 P and C-3/01 P. ECR 2004 page I-00023. ("Adalat".)

⁴³⁰ INN Nifedipine, one of the 219 INN's in the Sector Report.

⁴³¹ European Price Regulation at pp. 19-20.

⁴³² See Hesiod's Theogony (again) at lines 560-612.

policy based upon untested (and logically untenable) competition theories are simply not warranted.

5.6 Conclusion

As may be seen from the above analyses, the Preliminary Report failed to address its primary mandate, ignored the Commission's and other governmental studies conclusions regarding innovation in the pharmaceutical sector, contains information which contradicts its findings, contains statistical errors and assumptions and makes inefficient or impractical recommendations. In addition, the Report exhibits bias against the existence of IPR and fails to provide a balanced view of commercial practices in the sector from which any determination of whether or not a sector is distorted must be made. The Report ignores major holdings of the ECJ and makes inferences about patents which are also contradicted by ECJ case-law in order to reach its conclusions.

Accordingly, the Preliminary Report is a severely flawed and unbalanced document and should not be the basis for conclusions about performance in the pharmaceutical sector or recommendations for action.

6 ROADMAP FOR THE FUTURE: PROPOSALS

I propose a number of suggestions, which I believe, will create an atmosphere more conducive to pharmaceutical innovation in the EU and which would help reduce drug prices for consumers.

6.1.1 Regulatory Review creates far more delay to both originator and generic entry than posited for originator tool boxes

The Report in failing to analyze the effects of delay by Regulatory bodies ignored the fact that such delays are far more deleterious to market entry for both originator and generic than the delays it attributes to originator “tool boxes”. For example, the Report mentions delays in booking a slot for filing marketing authorization of up to two years⁴³³. This affects not only generic but originator filings as well. This is an enormous welfare loss compared to the alleged seven-month delay for generic entry. Professor Lichtenberg has calculated that for every year of use of a newer “vintage” drug (time that a newer or later vintage drug is in use) equates to a two-month increase in longevity⁴³⁴. If this statistic is applicable to delays in Marketing Authorization in the EU such a two year delay in overall grants conceivably could deny consumers an additional 4 months of longevity. It is not necessary to calculate the resulting societal costs in Euros

6.1.2 Centralizing the scientific approval process within the EMEA

Here are some suggestions. First, consolidate and centralize all clinical aspects and Exclusivity aspects of Marketing Authorizations under an amendment to Regulation 726/2004 and eliminate Member State Marketing Authorization other than for pricing and reimbursement. The present system of individual marketing authorizations and dependence upon RMS, reference products, or abbreviated procedures under Directive 2001/83 is duplicative, expensive and has too many costly variations. The EMEA should be able to handle all MA in a centralized fashion with fees modeled upon the example of EPC applications designating Member States where the final commercializing aspects will be undertaken. This eliminates differences in how clinical trials are conducted and enable originators and

⁴³³ Sector Report para. 1123.

⁴³⁴ Frank R. Lichtenberg, *WHY HAS LONGEVITY INCREASED MORE IN SOME STATES THAN IN OTHERS? The Role of Medical Innovation and other Factors*, Medical Progress Report No. 4, July 2007, (Manhattan Institute for Policy Research) Found at http://www.manhattan-institute.org/html/mpr_04.htm Last visited April 28, 2009.

generics alike to deal with the common issues of safety, purity, and efficacy in one place, leaving national issues for Member States. A mechanism, which may be adapted, exists today in the form of Regulation 726/2004 and the EMEA is already performing many of these tasks. Contracting out supervision of clinical trials to Member State organizations with surplus capacity and medical expertise may ease work overloads on the EMEA. Another, market-based method of speeding the conduct of clinical trials, suggested by Corinne and Robert Sauer⁴³⁵, could be to establish private certification boards for drug approvals competing on the basis of the safety, efficiency and cost of their drug approval process. The proponents argue that drug approval privatization could lower drug prices without creating IPR violation issues. Centralization of drug approvals would harmonize an EU wide process. Granting the EMEA authority to contract out trials to Regulatory authorities in Member States or private boards could be an efficient method of finding the most effective and cheapest means of satisfying safety concerns.

6.1.3 Establish a central registry of patents associated with Marketing Authority and SPC patent extension

Regulation 726/2004 Article 13(2) already provides for establishing a list of patents related to Marketing Authority. This requirement should be expanded to recording all patents asserted to be related to a drug when MA is granted or which has been granted MA in each Member State (much like the Orange Book in the US.) This sort of transparency is appropriate where multiple and overlapping levels of authorizations, IPR's and exclusivity regimes apply in 27 Member States.

6.1.4 Amend Directive 2004/48 to provide for Patent plaintiffs and defendants to have all related claims and defenses heard by one tribunal

If patents, especially secondary pharmaceutical patents are considered to be “weak” and the political consensus is that they must be tested, the best and cheapest method is to enable generics and originators to test all related claims in one litigation venue⁴³⁶. Since it is unlikely that Community Patent regime or Community Patent Court will be effected any time soon, and since there will still be huge numbers of National Patents even if enacted,

⁴³⁵ Corinne Sauer & Robert M. Sauer, *Is it Possible to Have Cheaper Drugs and Preserve the Incentive to Innovate? The Benefits of Privatizing the Drug Approval Process* January 2006 (“Privatizing Drug Approvals”) Found at <http://ssrn.com/abstract=875359> Last visited April 28, 2009. (

⁴³⁶ I except opposition proceedings under the EPC as they are governed by treaty. Complaints by generics that legal proceedings are sometimes stayed until opposition proceedings are concluded elide the fact that the generics are the parties bringing the opposition proceedings.

the problem should be attacked within each Member State's legal system. As previously noted, the HWA has been highly successful in the US in enabling the affected constituencies to try all of their claims in one unitary action. A similar system in the EU would provide for transactional efficiencies. Aspects of the HWA, which have proved problematical (such as MA priorities), may be corrected in the EU model. Existing Community rules can be amended to provide for the efficient determination in one tribunal of all claims that originators and generics may have against each other. The constituency best able to test pharmaceutical patent strengths are generics rather than a patent examiner or a competition authority. An examiner is in no position to know the properties of a new chemical, which often requires the results from clinical tests. However a commercial competitor who has knowledge of the properties of the invention and has had an opportunity to compare it with prior art or the results of clinical trials is in a far better information position to test the IPR and certainly has the motivation to do so⁴³⁷. Generics have the scientific expertise to identify highly technical patenting issues and a great deal of experience in such patent litigation⁴³⁸. Patent litigation is also part of the generic business model and the expenditure of relatively small sums for litigation costs have the potential to reap big rewards for them either in the form of verdicts permitting early market entry or settlements. It should also be pointed out that in the EU the winning side generally is awarded its costs and this represents the possibility of a net gain if there is a greater than 50/50 chance of winning.

Directive 2004/48 already contains many of the elements required including possibilities for injunctions, taking of evidence, damages, and costs. It would not be too difficult to amend it to provide for all counterclaims and defenses arising under the Member States law to be able to be asserted in one trial. Access to declaratory infringement or invalidity actions would permit entities to test IPR without incurring damages. This might require a small amendment to tribunal competency with respect to counterclaims under Regulation 44/2001 but that is not insurmountable. The establishment of a central patent, Marketing Authorization and SPC registry would, as noted create transparency sufficient for all to be on notice of applicable IPR's. An example of how a unitary HWA type system might work may be found in the recent US case of *Kaiser Foundation Health Plan, Inc. v. Abbott Laboratories et al.*⁴³⁹. Kaiser considered issues of generic entry patent invalidation, patent infringement, patent settlement and antitrust issues. Kaiser actually considered two tiers of issues. In the first set of trials involved issues regarding generic entry patent validity and settlement of originator/generic suits. In the second tier, a consumer entity brought antitrust actions against both the originator and generic and this was consolidated with other antitrust plaintiffs' claims filed in the first tier. The Federal Courts had jurisdiction over all of these claims and exercised it in a

⁴³⁷ Pharma's Nonobvious Problem, at p. 416.

⁴³⁸ See, e.g., Discussions of complex technical issues relating to chemistry in Patent-Related Barriers at pp. 12-16.

⁴³⁹ 552 F.3d 1033 (9th Cir. 2009) ("Kaiser").

uniform manner dealing with all related claims thus avoiding the risk of contradictory judgements.

In respect of competition law it would be relatively simple for DG Competition to provide guidelines on when it considered patent litigation and patent settlements to violate competition laws. Moreover, to the extent that DG Competition felt that pharmaceutical patent settlements might be anticompetitive it could provide for block exemptions or some system of notification to local competition authorities, which have better resources to deal with local linguistic and legal issues. The competition guidelines, however, should contain some sort of presumption that patent litigation is legitimate and contain competition law exceptions similar to the US Noerr-Pennington and Walker Process fraud exceptions for IPR obtained by fraud or inequitable conduct⁴⁴⁰. The Commission has already used similar guidelines in the ITT Promedia case. This is in line with Community law and Article 295 of the Treaty. This would also smooth out and harmonize many conflicts between trying to assert a legitimate monopoly under an IPR grant, and violations of competition law via sham litigation or litigation based upon fraudulently procured IPR.

6.1.5 Provide for flexibilities in grants of Exclusive Marketing authority to provide for protection relative to costs of investment

Much of the debate on the appropriate extent of patent protection for pharmaceuticals centers on originators trying to protect the enormous investments they make in bringing a drug to market. As pointed out by Benjamin Roin, the policies underlying patent laws are designed to reward innovation and this has little to do with protecting investment in commercializing the invention⁴⁴¹. Moreover, intellectual property protection provides few incentives for investments necessary for market entry⁴⁴². Considerations of patent vulnerability deter investment in valuable medicines that may become vulnerable to patent attack⁴⁴³. Much ink has

⁴⁴⁰ One example of how sham pharmaceutical patent litigation intended to delay generic entry may be deterred by stripping the litigant of antitrust immunity may be found in *In re Buspirone Antitrust Litigation* 185 F. Supp. 2d 363 (S.D.N.Y. 2002). There, a finding that a patent infringement suit was merely a sham to delay generic competition resulted in forcing the plaintiff to settle the Clayton Act suit for US \$220 Million.)

⁴⁴¹ Unpatentable Drugs at pp. 514-516.

⁴⁴² Market Experimentation (The authors argue for institution of intellectual property protection for market entry to balance the vulnerability to free riding of first movers who have invested heavily in market experimentation.)

⁴⁴³ Unpatentable Drugs at pp. 545-553 (Evidence that originators decide not to proceed with valuable drugs due to concerns that patents may be vulnerable to obviousness attacks.) (“When a drug is screened out of development under these circumstances, the resulting loss to the public is unlikely to be mitigated by the gain of some other drug developed in its place... The social costs of losing such drugs likely far outweigh any benefits to the public from faster access to inexpensive generics of the unpatentable drugs that actually reach the market.”)

been wasted on trying to harmonize the two differing policy issues but a way already exists to encourage commercialization divorced from innovation policy considerations. To wit: Data Protection and Marketing Exclusivity. Data Protection and Marketing Exclusivity are specifically aimed at rewarding or reimbursing originators for engaging in clinical trials and other efforts that commercialize an innovation. I agree with Professor Roin that it would be far simpler to enact a system of grants of Marketing Exclusivity based upon the time, effort and money required to obtain Marketing Authority than it would be to stretch Patent Law theories to cover commercialization efforts. This would encourage investment in commercializing useful medicinal products even if underlying patent protections might subsequently be invalidated. Flexibilities can include such non-IP law considerations as the length of time to bring a drug to market, the expense, and the merits of the medicinal product (which would be better understood after years of research and trials). Protection may be built in so that Marketing Exclusion terms would not be lock step based solely upon development expenditure. Firm term end dates would signal to generics when they may enter the market without the necessity to concentrate on litigating patent validity. A proper balance may thus be obtained between focusing on HWA type patent litigation and Regulatory Marketing Exclusivity.

6.1.6 Provide for Generic v. Generic Price Competition

It is curious that, in an Inquiry, which seeks to gauge the level of competition in a sector, the Report fails to look into generic versus generic competition and analyze its effects on prices and consumer welfare⁴⁴⁴. If consumer welfare is such great a concern, generic versus generic competition is no less important than post LoE originator versus generic competition. One only has to look at the effect of generic versus generic price competition in the US to gauge its importance. In the US, according to at least one Government Study the average ratio of generic price to originator price declines from 61% to 39% depending upon the number of competing generics manufacturing copies of the same drug⁴⁴⁵. The Sector Report finds that prices in the EU are subject to a far smaller drop over time from an initial 30% to about 40% (in other words, the drop in prices due to generic entry eventually equals the initial price drop in the US and, apparently no lower.) Such a price analysis of course, would also require

⁴⁴⁴ While paras 169-176 of the Sector Report measures the number of generics entering the market after LoE the next section measuring post LoE price drops only tangentially refers to generic v. generic competition in para. 189 stating that over time, generic prices go from 75% of originator pricing to about 60%.

⁴⁴⁵ See e.g. *HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY*, Congressional Budget Office Study July 1998, at page 33 Table 5. (“CBO Generic Pricing”) Found at www.cbo.gov/showdoc.cfm?index=655 Last Visited April 26, 2009.

analysis of governmental drug pricing. The deadweight loss here is far greater than the Report posits is due to delayed generic entry. If regulatory bodies only permit prices to be lowered by 25% upon generic entry why bother with generic entry at all and just reduce the price of branded drugs when they lose exclusivity? Otherwise only a fraction of the deadweight loss is transferred to consumers while the balance is transferred to generics after a lot of fuss and bother.

7 CONCLUSION

The Sector Report never got around to dealing with its key question and became enmeshed in complicated analyses of somewhat theoretical competition law violations having little if anything to do with pharmaceutical innovation in the EU. The Report failed to recognize other inquiries into the issue and harmonize itself with other studies by the Commission and by foreign governmental entities. Its basic theses are contradicted by its own data. There are open questions but the Report's lack of balance and obvious bias makes it manifestly unhelpful in answering those questions. This leaves open the issue of how to spur pharmaceutical innovation in the EU.

Perhaps the answer to why fewer NME's are getting to market may be found in another quote attributed to Yogi Berra. "Slump? I ain't in no slump. I just ain't hitting." It may well be that all of the "low hanging fruit", (targets that are more easily modulated by simple chemical formulations), have been harvested. Perhaps the advent of new technologies will create an increase in useful NME's. The increased use of targeted biologics appears to be the next "big wave". Perhaps more focus should be placed on less innovative but very effective modifications of existing drugs.

Broad predictions about the future of medicine are not within the core competence of DG Competition. Nor is Patent Reform. Competition law is important to commerce within the Internal Market. However it is not the appropriate surgical instrument to cure ills troubling innovative medicine in the EU. Any reforms to the European Patent system should be aimed at all sectors and are, in any event, exclusively within the Treaty-making competence of the Member States. Most of all, pharmaceutical innovation must be viewed as a global problem with application in the EU rather than the reverse.

Industry participants with far greater knowledge of the industry and its problems are better suited to engaging in the debate, whether in the markets, the legislature, or the courts. The parties best suited to resolve specific sector problems are the most efficient actors from a purely transaction cost point of view. Resolution by the parties costs far less than the agency and transaction costs of broad rule making and enforcement by a regulatory agency without the knowledge or resources required for the broad scale enforcement it calls for, and which displays a pronounced institutional bias.

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