

Authorship Declaration

I hereby declare and confirm that this thesis is entirely the result of my own work except where otherwise indicated. I gratefully acknowledge supervision and guidance I have received from Dr. Peter Camesasca and Dr. Avishalom Tor.

Date 10.8.06 Signature Dana

*Delaying Generic Entry in the EU and the US:
A Comparative Law & Economics Analysis*

Master thesis - EMLE program

Dana Gur, Israel

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...”Our message to brand-name manufacturers is clear: you deserve the fair rewards of your research and development – you do not have the right to keep generic drugs off the market for frivolous reasons”...

US President, George W. Bush, 2002

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I. Introduction¹

Generic drugs are chemically equivalent to brand-name drugs, and may replace them at a lower cost. Since prices of generics fall as the number of producers rises, generic manufacturers are most profitable when they are early to enter the market².

The delay of generic market entry is currently the focus of US and EU Member States' governments as well as antitrust enforcement institutions, due to its implications on soaring worldwide health-costs and on direct purchasers and consumers' welfare, allowing cheaper access to drugs.

In this paper, I intend to examine the practices and effects of generic delay in the US and EU contexts, by conducting a legal and economic comparative analysis.

I will inspect if there is a difference in the US and EU approach to the matter of generic delay and to the balance inherent to it, and will draw a public policy recommendation applicable to both systems that may put forward suggestions as to the socially optimal solutions.

¹ I would like to thank Prof. Daniel Rubinfeld from the University of Berkeley CU for suggesting to me that I write my thesis on this topic.

² Policy Relating to Generic Medicines in the OECD, Study carried out on behalf of the European Commission, 1998.

II. The Balance between the Importance of Generic Entry and its ‘Dynamic’ Cost

II.1. The Importance of Generic Entry

Much has been written about the importance of generic entry into the pharmaceutical market, bearing strong implications on its delay. Over the last four decades, there has been a continuing debate amidst policy makers regarding the proper balance between a competitive low-priced generic market³ and the encouragement of innovation in the pharmaceutical industry.

Generic entry is nowadays of increased public importance because cheaper and functionally identical generic versions of drugs may reduce the *growing impact of drug prices on healthcare costs around the world*⁴. Additionally, *allowing access to lower-priced drugs in the form of generics* is of crucial significance to those who may otherwise not afford what may be life-saving drugs⁵.

³ EuroActiv News, “G10 Medicines Group Makes Recommendations to Enhance Pharmaceutical Competitiveness”.

⁴ According to a recent report, drug expenditures in the USA are a substantial component of health expenditures (5.8% in 1992 and 10.5% in 2002) and are by far the fastest growing component of health care costs.

Kaiser Family Found., Trends and Indicators in The Changing Health Care Marketplace, at Exhibits 1.5, 1.6 & 1.7 (2004), available at <http://www.kkf.org/insurance/7031/index.cfm>.

Market researchers expect the European pharmaceutical market to grow by an average of 5.2% per year between 2002 and 2007. See “*Innovation in the Pharmaceutical Sector*”, A Study Undertaken for the European Commission by Charles River Associates, 8th November 2004.

M. Freeman, “*Sustainable, Fair and Pro-Generic*”, Chemist and Druggist, December 9, 2000 – According to Andrew Kay, chairman of the British Generics Manufacturer Association (BGMA), in the year 2000 alone there has been an addition of £200 million in the medicines bill.

⁵ This has been raised within the EU and US context and also in the global context of developed vis-à-vis developing countries.

II.2. The ‘Dynamic’ Cost Flowing from Generic Competition

The role of generics is to bid away, after patent expiry, the higher profits that are an essential reward to research-based manufacturers – if they are to take the risk of innovating⁶. Yet the innovative drug industry faces huge research and development (R&D) costs, also from drugs that are never introduced, all of which must be covered over the life of those drugs that *are* successful. Drug development has therefore been analogized to *drilling for oil ‘with many dry holes and a few gushers’*⁷. One recent study, in fact, estimated the success rate for compounds entering clinical testing at only 22 percent.

Many drugs would thus not be produced *but for the patent protection* allowing the branded companies to enjoy market power and reap supra-competitive profits.

With generic entry eroding the innovative-firms’ profits in a way that will not guarantee recouping of their costs also for unsuccessful developments, *one can not expect new R&D leading to the launching of new sometimes life-saving drugs*. This is what may be referred to as the ‘dynamic’ toll that generic entry takes on innovation.

Innovation and in particular pharmaceutical innovation are of tremendous importance to the technological development of a state, yet also for the purpose of finding life-saving treatments. The state of worldwide pharmaceutical innovation raised particular concern in recent years when it was suspected to have undergone a ‘crisis’, observed in the fact that

⁶ See *supra* note 1.

⁷ J. Langenfeld and W. Li, “Economic Analyses of Patent Settlement Agreements: The Implementation of Specific Economic Tests, the Evaluation of Dynamic Efficiency and the Scope of Patent Rights”, *University of San Francisco Law Review*, Vol. 39, pg. 57-80.

*the number of new products innovated has not risen whilst the overall level of R&D has risen dramatically*⁸.

II.3. The Challenge: What is the Right Balance to Strike?

The matter of generic delay raises questions regarding the inherent tradeoff between *static efficiencies*, allowing generic competition to decrease the high prices of brand drugs, and *dynamic efficiencies* that award patent exclusivity with substantial market power via intellectual property rights (IPRs), and are designed to furnish long-run incentives for innovation. In this framework, therefore, *there could be no long-run innovative benefits without the endurance of the short-run competitive welfare harms* flowing from the legal monopoly awarded by the patent.

On the one hand, putting emphasis on the static effects – namely, preventing substantial delay to generic entry whilst ignoring the exclusionary power awarded to patent holders – may discourage the research-based players from creating new vital drugs. On the other hand, failing to ‘crackdown’ on tactics of generic deferral may enable brand-drug companies to grow richer at the expense of consumers who may not afford the drugs and even suffer or die⁹. The right balance is therefore difficult to strike.

⁸ “Innovation in the Pharmaceutical Sector” – A Study Undertaken for the European Commission by Charles River Associates, November 8, 2004.

⁹ See Joshua P. Davis and Steig Olson, “Efforts to Delay Competition from Generic Drugs: Litigation along a Seismic Fault between Antitrust and Intellectual Property Law”, University of San Francisco, Vol. 39, pg. 1-10.

Theoretically speaking, static competitive harms must be tolerated because they are part of the supra-competitive return the government has granted to the IP owner under a social policy designed to encourage innovation¹⁰. *Yet encouraging dynamic efficiencies should not be absolute and should be balanced with the benefit arising from exercising patent rights.* Thus, it may be claimed that while the mere possession of monopoly power via a patent is not illegal by itself the *illegal willful acquisition or maintenance of that power through improper delaying tactics* strays from lawful boundaries.

The legal systems in both the EU and the US have attempted to craft a correct delicate balance between the static and dynamic efficiencies flowing from generic market entry and its delay, albeit in distinct manners. This may be seen in the different laws, case-law, antitrust policies and delaying tactics displayed in the EU and the US, and as will be discussed henceforth.

¹⁰ Herbert Hovenkamp et al., Anticompetitive Settlements of Intellectual Property Disputes, 87 Minn. L. Rev. 1719 (2003).

III. The Different Legal Aspects Regarding Delay of Generic Entry in the EU and the US

Different antitrust concerns involving the brand-name pharmaceutical companies and their generic competitors emerged from recent occurrences within the pharmaceutical industry,¹¹ both in the EU and the US. However, in this paper I intend to focus on anticompetitive affects flowing from delaying generic entry *conduct* of pharmaceutical manufacturers.

III.1. The Different Delaying Tactics Employed in the EU and the US

During these last years, the tactics used to delay generic companies' entry into the market have grown both in numbers and in their complexity to the point that some claim it has become more evident that the research-based industry will try to use any channel available to defer the entry of a generic version of its patent-protected drug¹².

¹¹ An apparent phenomenon is that of the pharmaceutical industry' restructuring, through mergers and acquisition, leading to consolidation in the USA – suggesting more *concentration*, albeit not necessarily *dominance* in supply.

See Roy Levy, Federal Trade Commission, *The Pharmaceutical Industry: A Discussion of Competitive and Antitrust Issues in an Environment of Change*: An FTC Report, (March 1999), available at <http://www.ftc.gov/reports/pharmaceutical/drugrep.pdf>.

Horizontal affiliations are also to be found in the EU, notably in the UK. Joint ventures and licensing agreements between brand-name pharmaceuticals and their generic competitors appear to represent another form of consolidation, in which research-based, generic and wholesaling companies are building their existing businesses rather than extending them upstream or down.

See also A. Jack, “*Rising Health Costs Open Way for Generics*”, Financial Times, London (UK), April 3, 2006, pg. 24 – describing a “recent wave of consolidation within Europe. Last year Novartis of Switzerland acquired Germany’s privately held Hexal, combining it with Sandoz unit to create the world’s second-largest generics business by sales. Acquisition activity has intensified...There is a clear drive towards scale and size...Eastern and Central Europe are a particular focus for several companies...”.

¹² A. S. Relman and M. Angell, “*How the Drug Industry Distorts Medicine and Politics – America’s Other Drug Problem*”, the New Republic, December 16, 2002.

The tactics used in the US are different from those used in the EU, due to differing regulatory regimes and methods of interpretation of both brand-name and generic companies' *conduct* by the Courts¹³.

In the U.S, evidence suggests both brand-name and generic drug manufacturers have discovered loopholes in the Drug Price Competition and Patent Term Restoration Act of 1984¹⁴, commonly known as the Hatch-Waxman Act¹⁵, and have exploited them, costing consumers billions of dollars. The main delaying tactics entail collusive “settlement” agreements in which generic companies are paid not to sell their drugs (payments referred to as “reverse payments”) or to sell them exclusively to the pioneer drug manufacturer¹⁶; the filing of sham patent-infringement suits designed to invoke “stays” of FDA marketing approval of generics¹⁷; and “gaming” the drug approval process by the Food and Drug Administration (FDA) through alleged fraudulent or improper listing of the brand products in FDA’s “Orange Book”.

In the EU context, case law and legal treatises indicate that the main types of delaying tactics detected were regulatory abuse methods, be it centralized EU regulations or Member States’ (MS) patent laws, for the fraudulent or “frivolous” procurement of patented drugs.

¹³ This matter will be elaborated upon in the following chapters.

¹⁴ Act of 1984, Pub. L. No 98-417, 98 Stat. 1585 (codified as amended at 21 U.S.C § 355 (1994)), codified in scattered portions of 21 & 35 U.S.C - the United States Code.

¹⁵ Hereinafter: the Hatch-Waxman Act.

¹⁶ These agreements are reached as part of “settlements” of patent infringement litigation or pending the outcome of the litigation.

¹⁷ Federal Trade Commission, *Generic Drug Entry Prior to Patent Expiration: An FTC Study*, 25-52 (July 2002) [hereinafter: FTC Study], available at: www.ftc.gov/os/2002/07/genericdrugstudy.pdf (last accessed July 24, 2006).

III.1.1. Litigation Abuse in the US

*The US Hatch-Waxman Act recognizes the importance of protecting patents by ensuring that the pioneer drug manufacturer, i.e., the NDA-holder¹⁸ is notified and may sue for infringement when a generic manufacturer applies for FDA approval (ANDA)¹⁹. If the innovator files for a patent-infringement suit in response to the generic application he/she is then granted either an *automatic* thirty-month stay of *generic FDA approval* or a stay until the patent dispute is resolved²⁰.*

Manufacturers of brand-name drugs in the US have been accused of abusing this provision of the act through filing “sham” patent-infringement suits aimed to trigger the automatic stay period²¹.

III.1.2. Collusive Settlement Agreements to Prevent Generic Entry in the US

Delaying tactics also included collusive agreements entered into by brand-name and generic manufacturers in the USA²². The general pattern of such “pay for delay/stay” agreements involves a brand-name manufacturer paying an ANDA applicant in exchange for the *generic’s agreement to refrain from coming to market*. These agreements were

¹⁸ The pioneer manufacturer applies for a “New Drug Application” approval, and is therefore an NDA-holder.

¹⁹ When a generic manufacturer applies for FDA approval, he/she may follow an abbreviated procedure called an ANDA – “Abbreviated New Drug Application”, which will be elaborated upon hereafter.

²⁰ See 21 U.S.C.S § 355(j)(5)(B)(iii) (Law. Co-op. 2002)

²¹ A notable case in this context is that of *Walker Process Equip., Inc. v. Food Mach. & Chem. Corp.*, 382 U.S. 172 (1965), in which it was established that enforcement of fraudulently obtained patent by means of groundless infringement litigation exposes patentee to liability under Section 2 of Sherman Act.

²² Usually at the stage of the generic application for the ANDA.

seen by the Federal Trade Commission (FTC), consumers, and pharmaceutical competitors as damaging competition by means of delaying generic market entry²³.

The Hatch-Waxman Act awards the *first* generic manufacturer to follow the Paragraph IV track a *180-day exclusivity period*, in which the FDA may not approve the ANDA of a subsequent generic applicant²⁴. The act provided that the exclusivity period began either on the date of the first commercial marketing of the generic or the date of a “court decision”²⁵ declaring the patent invalid or not infringed, whichever was sooner²⁶. Yet the exclusion agreements were usually concluded *before* a court decision regarding the infringement, and *stalled* the first day of marketing of the generic drug. They thus allowed brand-name companies and first generic applicants to reach agreements “parking” the first generic applicant’s exclusivity period²⁷ and holding up the approval of *subsequent* ANDAs. These agreements therefore reveal an example of *generic manufacturers* delaying generic entry along with the brand manufacturers²⁸.

²³ See *supra* note 16, at pg. 11.

²⁴ 21 U.S.C.S. § 355(j)(5)(B)(iv) (Law. Co-op. 2002) – Consequently, the new generic product competes with only the brand-name manufacturer for 180 days.

²⁵ The meaning of the statutory term “court decision” has caused particular difficulty in determining when the exclusivity term began.

²⁶ *Id.* However, provisions of the Hatch-Waxman Act relating to the 180-day exclusivity period have been amended by the Medicare Prescription Drug and Modernization Act of 2003, as will be discussed in further chapters.

²⁷ See *supra* note 16, pg. 10. This matter will be further elaborated upon in the next chapters, discussing case law in the USA.

²⁸ In the EU context, Tom McKillop, chief executive of AstraZeneca, argued with regards to the generics industry, that it is not always the innocent *victim* of anticompetitive practices. “*The generic boys are all lily white,*” he said with heavy irony. “*They're all in it for Joe Public.*” David Pilling and Richard Wolffe, “*Drug Abuses: as Pharmaceutical Companies Go to Extraordinary Lengths to Protect Expiring Patents, Regulators Are Starting to Pay Close Attention. Comment and Analysis*”, Financial Times, 20 April, 2000.

III.1.3. Regulatory Abuse both in the EU and the US

III.1.3.1. In the U.S. – Orange Book Listings of Frivolous Patents and the Trigger of the Thirty-Month Stay

The name of the patent owner, number, and the date in which it expires are listed by the FDA in the *Approved Drug Product with Therapeutic Equivalence Evaluations* publication, commonly known as the “Orange Book”²⁹. When a generic applicant submits an Abbreviated New Drug Application (ANDA), allowing him/her to enjoy from an expedited process of review and rely on the clinical data of the pioneer-manufacturer, he/she must check all patents claimed by the innovator or NDA-holder that are listed in the Orange Book and must certify that its generic drug will not infringe them or that the listed patents are invalid or unenforceable³⁰.

This provision has enticed innovators to list with the FDA *patents that may not properly claim the patent in question*. For instance, some brand-name drug companies in the USA file what is known as “*submarine*” *patents*: an additional patent covering other elements of the drug different from the original active ingredient approved³¹. Others have

²⁹ Ctr. for Drug Evaluation & Research, Food & Drug Administration, *Approved Drug Products with Therapeutic Equivalence Evaluations available at: <http://www.fda.gov/cder/ob/docs/preface/ecpreface.htm>*. 21 U.S.C.S. § 355(b)(1) (Law. Co-op. 2002).

³⁰ 21 U.S.C.S § 355(j) (Law. Co-op. 2002).

³¹ SmithKline won its extension on Augmentin, first launched in 1981, by filing an additional patent covering an element (including an acid that stops amoxicillin degrading) different from the active ingredient for which it was first approved a patent (amoxicillin, the active ingredient of Augmentin) – before its original protection on amoxicillin expired.

listed "*cleaned-up*" versions of old drugs, called 'single isomers'³². Branded companies enjoy the benefit of sales' representatives and advertising budgets "trumpeting" even the most marginal advantages. Crucially, the "new molecule" is treated as a separate drug, with an entirely new patent life³³.

The improper listing of patents based on the Hatch-Waxman Act, allowed innovators to stack *successive* thirty-month stays triggered by filing patent-infringement suits for every 'new' patent listed. The provision allowing for consecutive stays, however, has since changed.

III.1.3.2. In the E.U. – Withdrawal of "Reference Product" from Market Before Patent Expires and Obtaining Frivolous Patents

In Europe, too, a similar strategy was being employed by brand companies, notwithstanding the different regulatory schemes. According to Article 10 of Directive 2004/27/EC³⁴, a generic applying for approval does not need to furnish an entire dossier

³² Most drug molecules can exist in two mirror-image forms, only one of which is active. New techniques have been developed to discard the non-active (and possibly harmful) component, enabling drug companies to demonstrate greater potency or fewer side-effects, yet without bringing a significant change to the drug itself.

³³ This strategy has generated a launch of a large number of single-isomer versions of medicines that might otherwise have been expired. These include Prozac Jr., a single-isomer version of Losec called Nexium, and desloratadine, the single-isomer offspring of Claritin.

See *supra* note 27, David Pilling and Richard Wolfe, Article in Financial Times.

³⁴ 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. OJ C 75 E, 26.3.2002, p. 216 and OJ C (not yet published in the Official Journal).

Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use. Official Journal L – 311, 28/11/2004, p. 67 – 128.

of data on safety and efficacy, but rather it has to prove “bio-equivalence” with the original branded medicine known as the “reference” product³⁵.

Pharmaceutical companies, however, have taken to withdrawing the reference product from the market shortly before its patent expiry and replacing it with what may be a ‘new and improved version’ of the drug – such as a *capsule form, instead of a tablet*. If the generic manufacturer then sought regulatory clearance for its product it ran the risk of rejection because there was no longer a marketed reference-product with which to compare its medicine.

Such was the case of AstraZeneca: according to the European Commission, AstraZeneca misused regulatory procedures by withdrawing marketing authorizations for the *capsule* form of its successful drug and replacing them with marketing authorizations for a *tablet* form³⁶. This inhibited generic entry, as *the withdrawal of a marketing authorization* within the MS in which the generic sought approval, *prevented generic applications from being assessed within the abridged procedure*³⁷ under the former regulatory EU pharmaceutical regime³⁸.

³⁵ This is referred to as the “Abridged Procedure” which is equivalent to the US “Abbreviated Procedure”.

³⁶ *Id.* 4.

³⁷ The European Commission's *AstraZeneca* decision of 15 June 2005 found that AstraZeneca committed another regulatory abuse, by *providing misleading information to national patent offices in applications for supplementary protection certificates (SPCs)*, which enabled it to delay generic entry to its product market. *Id.* 3.

³⁸ Currently, under Article 10 of Directive 2004/27/EC, the abridged procedure will apply even if the reference medicinal product was not authorized in the Member State in which the application for the generic medicinal product is submitted, but rather in another Member State within the European Community. However, the *AstraZeneca* decision refers to Directive 65/65/EEC, as amended, since that was the Directive applicable at the time of the behavior examined in the case.

This form of improper procurement of patents such as the filing of “frivolous” patents or Incrementally Modified Drugs (“IMDs”) often covering spurious innovations such as the *shape or color of a pill*, seems to take place both in the USA and in the EU. In this manner, brand-name drug companies may file not just one patent on their drugs, but a series of them throughout the life of the first patent.

Some consequently argue that “stretching” the privileged time awarded legally by the patent³⁹ through the usage of a variety of ‘stratagems’ is the most innovative activity of today’s drug companies⁴⁰.

Evidence suggests of additional tactics less commonly used by pharmaceutical manufacturers to curb generic competition, which are beyond the scope of this paper. Those include, *inter alia*, instituting a strict test requirement prior to patent expiry by brand-name manufacturers⁴¹, testing the drugs on children in order to obtain six more months of patent protection whether the drugs are meant to be used by children or not⁴², fixing prices of generic versions of drugs by both generic and brand-name drug companies⁴³ or blocking generic manufacturers from access to the material source of

³⁹ Through the approval of the patent either by the FDA or the European Medicines Agency (EMA) and competent Member States’ patent offices.

The EMA was formerly known as the “Agency for the Evaluation of Medicinal Products” and its name has been recently modified by Regulation (EC) No 726/2004 of the European Parliament and of the Council, of 31 March 2004 into “*the European Medicines Agency*”, in order to ‘simplify’ it.

⁴⁰ See *supra* note 11.

⁴¹ Chain Pharmacy, Category News, “*Generic Accutane Faces Potential Delays*”, March 25, 2002; 24, 4, pg. 49. Before losing patent protection, Roche instituted a strict pregnancy test requirement to prevent pregnant women from taking Accutane. Roche’s move is viewed by some as an attempt to retain the last of Accutane’s profits by delaying generic entries.

⁴² Both the USA and the EU award a period of patent exclusivity in the case of clinical testing on children.

⁴³ Two senior executives of Goldshield Group plc. were arrested on March 28, 2005, on suspicion of fixing the price of generic drugs. Wilmer Cutler Pickering Hale and Dorr LLP, Pharmabulletin, Issue 2, Summer 2005.

production of the drug⁴⁴. The FTC suspects anticompetitive conduct may have been also carried out in the case of “authorized generics” – generics introduced by the *brand-name manufacturer* usually at the time the first independent generic intends to enter the market. Another conduct addressed by the FTC is that of exploitation of citizen petitions in the US, intended to signal to the FDA of potential problems of a product prior to its marketing, used to delay generic entry by pioneer drug makers⁴⁵.

⁴⁴ “Barr Settles with Invamed, Apoteco; Litigation Over Warfarin Sodium Ended”, *Pharmaceutical Law & Industry*, Vol. 4 No 24, June 16, 2006, pg. 712.

⁴⁵ The FTC is set to conduct a study regarding “authorized generics” – using its 6(b) subpoena authority, which is expected to be completed by the year 2007. Press Release, Federal Trade Commission, FTC Proposes Study of Competitive Impacts of Authorized Generic Drugs (Mar. 29, 2006), available at <http://www.ftc.gov/opa/2006/03/authgenerics.htm>.

III.2. The Different Pharmaceutical, Patent and Antitrust Legislation in the EU and the USA

III.2.1. The Legal Framework in the USA

Defining questions that are related to the behavior of pharmaceutical companies requires an understanding of the role of government regulation of the industry.

R&D investments and the marketing of pharmaceuticals are heavily regulated by the FDA. Under the Federal Food Drug Cosmetic Act (FFDCA)⁴⁶, any person seeking to market a new drug must first obtain FDA approval by filing a New Drug Application (NDA) establishing the drug is safe and effective for its intended use⁴⁷.

IP law also significantly influences the pharmaceutical industry. Studies have proven that the industry is heavily dependent on patent laws to justify investment in R&D⁴⁸.

In 1984, the US Congress amended the FFDCA, and passed the Hatch-Waxman Act⁴⁹ aimed to *strike a balance between generic and brand-drug manufacturers' interests*. On the one hand, it enabled to bring generics into the market more quickly⁵⁰

⁴⁶ 21 U.S.C.S. § § 301-397 (Law. Co-op. 2002).

⁴⁷ *Id.* § 355.

⁴⁸ Richard C. Levin, Testimony Before FTC/DOJ Joint Hearings on Competition and Intellectual Property Law (Feb. 6, 2002), *available at*:

<http://www.ftc.gov/os/comments/intelpropertycomments/levinrichardc.htm>

⁴⁹ The Hatch-Waxman Act is known after its sponsors – Senator Orrin Hatch (R-Utah) and Representative Henry Waxman (D-Cal).

⁵⁰ Title I of the Act aimed to “*make available more low cost generic drugs* by establishing a generic drug approval procedure for pioneer drugs first approved after 1962.” H.R. Rep. No. 857 (Part I), 98th Cong., 2d Sess. At 14 (1984).

See Roche Products, Inc. v. Bolar Pharm. Co., Inc., 733 F.2d 858 (Fed. Cir. 1984) explaining Section 505 of the FFDCA, ch. 675, 52 Stat. 1052 (1938)) and referring to the Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780). *See* G. Mossinghoff, “*Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*”, Food and Drug Law Journal, Vol. 54, pg. 188-194.

while on the other hand it allowed the pioneer manufacturers to be compensated for the patent-protection term lost during the long FDA approval process⁵¹.

Title I of the Act specifically authorizes an abbreviated procedure (ANDAs), allowing the generic applicant to take advantage of the NDA-holder's time and expenses⁵². An ANDA applicant must show that its proposed generic product has, *inter alia*, the same active ingredient as the brand drug⁵³. Because the ANDA process may be conducted *while the patent for the brand product is still in force*, he may obtain FDA approval and commercially market its product the moment the patent expires. This provision, referred to as the Bolar Amendment, allows the generics a *unique exception to the patent laws*⁵⁴, or a 'safe harbor' against patent infringement⁵⁵.

It may thus be noted that the *balance sought between the dynamic and static efficiencies within the Hatch-Waxman Act* has awarded advantages to both generic and pioneer manufacturers, yet it also caused it to be extremely complex, with loopholes allowing for the very delaying tactics mentioned above.

Evidence shows nonetheless that the act has been *successful in improving generic competition*, to the point that some argue that the vigorous generic drug industry owes its very existence to it⁵⁶.

⁵¹ For term restoration the pioneer manufacturer received an extension term equal to *half* the time of the investigational new drug (IND) period, yet the maximum extension period is 5 years and the total market exclusivity time can't exceed 14 years. The patent term restoration part of the Act appears in title 35 of the *United States Code*.

⁵² 21 U.S.C.S. § 355(j) (Law. Co-op. 1998 & Supp. 2004)

⁵³ Generics typically contain the same active ingredient yet not necessarily the same inactive ingredients as the pioneer drug.

⁵⁴ 35 U.S.C.S. § 271 (a) (Law. Co-op. 2004) – Patent Law provides that “whoever without authority makes, uses or sells any patented invention, within the United States during the term of the patent therefore, infringes the patent”.

The famous case of *Roche Products v. Bolar Pharmaceuticals* was reversed specifically in Section 271(e)(1) of title 35 of the United States Code.

⁵⁵ 35 U.S.C.S. § 271(e)(1) (Law. Co-op. 2000 & Supp. 2004).

⁵⁶ *Id.* 33.

Partially due to the display of delaying tactics, but also because of other forms of abuse of its provisions, there were calls for a substantial reform to the Hatch-Waxman act⁵⁷, one which was finally carried out by the Medicare Act⁵⁸.

The Medicare Act succeeded in amending the provisions of Hatch-Waxman which contributed to the most costly and substantial generic delays, while making an effort not to encroach the patentees' rights⁵⁹. Thus, the act established that collusive agreements which affect the marketing of the generic drug or the 180-day exclusivity period *must be filed with the FTC and the US Department of Justice*⁶⁰. The problem of successive thirty-month stays was solved by establishing *one stay per ANDA applicant*. The new law is more specific regarding the event that triggers the 180-day exclusivity period⁶¹ and operates on a “use it or lose it” premise, requiring the first ANDA filer to use the 180-day period within certain time constraints or forfeit it⁶².

Although earlier proposals for revising Hatch-Waxman called to grant *a private cause of action for delisting patents from the Orange Book* as a manner to solve improper filing of false patents – the Medicare allows a delisting claim to be only a *counterclaim*

⁵⁷ The Boston Consulting Group, “*Sustaining Innovation in U.S. Pharmaceuticals, Intellectual Property Protection & the Role of Patents*” (Jan. 1996).

⁵⁸ The Medicare Prescription Drug and Modernization Act of 2003. Pub. L. No. 108-173, Title XI, § § 1101, 1102 (codified as amended at 21 U.S.C. 355 (j)(2) and (5) (2004)).

⁵⁹ The FTC Study investigating the behavior of drug manufacturers and its recommendations (See *supra* note 16) served as the basis for the changes that were signed into law by U.S. President George W. Bush on December 8, 2003, as Title XI of the Medicare Act.

⁶⁰ Medicare Act, Pub. L. No. 108-173, §§ 1112-1113, 117 Stat, 2066 (2004), The Act amends Section 505(j) of the FDCA (21 U.S.C.S, 355(j)). See also <http://www.ftc.gov/os/2004/01/040106pharmrules.pdf> (last visited Sept. 16, 2004).

⁶¹ The FTC Study recommendation was adopted into the Medicare Law, clarifying that “commercial marketing” includes the first generic applicant’s marketing of the brand-name product. See *supra* note 16, pg. 11.

⁶² Thus, the ANDA applicant must market its product within 75 days after final FDA approval or thirty months after submission of its ANDA, whichever is earlier. See 21 U.S.C.S, § 355a)(5)(D) (Law Co-op, 2004).

and does not permit recovery of damages by the generic applicant⁶³. However, the new law allows for generic applicants to seek patent certainty through a declaratory judgment, as long as neither the NDA-holder nor the patent-owner files an infringement suit⁶⁴.

The Sherman Act must also be considered in matters of *pharmaceutical competition*, in the examination of whether conduct delaying generic entry yields “anticompetitive effects” under Section 1 of Act⁶⁵, or the creation or maintenance of “monopoly power” under Section 2 of the Act⁶⁶. Proving these threshold elements of antitrust claims requires, *inter alia*, to define the relevant pharmaceutical product market⁶⁷ and establish whether the conduct is to be subject to the “per-se illegal” rule or to the “rule of reason”⁶⁸.

⁶³ Medicare Act, *supra* note 47, § 1101. Nonetheless, the provision doesn’t prevent a generic’s ability to collect antitrust damages for improper Orange Book listing.

⁶⁴ This provision may be less effective, unless the generic obtains an assurance from the NDA-holder or patent-owner that they will sue for infringement, which will estop them later on from filing suit.

at <http://world.std.com/~goldberg/hr1confrpt.html> (last visited Jan. 16, 2004),

⁶⁵ 15 U.S.C. § 1 (2000).

⁶⁶ *Id.* § 2.

⁶⁷ M.H. Morse, “*Product Market Definition in the Pharmaceutical in the Pharmaceutical Industry*”, *Antitrust Law Journal*, Vol. 71, pg. 633-676.

⁶⁸ Courts differed on whether the agreements entered into by branded and generic manufacturers retarding generic entry should be subject to the per se rule or not.

III.2.2. The Legal Framework in the EU

The first EU pharmaceutical directive, Directive 65/65/EEC⁶⁹ stemmed from determination to maintain a high level of protection of public health⁷⁰. A decade later, two landmark Directives, 75/318/EEC⁷¹ and 75/319/EEC⁷² introduced the procedure of *mutual recognition* of MS of their respective national marketing-authorizations. These two directives were in line with the 1957 Treaty of Rome providing for the free movement of goods⁷³.

A new European system for authorizing drugs was adopted in January 1995, offering a “centralized” procedure, with applications made directly to the EMEA⁷⁴, leading to the grant of an authorization by the European Commission⁷⁵ and a “Mutual Recognition” procedure, applicable to the majority of conventional drugs⁷⁶.

Directive 87/21/EEC which amended Directive 65/65 established in its Article 4 that an undertaking may use an *abridged procedure after a period of six to ten years*, to

⁶⁹ Directive 65/65/EEC of the Council of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ No 022, 09/02/1965 p. 0369-0373).

⁷⁰ Since the Treaties of Maastricht and Amsterdam, the legal basis for Community health policy is laid down in articles 95, 152-153 of the EC Treaty.

⁷¹ OJ No L 147, 09/06/1975 p. 0001-0012.

⁷² OJ No L 147, 09/06/1975 p. 0013-0022.

⁷³ Pharmaceuticals in the European Union, Report of European Commission, Enterprise Directorate-General, available at dg3.eudra.org/F2/pharmacos/docs/brochure/pharmaeu.pdf.

⁷⁴ See *Supra note 38* with regards to the name change of the EMEA.

⁷⁵ The centralized procedure is laid down in Council Regulation (EEC) No 2309/93, Official Journal No L 214, 24/08/1993 p. 0001-0002), as amended by Council Regulation (EEC) No 649/98 (OJ L 88, 24.3.1998, pg. 7) and Directive 93/41/EEC (Official Journal No L 214, 24.08.1993 p. 40).

See E. Liikanen, “Changes to the European Union Pharmaceutical Legislation: Implications of the ‘Pharma Review’ for Biotechnology Companies”, Journal of Commercial Biotechnology, Vol. 11, No. 1, pg. 38-43, October 2004.

⁷⁶ The Mutual Recognition Procedure is laid down in Council Directive 93/39/EEC (OJ L 015, 17.1.1987, p. 0038-0041), in accordance (and amending) with Council Directives 65/65/EEC, 75/318/EEC and 75/319/EEC in respect of medicinal products.

obtain a marketing authorization for a generic product “*essentially similar*” to the original product approved⁷⁷. *The simplified procedure strikes a balance between the interests of innovative and generic producers*, by relieving generic applicants from the repetition of tests unless absolutely necessary⁷⁸, yet by authorizing a generic *only after the innovator has enjoyed a period of data exclusivity*⁷⁹.

Between 2004 and 2005, a global revision of the regulatory framework for medicines, the ‘Pharma Review’, has been adopted by Europe⁸⁰, responding to calls for the enhancement of generic competition⁸¹ in the EU vis-à-vis the USA and the striking of a better dynamic-static efficiencies’ balance.

The primary modifications entailed the replacement of the former reliance on the “*essentially similar*” test with a codified definition of “generic product”, as a product having the same active substance and being ‘bioequivalent’ to the original⁸².

Furthermore, the data-protection period granted to the pioneer manufacturers was *reduced* from a ten-year period to an *eight-year period* of protection. In order to

⁷⁷ Council Directive 87/21/EEC of 22 December 1986, amending Council Directive 65/65/EEC of 26 January 1965 on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 1987 L 15, p. 36).

⁷⁸ Fourth recital in the preamble to Directive 87/21/EEC.

⁷⁹ Second recital in the preamble to Directive 87/21/EEC.

⁸⁰ Proposal for a Regulation of the European Parliament and of the Council 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 (2001/0252/COD) + Proposal for a Directive of the European Parliament and of the Council Amending Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use (2001/0253/COD).

⁸¹ Wilmer Cutler Pickering Hale and Dorr LLP, Pharmabulletin, Spring 2005: “*The European Parliaments stated in 1996 that in order for the EU to remain competitive in the expanding European and international non-proprietary markets, measures should be introduced at the EU level permitting generic pharmaceutical companies to initiate experiments...prior to patent and supplementary protection certificate expiration, although the marketing of their products should not be permitted until after this date*”.

K. Gopal, “Generics Grumble”, Pharmaceutical Executive, Dec 2000, Vol. 20, pg. 26: “We are in the absurd situation in Europe of importing generics in new areas”, said Greg Perry, director of EGA.

⁸² Article 10 2(b) of Directive 2004/27/EC on the Community Code Relating to Medicinal Products for Human Use, defines “*generic medicinal product*” + “*bioequivalence*” (See *supra* note 19 for reference).

compensate brand-manufacturers for this reduction, it was established that the *marketing* of a generic will not be allowed until *ten years* from the initial authorization of the reference product. Additionally, there is an option for the data-protection period to be extended to a maximum of 11 years if, during the eight years of data exclusivity, the brand-manufacturer is approved a *new therapeutic indication* held to bring a *significant clinical benefit*⁸³. The purpose of this provision is to reward R&D on existing molecules, whose potential may not be fully exploited.

The reformed legislation⁸⁴ therefore tries to strike a ‘new and improved’ balance, allowing the generics to enjoy the important Bolar provision in the EU scheme for the first time – several years after its introduction in the USA, Japan and Canada⁸⁵, yet at the same time offsetting this ‘exception to the patent’ with enhanced protection of patented-drugs’ data⁸⁶ prior to generic entry.

Further EU legislation relevant to antitrust issues within the pharmaceutical industry are Articles 81 and 82 of the EC Treaty⁸⁷. Article 81 prohibits agreements and concerted practices which may affect trade between MS and have as their object or effect the restriction of competition within the EU, whereas Article 82 prohibits any abuse of a dominant position within the EU, insofar as it affects trade between MS.

⁸³ Article 14(11) of Regulation (EC) No 726/2004 (see *supra* note 76 for reference).

⁸⁴ An agreement with the European Parliament with regards to the ‘Pharma Review’ was reached on 17th December, 2003, and was formally adopted by the Council of the European Union on 11th March, 2004. See EuractivNews, “*Landmark agreement on reform of EU pharmaceutical legislation*” and European Commission’s press release IP/03/1771, 18th December, 2003 and 2570th Council Meeting, Competitiveness (Internal Market, Industry and Research) Brussels, 11th March, 2004 (C/04/62). See EuractivNews, “*Council adopts a new fees scheme for registration of medicines*”, 17 November 2005.

⁸⁵ Other countries also allow for the Bolar exception, such as Israel, that provides for it in its Patent Law.

⁸⁶ Another important revision is that which allows a generic producer to apply for an abridged procedure in the EU even in a MS where the reference product either did not receive a marketing authorization or the authorization was withdrawn, Article 10(1) of Directive 2004/27/EC.

⁸⁷ Ex Article 85 and 86 of the Treaty establishing the European Community.

III.3. Pharmaceutical Antitrust Case-law in the EU and the USA

The practice of hindering generic entry has recently taken on increased importance from a US case-law perspective, particularly in light of substantial court cases that the FTC has taken an interest in, as well as private suits submitted by direct purchasers, third-party payors and consumers.

Conversely, in the EU sphere, much less case-law explicitly relating to generic entry may be found, albeit other issues of competition in the pharmaceutical industry such as the integrity of the European common market and parallel trade were addressed.

III.4. The Strike of the Balance Within US Case-law

In view of the fact that US case-law pertaining to this topic is abundant, it will be beyond the scope of this paper to cover it all. The relevant case-law discusses mainly whether the conduct on part of the drug manufacturers comprises a violation of Article 1 or Article 2 of the Sherman Act, examining the different inter-related threshold elements for the establishment of violation. The analysis of these elements was controversial and has an economic and EU-comparative bearing, yet *its main underlying question is that of the dynamic-static balance.*

The US appellate courts disagreed on whether the delaying tactic of collusive agreements entered into by branded and generic manufacturers should be subject to the

‘rule of reason’ or the ‘per-se illegal’ rule. The different approaches taken by the Sixth and Eleventh Circuits illustrate the tension between the dynamic and static-efficiency approaches.

*In re Cardizem CD Antitrust Litigation*⁸⁸, the brand-name manufacturer, HMRI⁸⁹, entered into a “pay for stay” agreement with the first generic applicant, Andrx, after suing it for patent infringement and triggering the thirty-month stay period. The second generic company to apply for an ANDA, Biovail, was not sued by HMRI, yet its FDA approval was held up due to the stay. Biovail then sued Andrx for the agreement it entered into, which prohibited Andrx from selling its generic product and from transferring the 180-day market exclusivity period. While the district court dismissed Biovail’s claim, for failing to establish the causal connection between its injury and anticompetitive behavior, the Court of Appeals established that the agreement *strongly suggests anticompetitive and rent-preserving effects*. In a private suit brought by direct and indirect purchasers of the branded product⁹⁰, the Court of Appeals for the Sixth Circuit held that the agreement *was illegal per se* because it amounted to *a horizontal market allocation agreement eliminating competition for the product*.

Conversely, in the case of *Valley Drug v. Geneva Pharmaceuticals Inc.*⁹¹, the Court of Eleventh Circuit rejected the per se analysis, holding that *such an analysis is inappropriate in agreements involving patent litigation*. In this case, Abbott initially sued both Zenith and Geneva following ANDA applications for approval of their generic version, yet subsequently entered into agreements with both companies, in which both

⁸⁸ *In Andrx Pharmaceuticals, Inc. v. Biovail Corp.*, 256 F.3d 799 (D.C. Cir. 2001).

⁸⁹ Hoechst, Marion, Roussel, Inc.

⁹⁰ *In re Cardizem CD Antitrust Litigation*, 332 F.3d 896 (6th Cir. 2003).

⁹¹ *Valley Drug v. Geneva Pharm., Inc.* 344 F.3d 1294 (11th Cir. 2003).

agreed not to sell their generic products or their 180-day exclusivity period. The district court established that Abbott, Geneva, and Zenith were horizontal competitors who conspired to allocate the entire market of the branded product, relying also on the fact that the Abbott patents were eventually held invalid. However, the Court of Appeals for the Eleventh Circuit rejected that conclusion stating that “*exposing the parties to antitrust liability for the exclusionary effects of a settlement reasonably within the scope of the patent merely because the patent is subsequently declared invalid would undermine the patent incentives*”⁹². The Court therefore objected to the per-se antitrust analysis solely on the basis of such payments.

The FTC has taken an active role in cases of alleged Hatch-Waxman abuse⁹³, yet two FTC actions, with distinct outcomes, demonstrate together with the above Appellate Court decisions, what may lead to *legal uncertainty* in the matter of settlement agreements.

In the case of *Abbott Labs*⁹⁴, Geneva agreed not to enter the brand-drug market of Abbott until either the patent infringement-suit against it was resolved or another generic manufacturer entered. It also agreed not to transfer its 180-day market exclusivity rights.

⁹² *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 261 F. Supp. 2d 188, 249 (H.D.N.Y. 2003).

⁹³ *See, e.g.*, Federal Trade Commission, Petition for a Writ of Certiorari, *FTC v. Schering-Plough Corp.*, No. 05-273 (June 26, 2006) (denying cert. petition); *Schering-Plough Corp. v. F.T.C.*, 402 F.3d 1056 (11th Cir. 2005); *Schering-Plough Corp.*, No. 9297, 2003 WL 22989651 (F.T.C.) (Dec. 8, 2003) (Commission decision and final order); *Schering-Plough Corp., Upsher-Smith Labs., and American Home Products Corp.*, Dkt. No. 9297 (Apr. 5, 2002) (consent order as to American Home Products); *FTC v. Perrigo and Alparma*, Civ. Action No. 1:04CV01397 (D.D.C. Aug. 12, 2004) (stipulated judgment); *Bristol-Myers Squibb Co.*, Dkt. No. C-4076 (Apr. 13, 2003) (consent order); *Biovail Corp. and Elan Corp. PLC*, Dkt. No. C-4057 (Aug. 20, 2002) (consent order); *Biovail Corp.*, Dkt. No. C-4060 (Oct. 4, 2002) (consent order); *Abbott Labs.*, Dkt. No. C-3945 (May 26, 2002) (consent order); *Geneva Pharms., Inc.*, Dkt. No. C-3946 (May 22, 2000); *Hoechst Marion Roussel, Inc.*, Dkt. No. 9293 (Apr. 4, 2001) (consent order); *FTC v. Mylan Labs., Inc. et al.*, 62 F. Supp. 2d 25 (D.D.C. 1999).

⁹⁴ *E.g.*, Abbott Laboratories, No. C-3945 available at: <http://www.ftc.gov/os/2000/05/c3945complaint.htm>; Geneva Pharm., Inc., No. C-3946, available at: <http://www.ftc.gov/os/2000/05/c3946complaint.htm>; Hoechst Marion Roussel, Inc., No. 9293, available at: <http://www.ftc.gov/os/2000/03/hoechstandrxcplaint.htm>; Schering-Plough Corp., No. 9297, available at: <http://www.ftc.gov/os/2001/04/scheringpart3cmp.pdf>.

For Geneva, therefore, the agreement was the optimal answer because it was assured a risk-free payment until litigation was resolved, while preserving its rights to enjoy the 180-day exclusivity period. According to the FTC's complaint, "*the agreement was not justified by any countervailing efficiency*" and imposed restraints *beyond what would be available in a court-ordered preliminary injunction*. Ultimately, the FTC investigation led to a consent order which barred the parties from entering into similar agreements in the future.

Under similar circumstances, the Schering-Plough case resulted in considerably different outcomes for the FTC investigation. The case is still pending a Supreme Court certiorari⁹⁵ to review the proceeding in the US, and seems to raise genuine concerns among FTC officials⁹⁶. The FTC contended that Schering-Plough conspired with generic manufacturers to keep a generic version of its drug from entering the market. In June, 2002, the administrative law judge dismissed the FTC's complaint, finding that *there was insufficient evidence to conclude that the payment involved was for delaying market entry of the generic product*.

In December, 2003, however, the Commission overturned the decision of the administrative law judge, finding that the settlement agreement constituted unfair competition⁹⁷.

⁹⁵ Schering-Plough Corp., No. 9297 2003 WL 22989651 (F.T.C. Dec. 8, 2003), vacated, Schering-Plough Corp. v. FTC, 402 F.3d 1056 (11th Cir. 2005), petition for cert filed (Aug. 29, 2005) (No. 05-273), available at: <http://www.ftc.gov/os/2005/08/050829scheringploughpet.pdf> (last accessed July 25, 2006).

⁹⁶ See "Exclusion Payments to Settle Pharmaceutical Patent Cases: They're B-a-a-a-ck!, The Role of the Commission, Congress, and the Courts", available at: <http://www.ftc.gov/speeches/leibowitz/060424PharmaSpeechACI.pdf> (last accessed July 25, 2006).

⁹⁷ See Schering-Plough Corp., No. 9297 (F.T.C. Dec. 18, 2003) final order, available at: <http://www.ftc.gov/os/adjpro/d9297/031218finalorder.pdf>, (last accessed July 25, 2006) + opinion of the Commission, available at: <http://www.ftc.gov/os/adjpro/d9297/031218commissionopinion.pdf> (last accessed July 25, 2006).

Schering and Upsher followed by appealing the case to the Eleventh Circuit Court of Appeals, which on March 8, 2005, issued a decision in the matter reversing the Commission's ruling. In response, the FTC filed on August 29, 2005 a petition for a writ of certiorari with the court, yet on May, 2006, the US Solicitor General submitted an *amicus brief* urging the court to deny said certiorari⁹⁸, alleging that the payments in question were bona fide royalty payments which do not require a categorical condemnation of patent-dispute settlements. The FTC followed by replying on June 12, 2006, in a supplemental brief that "*In its observations on the merits, the United States fails to appreciate the... fundamental inconsistency between such a rule of law and the policies of Congress, as set forth in the Hatch-Waxman Act*"⁹⁹.

FTC Commissioner, Mr. Jon Leibowitz, asserted that he finds a correlation between Schering-Plough and other recent Court decisions and a more de-facto widespread practice of "pay for stay" settlements, to the extent that they "*appear to be the new way to do business*". He further declared that if the Schering-Plough petition for cert will be rejected, the FTC will either look for more appropriate cases which may create a clearer split in the circuits or encourage Congress to change the legislation, as it has done with the Medicare Act.

Thus, in the aforementioned *In re Abbott Labs* case, the Eleventh Circuit Court of Appeals *favored the dynamic efficiency* in its recognition that "pay for stay" agreements

⁹⁸ Solicitor General Brief for the United States as Amicus Curiae: FTC, Petitioner v. Schering-Plough Corporation, et Al., May 17, 2006, available at: <http://www.usdoj.gov/atr/cases/f216300/216358.htm> (last accessed on July 25, 2006).

⁹⁹ Supplemental Brief for the Petitioner, June 12, 2006, available at: <http://www.ftc.gov/os/adjpro/d9297/060612certiorarisupplementalbrief.pdf> (last accessed July 25, 2006). See "FTC's Schering Brief Says Solicitor General Errs in Recommending Court Deny Review", Antitrust, Vol. 4 Number 24, Pg. 697, June 16, 2006.

were no broader than the exclusionary effect awarded by patents, whereas in the *In re Cardizem* case, the Sixth Circuit Court of Appeals *accentuated the static efficiencies*, establishing that there are anticompetitive effects flowing from the “pay for stay” agreements.

The view voiced in recent US case-law, including Leibowitz’s claim regarding the Schering-Plough case, demonstrates *that while the patentee rightfully merits the dynamic right of exclusion, enabling it to recoup its high initial R&D costs and giving it incentives to further innovate – the legal reward does not extend to certain strategies of delay*, which manipulate the legislation in a way not intended by the legislators.

In the case of *Abbott Laboratories v. Teva*¹⁰⁰, for instance, the court asserted that it will *weigh the generic applicants’ anticompetitive harm from changes to the drug against the benefits created by the changes*¹⁰¹. In this case, the patent-owner repeatedly reformulated the patented drug from capsule to tablet form, whilst registering the former formulation as ‘obsolete’ in the National Drug Data File. The court concluded that *the generic manufacturers suffered harm greater than the benefit of the ‘improvement’ to the drugs*¹⁰² and thus preferred the *specific static effects* of the case to the *specific dynamic effects*. The court in fact established that here too the new ‘improvement’ strayed from what may be rightfully claimed under patent law.

¹⁰⁰ See *infra* note 149.

¹⁰¹ The Court chose to adopt the balancing test used by the Court in *United States v. Microsoft Corp.*, 253 F. 3d 24 (D.C. Cir. 2001) and apply the “rule of reason”.

¹⁰² The court established that the reformulation of the drug along with the FDA approval process and pharmacies’ required use of the National Drug Data File did not permit consumer choice of the generic drugs and therefore caused competitive harm to the generic manufacturers.

III.5. Questions rising from Case law in the EU

It is possible that the European Commission will in the future focus its interest on alleged delays of generic entry with the same zealousness that has characterized the US antitrust authorities these last years, despite the considerably different regulatory framework. Yet, due to the particular facts of the AstraZeneca case and the changes in legislation since then¹⁰³, it is unlikely that there will be cases similar to it. It must be noted however, that certain tactics of delay of generic entry, mainly those relating to the procurement of “frivolous” patents, have been challenged in MS’ courts, particularly in the UK¹⁰⁴ as its case-law demonstrated and as will be discussed further on.

The EU case-law regarding the deferral of generic entry involves contexts that are idiosyncratic to the European Community and European Market such as *parallel trade*, the *European price regulation* and *European market integration*. Yet it may be noted that these issues, specifically that of parallel trade, also underline the basic tension between dynamic and static efficiencies within the pharmaceutical industry.

¹⁰³ See supra note 37.

¹⁰⁴ These cases will be discussed hereinafter.

III.5.1. Parallel Trade

Parallel trade (PT) in medicines involves medicinal products genuinely produced under the protection of an IPR¹⁰⁵ which are placed into circulation in one market, and then traded by an intermediary in a second market – without the authorization of the local owner of the IPR¹⁰⁶. IPRs may provide inventors of new medicinal products the legal right to exclude rivals from making, selling and distributing those inventions. A country's law concerning the territorial exhaustion of these rights is therefore an important component of how it regulates and limits their use. The policy used in the EU is that of regional exhaustion, i.e. PT is legal within the EU as well as the EEA¹⁰⁷, but importation from outside this area is disallowed.

The European Court of Justice (ECJ) consistently upheld the view that, under Article 30 of the Treaty of Rome, free circulation of goods takes precedence over IPRs¹⁰⁸. Hence, countries may not use the existence of differential price controls in pharmaceuticals to justify restrictions on PT within the EU¹⁰⁹. An important exception is that if products are placed on the market under a *compulsory license*, they may not be parallel imported¹¹⁰.

However, debate with regards to the costs and benefits of pharmaceutical PT has been ongoing in the EU context and has increased over the past years for a number of reasons, among them the different regulatory regimes among the MS, resulting in significant price differentials and the important place that PT takes in MS'

¹⁰⁵ Namely: a trademark, patent, or copyright.

¹⁰⁶ Keith E. Maskus, "*Parallel Imports in Pharmaceuticals: Implications for Competition and Prices in Developing Countries*", Final Report to World Intellectual Property Organization, April 2001.

¹⁰⁷ States which form part of the European Economic Area, in accordance with the Agreement on the European Economic Area, such as Norway, Iceland and Liechtenstein.

¹⁰⁸ In the case of patents it was *Merck v. Stephar* (C-187/80).

¹⁰⁹ *Merck v. Primetown* (C-267/95 and C-268/95).

¹¹⁰ *Pharmon v. Hoechst* (C-19/84).

pharmaceutical expenditure schemes, particularly MS with high pharmaceutical prices such as the UK, Germany, the Netherlands and Sweden.

Furthermore, PT embodies within it the question of *the proper balance between competition and innovation* or the static versus the dynamic efficiencies. On the one hand it involves MS exercising their legal right and autonomy to determine their own health policies¹¹¹ as well as parallel distributors exercising their legal right embedded in the principle of free movement of goods within the EU. On the other hand, there are the research-based companies, which lose a stake of their sale revenues due to the exportation of their products to a low-priced European state, which *may discourage incentives of development in drug R&D*.

A ban per-se of parallel importation in the EU, however, will not achieve the dynamic effects desired by the research-based industry, because it will not prevent imports of *generic drugs* that impact prices of locally sourced (LS) originals more than parallel imported drugs. This is mainly so because prices of LS drugs are not sensitive to the presence of PT products. One reason for the price-insensitivity is that LS drug manufacturers do not reduce their prices so as not to let PT products pose a threat to their interests – instead, they offer ‘price equalization deals’ to their *own distributors and pharmacists*. Another cause is that PT distributors in the EU are subject to certain *particular pressures* such as the coverage of the market by the distributor, transportation costs, relabelling or repackaging costs and perhaps most significantly – product

¹¹¹ Promotional policies relate to directly encouraging the dispensing of PI products via incentives. Denmark, Germany, the Netherlands, Norway, Sweden and the UK, which are considered to be high-price countries, and therefore significant parallel importers of pharmaceuticals, have such policies in place, *See supra* note 105.

availability. Consequently, it is questionable whether PT leads to downward price convergence over time, and it may be concluded that the effect of price competition from PT is ambiguous¹¹².

Conversely, it is evident from the partition between in-patent and off-patent drugs that generic competition *does indeed lead to a downward price adjustment*. This is compatible with both economic theory and the fact that generic drugs are cheaper than the branded originals, including their parallel imported versions.

A recent research of PT in the EU showed that most of the arguments raised by opponents of PT were correct. Mainly, that PT in drugs may cause *shortages in drugs* in the exporting countries and that the *gains from PT accrue mostly to the distribution chain* rather than to healthcare systems and consumers. Additionally, findings proved that PT, albeit it is a form of arbitrage in the EU, *does not produce statistically significant price competition effects in destination countries*, and leads to a ‘convergence to the top’ rather than ‘a convergence to the bottom’. This is largely due to price regulation in different MS. Finally, it was concluded that *PT erodes the research-based industry’s sales and profits*.

Consequently, it may be claimed that the *price paid by the research-based industry for PT in terms of dynamic efficiencies is significant*, critically so because the EU pharmaceutical industry is competing with other international industries and has already in the past decade increasingly relocated some of its activities from Europe to North America. Furthermore, it may be suggested that in order to raise cost-containment savings accrued by healthcare systems in the EU from PT, an agreement between the

¹¹² There is evidence of product shortages in some countries that parallel-export extensively.

insurance and research-based companies should be reached, in a way that will balance the objectives of health policies and the dynamic efficiencies in terms of R&D investments.

Advocate General Jacobs' opinion in the Syfait case voiced these conclusions and was welcomed by the brand-name drug companies. At the same time, however, these companies were frustrated by the lack of ruling on the matter by the ECJ, which chose not to incorporate AG Jacobs' opinion into its ruling¹¹³.

III.5.2. The AstraZeneca Case

The AstraZeneca case¹¹⁴ is the first and to date the *only case* in which generic delaying tactics were established by the EC to be *a novel type of abuse of Article 82 EC Treaty*, addressing both dominant position abuse and abusive conduct. Furthermore, AstraZeneca represents the first time in which the EC analyzed market definition and dominance in the pharmaceutical industry, outside the merger control context¹¹⁵.

However, the abuses in this case concern not only market access for generic producers but also market access for parallel traded products on a number of EEA markets. The EC eventually fined AstraZeneca for the abuses with a sum of €60 million.

Based on the facts of the case, the violation of Article 82 consisted of two forms of abuse, both of which can be classified as 'regulatory abuse', namely the furnishing of misleading information to national patent offices within the EEA in order to obtain

¹¹³ EuractivNews, "Drug Firms Frustrated by Lack of Ruling on Parallel Trade", 2 June 2005.

¹¹⁴ Commission Decision of June 15, 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).

¹¹⁵ It is important to note that AstraZeneca has appealed the decision to the European Court of First Instance (CFI).

Supplementary Protection Certificates (SPCs) and effectively extend the basic patent protection for AstraZeneca's patented medicine Losec¹¹⁶; and misusing regulatory procedures by switching from capsule to tablet formulations of Losec, thereby withdrawing marketing authorizations from certain EEA markets.

In its decision, the EC emphasized the importance awarded to *static efficiencies*, in the form of the Community pharmaceutical legislation and policy¹¹⁷. The Commission stressed that while the mere possession of a patent or IPR does not, in principle, violate Article 82 – the argument that the acquisition of an SPC cannot constitute an infringement of the article because it relates to an existing IPR – must be rejected¹¹⁸. The Commission clarified that incentives for innovation will not be discouraged by qualifying as abusive misleading representations made in the context of applications for IPRs – or in other words, *the dynamic efficiencies will not be harmed if static abuses are prohibited*.

Albeit the initiative taken by the Commission and the severe stance it has adapted in its decision to practices of generic delay, the Commission's decision raised substantial criticisms¹¹⁹, voicing mainly the concern that this decision will have on the dynamic incentives to innovate.

Thus, it was argued that with this decision, the Commission introduced a new form of abuse of a dominant position that may have overstepped the boundaries of Article

¹¹⁶ On the basis of Council Regulation (EEC) No 1768/92 of 18 June 1992, concerning the creation of Supplementary Protection Certificate for medicinal products.

¹¹⁷ See inter alia the Commission's Communication of 25 November 1998 (COM (98) 588 final) (in particular p. 15) and the Council Conclusions of 29 June 2000 (OJ C 218, 31.7.2000, p. 10).

¹¹⁸ See *supra* note 105, at pg. 159.

¹¹⁹ Sophie Lawrance and Pat Treacy, "The Commission's AstraZeneca decision: delaying generic entry is an abuse of a dominant position".

82. For instance, if AstraZeneca's conduct is compared with the established abuse of *refusing to supply*¹²⁰, the decision would imply that a dominant company is under *an obligation to supply both existing and new customers*, whereas under existing case law, obligations to supply new customers have been imposed only in very unusual circumstances, such as 'essential facilities' cases. These criticisms voice the pioneer companies' concerns regarding possible infringement of their dynamic and innovative incentives.

¹²⁰ The withdrawal of the "Losec" marketing authorization in fact deprived generic competitors of an element they needed to be able to enter the market and it is for that reason that it is compared with an abuse of refusal to supply.

III.5.3. The Syfait Case – the Judgment and Opinion of Advocate General Jacobs

While the AstraZeneca case dealt with imposing barriers to entry to both generic and parallel trade products, the Syfait case discusses trade restrictions with regards to parallel trade alone.

However, *both the Syfait case¹²¹ and the AstraZeneca case are the only cases to recently address the issue of the application of Article 82 to the pharmaceutical sector.*

The Syfait case concerns the supply of three proprietary medicinal products, owned and manufactured by GlaxoSmithKline (GSK), to Greek pharmaceutical wholesalers and their parallel trade in these products. Until November 2000, GSK met in full the orders that it received from the Greek wholesalers – orders which were then mostly exported by the wholesalers to other EU MS where prices were much higher. However, from early November 2000, GSK stopped meeting orders from pharmaceutical wholesalers and started supplying Greek hospitals and pharmacies *directly*. It asserted that the export of the relevant products by wholesalers was leading to *significant shortages* on the Greek market and refused to meet their orders *in full*. It is the latter refusal that formed the subject of proceedings before the Greek Competition Commission, which referred certain questions to the ECJ for a preliminary ruling. In particular, the Greek Commission wished to know whether the refusal constitutes *a per-se abuse* within the meaning of Article 82 in circumstances it is due to GSK's *intention to limit PT*. The resolution of this question was of particular importance because ECJ case-

¹²¹ Case C-53/03, Syfait and others v. GlaxoSmithKline AEEVE, opinion of Advocate General Jacobs, 28 October 2004.

law confirmed that *a dominant undertaking is permitted to take reasonable steps to protect its legitimate commercial interests, provided they are proportionate to the threat and aren't aimed at strengthening or abusing its dominant position*¹²². ECJ case-law specifically held that limitation of PT does not constitute a per-se abusive practice when engaged by an undertaking holding a dominant position. Instead, it would be abusive where the customer concerned has *suffered obvious, immediate and substantial competitive disadvantage*, has been placed at the risk of elimination¹²³, or where *there was no objective justification* for the abuse.

In the Syfait case, both the AG and the Commission, as intervening party, recognized that a refusal to supply aimed at restricting PT does not amount to a *per-se infringement*. However, the Commission argued that an *intention* to limit PT should 'ordinarily' render a refusal to supply abusive. AG Jacobs considered the Commission's view reasonable when 'such conduct is aimed at removing a source of competition in the MS of import' yet not in the case where it is "*rather an inevitable consequence, given the characteristics of the market*", and of GSK's attempt to "*protect what it sees as its legitimate commercial interests*".

Furthermore, the AG considered a refusal to supply *capable of justification* where the price differential giving rise to PT is the result of *government intervention in the states of export* to fix the price there at a lower level than elsewhere in the EU.

AG Jacobs asserted that *certain idiosyncratic characteristics of the pharmaceutical sector must be considered*, among others, the pervasive and diverse state intervention in the pricing of pharmaceutical products, obligations upon pharmaceutical undertakings

¹²² See Case 27/76 United Brands v Commission, Case 85/76 Hoffman-La Roche v Commission and Case 322/81 Michelin v Commission.

¹²³ E.g. Joined cases 6/73 and 7/73, Commercial Solvents v. Commission.

and wholesalers to ensure the availability of adequate stocks of products, *the potentially negative consequences of PT for competition and incentives to innovate* and the fact that end-users of pharmaceutical products do not always benefit from PT. He further maintained that public authorities in EU MS, as the main purchasers of pharmaceutical PT products, cannot be assumed to benefit from lower prices – given that they are themselves responsible for fixing them.

Hence, AG Jacobs concluded that as long as the above conditions are fulfilled, a refusal to supply (in full) *would in principle be justifiable* according to Article 82. However, he emphasized that this justification cannot necessarily be applied to other types of refusal or abuse.

It must be noted that in accordance with ECJ procedure, the AG’s opinion was not binding on the Court, which declared the application by the Greek Commission inadmissible because it was not a “court or tribunal” of a MS, within the meaning of its case-law¹²⁴. Due to the ECJ’s decision, the substance of the case remains unsettled.

It may therefore be observed that AG Jacobs finally favored the *dynamic, research-based efficiencies*. Aside from establishing that *PT may have negative effects on distribution* or may lead to under-supply, the decision *highlighted the potentially negative consequences of PT on incentives to innovate* or on the timely introduction of innovative products in low-priced countries. Jacob’s decision was eventually derived from a cost-benefit analysis determining that the ‘dynamic’ price pharmaceutical companies’ pay for PT should not be greater than the benefits flowing from it.

¹²⁴ Case C-53/03, Syfait and others v. GlaxoSmithKline AEEVE, judgment of 31 May 2005. Only courts and tribunals may refer questions to the ECJ for preliminary ruling.

IV. The Common and Different Economic Aspects Regarding Delay of Generic Entry in the EU and the US

Some of the economic aspects of generic delay are common to the EU and the US contexts while others are unique either to the EU market. The idiosyncratic features of the EU pharmaceutical market lead to a distinct economic analysis of generic delay and to a distinct strike of the balance between the dynamic and static efficiencies.

IV.1. Economic Features of Generics Common to the EU and the US Markets

Generic drugs may usually be marketed at prices lower than those of original brand drugs because *their manufacturers don't have to incur the research, development, and promotional costs normally associated with the creation and marketing of an original product* – costs that are *fixed and sunk*¹²⁵.

The *generic manufacturers also incur fixed costs associated with their entry*, albeit substantially lower than those borne by the pioneer drug manufacturers.

It is noteworthy that the abridged and abbreviated procedures for generics, provided for both in the EU and the US environments, respectively allow for a *large drop in the cost of generic entry* in comparison with previous arrangements and thus facilitate generic access. Relaxation of brand-generic substitution laws or health schemes, both in

¹²⁵ Fixed costs are costs incurred regardless of the quantity of output to be manufactured, i.e. – costs that are not affected by the quantity of units manufactured, whereas variable costs vary depending on the quantity of output.

EU MS and the US, also gave rise to more extensive generic entry *thereby strengthening the static efficiencies* accompanying it.

Yet the application procedures both in the EU and the US still require inspections of the FDA or MS' authorities, obligating the entrant to be ready to make the product, at times by means of purchasing new equipment or bringing it to an operational stage months before it is legally permitted to sell the product. *These expenditures form fixed and sunk costs that the generic firms must pay* in order to have the ability to enter the market.

IV.1.1. Factors Inducing Generic Entry

A generic firm will want to enter the brand-name product market *only if it expects the markup over variable costs and quantity sold to be large enough to cover its fixed costs*¹²⁶. The larger expected profit in the brand product-market to which the generic aspires to enter, the more generic firms will enter. *In equilibrium, the correct number of entrants will enter for the size of expected profits and a zero-profit condition will hold*¹²⁷.

The number of entrants is therefore a function of the expected entry profits:

$$E[N_i] = f(E[\pi])^{128}.$$

¹²⁶ Fiona M. Scott Morton, "Entry Decisions in the Generic Pharmaceutical Industry", RAND Journal of Economics, Vol. 30, No. 3, Autumn 1999, pp. 421-440.

¹²⁷ As economic theory teaches, positive profits in a monopoly/incumbent product market serve as a signal for generics or potential competitors that potential positive profits are also feasible for them, and that the market may also contain them. However, equilibrium represents the point in which entrants don't earn *negative profits* yet neither above-zero profits.

¹²⁸ The number of entrants is denoted by N, whereas entry is denoted by E.

Characteristics of a drug market before the brand's patent expires are significant predictors of generic entry. The revenue of the brand in *the year before patent expiration* was found to be the most important indicator to generic entry. Another feature of the market affecting generic entry is the *size of the brand market*, which is likely to be a *function of both the age of the drug and the period since patent expiry*.

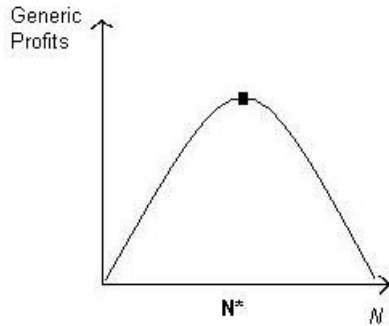
Evidence indicates that the *generic regulatory approval procedure negatively affects the number of generic entrants*, due to expectations to incur costs flowing from it.

Another feature *not yet considered by the literature* that I believe may affect generic entry is the *frequency of use of generic delaying tactics* by the brand company whose product market is entered. Especially in these last decades in which the phenomena prevailed, *the recurrent employment of generic delaying stratagems may serve as a 'signal' negatively affecting the number of generic entrants*. However, this will still depend on the size of the expected profits and the market of the brand. This feature will probably affect generic entry less in the case of a 'blockbuster drug' market – in which expected profits are assumed to cover litigation costs and fixed costs for entry.

The entry function of generics is therefore concave¹²⁹, albeit the fact that the amount of entry as a function of market revenue is positive – due to *additional entrants gradually eroding price-cost margins¹³⁰*.

¹²⁹ For the reasons mentioned above: the number of entrants is inversely related to their predicted profits: the more firms enter – the less profits they are bound to earn.

¹³⁰ The function may be explained in the following way: more generic entrants will enter, therefore as a whole, they will earn more profits – until a certain point in which the profits decline because they apply to *all* the number of entrants, which will be too numerous to sustain the profit potential of the market.



The entry decision is complex, because it is dependent on the number of firms in the market – which affects the *price-cost margin*¹³¹ and the quantity per firm. The decision is therefore made, *given others' entry decisions, representing a prisoner's dilemma*¹³² and a *Nash equilibrium situation*¹³³.

In addition, entrants may enter *simultaneously* and *secretly*, because entry information is kept secret by the regulatory approving bodies, until decision is made.

Generic manufacturers *do not announce their entry decisions* because they do not want to signal to potential competitors that they think a particular market is a good one to enter into, so as not to tempt them to enter. Another reason for *not committing* to an entry decision is that there is no guarantee that approval will be eventually granted. A delay in the approval process may cause the first firm's generic to be approved *after* that of a competitor responding to the announcement. Some entrants, who are "late" in applying, can still withdraw their application when a rival is approved, and thereby save a

¹³¹ The difference between the variable and fixed production costs of the product and the price consumers will pay for it, times the quantity sold.

¹³² A prisoner's dilemma describes a situation, in which cooperation may be more profitable, yet cooperation depends on other's decisions – In this case too, because the generic entrants are unaware of other generic manufacturers' decisions and depend on them – they may benefit from cooperation among them, yet this cooperation is subject to their rivals' compliance with the decisions, albeit breaching may be the dominant strategy: if others keep the decision, breaching (such as pricing the product lower than decided) may grant an advantage in the market and if other rivals don't keep the agreement, breaching is better.

¹³³ Nash equilibrium is a situation in which economic actors interacting with each other choose their best strategy *given* the strategies others have chosen.

significant part of the entry cost. As a result, generic firms *sink entry costs simultaneously*¹³⁴.

The *entrant's estimates of its own rank in the order of entry* as well as its beliefs about *relative costs* it may have to incur, also play a role in entry decisions¹³⁵. *A firm will expect itself to enter a market and others to stay out if its rank order is equal or less than the expected number of entrants, i.e. – if its rank is either last or second-to-last and upwards.*

Entry by a firm is usually an *irreversible decision* in the sense that although an ANDA or abridged procedure requires much less than producing an original pioneer drug, *entry costs are nevertheless significant when there is likely to be strong price competition*¹³⁶.

Consequently, the interrelation between *the number of entrants* and the *concealment of that number*, leads to a *risk to profits from unanticipated excessive entry of competitors*, which may lead to an *unexpected failure of a product* to be profitable.

A pure-strategy Nash equilibrium exists when all entrants earn positive profits and all other non-entrants would not earn a positive profit if they entered. The Nash equilibrium holds that the most profitable N^* entrants enter, where (N^*+1) would already earn a negative profit. This equilibrium maximizes social welfare and may be sustained due

¹³⁴ I.e., pay for the sunk costs – which are costs such as for the purchase of machinery or other fixed costs, which will not necessarily be recovered during the manufacturing process and may depend, inter alia, on the success of the product in the market. The potential of losing these costs is what makes them be regarded as 'sunk'.

¹³⁵ Due to the fact that the generic entry occurs under a veil of secrecy – the generic may not know his rank of entry, given its rivals' positions, in objective terms. It will therefore be his perception of his rank, comparing with the others'.

¹³⁶ An example from the US: the average size of brand markets that attract generic entrance is one of at least \$22 million in annual revenue (data is relevant to 1999; the estimate must be much higher these days), from which generic pharmaceuticals usually capture half of the molecule volume, albeit at prices 30%-50% lower than the brand – i.e., generic annual revenues may be less than \$10 million per year. However, the estimated costs of filing an ANDA is from \$250,000 to \$20 million (the variability is due to substantial heterogeneity of entry costs, depending on the specific drugs and firm-drug combinations).

to the entry costs. Entry costs may differ across markets, yet *those with the lowest fixed costs would enter*, as long as the *cut-off value for the market is higher* than their expected costs of entry¹³⁷.

IV.1.2. The ‘Relevant Market’ Definition

The *relevant market definition* does not differ to a great extent in the EU and the US settings.

Both the US courts and the ECJ and Commission in the EU use evidence of “reasonable interchangeability of use” and “cross elasticity of demand” in order to define a relevant market, with the most widely-used tool being the so-called ‘small but significant non-transitory increase in price’, or SSNIP test.

The courts however also take into account the *specific characteristics of the pharmaceutical market*, inter alia, those that cause for less price-sensitivity and price elasticity of demand.

In the AstraZeneca case the EU Commission based its market definition on the Commission Notice confirming the above SSNIP test, yet *it too emphasized that features specific to the pharmaceutical market* in the EU such as a low degree of involvement by consumers and a high degree of public regulation must be considered.

To date, *therapeutic substitution* has been the most commonly established market definition in the analysis of generic delay cases, both in the US and in the EU.

However, some claim that the relevant market in cases involving delayed generic entry must be *the molecule itself* because of idiosyncratic features of the pharmaceutical

¹³⁷ See *supra* note 219.

industry such as IP protections and the uniqueness of individual patients – which *make cross-price elasticity of demand between drugs within a therapeutic class low*¹³⁸.

Proponents of the generic industry thus argue that by claiming the “*relevant market*” should include all of the “*competing*” drugs in a therapeutic class, research-based manufacturers improperly manipulate a conclusion that *delaying generic entry cannot involve maintenance of market power* – thereby *negatively affecting static efficiencies*.

IV.1.3. Requirements for the Grant of Generic Market Authorizations

The requirements for granting market authorizations for generic products are significantly harmonized between the EU and the US in terms of acceptance of either *abridged* or *abbreviated* marketing applications. Technical requirements for the demonstration of quality, *safety and efficacy* of new medicinal products have also been harmonized between the EU and the US, under the ICH (International Conferences on Harmonization). This allowed for mutual recognition agreements and substantial savings for manufacturers, and ultimately consumers and social security institutions.

IV.1.4. The Bolar Exception

Some maintain that the main incentive for diffusion of generics in the US came from the Hatch-Waxman Act and its Bolar amendment. In the EU, until recently, generics were not allowed to file for abridged applications, test or develop their product *before*

¹³⁸ See *supra* note 69.

patent expiration of the reference product. However, with the recent EU reform to the legislation the Bolar provision was introduced, symbolizing a step towards enhanced competition and static efficiencies, as is the case in the US, as well as many other countries across the world.

IV.1.5. Delay of Generic Entry and the Extension of Monopoly Power

In principle, the expected monopoly profits from sales during the patent life *reimburse* the innovator for his/her risky investment, while *competition with generics after the expiry of the patent reduces society's costs reflected in the deadweight losses* flowing from monopoly pricing under patent¹³⁹.

The deadweight loss produced by the monopoly is therefore the 'cost' of the 'dynamic' effects which are offset by generic competition, or the 'static' benefits. Generic competition which erodes the monopolist profits to an extent that it cannot reimburse its R&D costs is on the other hand the 'cost' of the 'static' effects, offsetting the 'dynamic' innovative benefits.

The issue of delaying generic entry therefore raises fundamental questions relating to dynamic and static efficiencies, namely – does the delay fall within the scope of the legitimate monopoly power granted via the patent? Were these methods of delay

¹³⁹ A monopolist, seeking to maximize its profits, charges a price *above the product's unit production cost*. However, some consumers whose *willingness to pay* for the monopolist's product will *be higher than its unit cost*, because the monopolist will charge an even higher price than their willingness to pay. Monopoly pricing therefore causes a part of the market not to be served, in an inefficient way. This is the deadweight loss.

foreseen and desired by US Congress or EU legislators, or are they rather a cynical extension of the legal monopoly power, aimed not to reimburse for the risk, but rather to allow prolonged rent-preserving?

The answer to these questions would depend on, *inter alia*, whether the brand-name drug manufacturer is considered to indeed have *monopoly power* in the strict sense resulting from the patent protection, a question related also to the definition of the relevant market.

Market power cannot be presumed from the existence of a patent, however, because like real property, IP gives one only the right to exclude. Whether or not a patent confers monopoly power depends on the availability of substitutes.

Focusing on the relationship between price and short-term marginal costs cannot be said to provide useful evidence of market power, because the most significant costs are the initial fixed costs of R&D whereas marginal costs are often small. Accordingly, the technically correct way to measure whether IP produces returns above cost is to *compare development costs with profits generated during the product's marketable life*. In a high-risk enterprise, moreover, *one must take into account the failed products as well as the successive ones*.

Consequently, market power cannot be assumed from the existence of patents, the pricing above short-run marginal cost, from generic entry below the price of a branded drug or from reduced output of the branded-drug upon generic entry. Therefore, a narrow market definition that does not include both patented and off-patent therapeutic

substitutes should be rejected unless a “formal test” is presented – showing the various drugs’ impact on the price and quantity of sales.

The conclusion for this paper’s purposes would thus be that just as market power cannot be presumed based on the existence of patents alone, so the prolongation of a patent, at times causing generic delay, cannot be presumed on its own to be an extension of monopoly power.

Another claim that has been made by proponents of the pharmaceutical industry is that it is not monopoly power which enables *abnormal profits for the branded-drugs firms to persist over time*, but rather *innovative propensity*, which strengthens the dynamic benefits. While it may be true that the firms at first receive a temporary monopoly, their superior financial advantages flow from their *later introduction of valuable innovations* to the market¹⁴⁰.

This persistent profitability theory may account for the supra-competitive brand-manufacturers’ *gains even subsequent to generic entry*. It also implies *a positive welfare-enhancing factor* – i.e., that of enhanced technological innovation. On the other hand, persistence of the firm’s supra-normal profits may also indicate its *ability to avoid or delay competition*.

It may additionally be argued that the fact brand-name firms do not lose all of their sales and market dominance immediately after patent expiry but only over a period

¹⁴⁰ Peter W. Roberts, “Product Innovation, Product-Market Competition and Persistent Profitability in the US Pharmaceutical Industry”, *Strategic Management Journal, Strat. Mgmt. J.*, 20: 655-670.

of time – is proof that the *value of a patent exceeds beyond the actual period of patent protection*. However, while this dominance is *legitimate* and intended by the legislators, employing generic delay tactics in order to deliberately hinder generic competition – strays from the legal protection provided for.

IV.1.6. The Policies Affecting Demand for Generics in the EU and the US

Policies in the EU and US by which governments influence demand for generics include permitting generic and therapeutic substitution, providing doctors or pharmacists with incentives to dispense generics, exerting price controls on generic or research-based manufacturers, using reimbursement systems and co-payment schemes – all of which are *aimed to make consumers more price-sensitive* and favor cheaper generic medicines over branded drugs – thereby facilitating generic competition and its static efficiencies.

In the US, generic substitution is permitted, while the consumer is permitted to refuse it. There are non-financial influences on doctors and financial incentives to pharmacists. Over the last two decades, developments in state drug substitution laws, federal legislation and the emergence of Health Maintenance Organizations (HMO) and Pharmacy Benefit Managers (PBMs) – have lead to an alteration of the pricing and other competitive strategies of pharmaceutical companies. And so today pharmacists are typically part of PBM networks, enabling them to check which branded or generic substitutions are required by the patient's health insurer, whether the doctor is prescribing according to health plan policy and what co-payment amount applies.

This information enables insurers and other drug buyers to focus more attention on comparisons of drug alternatives¹⁴¹ and subsequently strongly encourage use of generic drugs, particularly through use of lower co-payments required from consumers and higher dispensing fees paid to pharmacists.

In some of the European countries, the same systems are allowed for generic substitution yet financial incentives to pharmacists are not common. In the context of co-payment systems – in some EU states prescribed medicines are paid for *in full* while in others patients either pay in part or in full for medicines up to a threshold.

Co-payments up to a threshold sensitise end-users to the cost of their individual prescribed medicines – up to the threshold. They do not openly favor generic medicines, yet they are likely to have that effect because prescribers who know that their patients will pay from their own pockets up to a certain threshold, may be more likely to ask the patients regarding generic substitution¹⁴².

The “*reference pricing*” system used in the EU allows for health-funds to cover or reimburse the cost of drugs within a therapeutic level *only up to the reference price, fixed against the cheapest product in the category* – i.e., enabling them to reimburse for a generic instead of for a brand. *From the consumer’s point of view, reference pricing offers an element of choice, because they can decide whether a product priced at the reference price, requiring no co-payment, is satisfactory for their needs.* However,

¹⁴¹ This evolving information technology has also increasingly prompted drug companies to charge different prices to different groups of buyers.

¹⁴² Threshold co-payment also preserve social solidarity by providing free or subsidized medicines above the threshold.

reference pricing is likely to distort consumers' choice because they will most likely choose *paying nothing* over *paying something*, regardless of the quality of the product.

Fixed rate co-payments used in some EU MS can influence consumer demand but they do not sensitise prescribers or consumers to make choices between original and generic drugs because the consumers will have to pay up-to a fixed rate in any case.

EU MS' health funds, which are the final payers, make savings when generics enter the market because of certain pricing and reimbursement regimes that are specific to generics, yet some of them specifically set a lower price of reimbursement for generics – requiring the consumer to pay any supplement above it.

Both the US and the EU settings are therefore characterized by a demand for medicines which is *inelastic to changes in the price paid by the patients/consumers*¹⁴³, because of complex interactions among providers, patients and third-party payers, as well as price-insensitivity on part of prescribing doctors¹⁴⁴.

Nonetheless, there are certain typical traits to the EU regime, making the demand and supply of its pharmaceutical market *even less subject to free market forces*. Such is the direct government intervention on the demand side – setting the prices for pharmaceuticals and the indirect intervention in matters of marketing authorizations and IPRs affecting the supply side¹⁴⁵. Another unique attribute of the European market generally, albeit more acute in the pharmaceutical context, is that of the divergence

¹⁴³ Gerdtham U G and Johanneson M. “The Impact of User Charges on the Consumption of Drugs. Empirical Evidence and Economic Implications”. *Pharmacoeconomics*, 1996, June 9 (6), pg. 478-483.

¹⁴⁴ These aspects lead both the EU and US pharmaceutical markets to put a strong emphasis on *non-price factors of competition* such as advertising.

¹⁴⁵ See *supra* note 1, Policy Relating to Generic Medicines in the OECD, Study carried out on behalf of the European Commission.

between MS across the European continent, especially with the EU enlargement. This divergence exists alongside the goal of creating a single European market, raising difficulties in that sense.

IV.2. Economic Features of Generics Unique to the EU Market

IV.2.1. Price Regulation of Generics in the EU

The dynamics of prices and the diffusion of generic products differ between the US and the EU.

On the one hand, in the US system, which relies on market-based competition in pharmaceuticals, there is a clear distinction between firms that are innovators and generic firms that act as imitators, after patent expiry. Hence, *original pharmaceutical products enjoy premium prices and exclusivity profits under patent protection, and face fierce competition after patent expiry.*

On the other hand, the EU system relies on *administered prices*, causing the diffusion of generics after patent expiry to be rather limited, even in the long run. In European countries, *prices of original products decrease over time*, especially in regulated countries where prices are set when the drug is launched and then are seldom allowed to be increased. In this setting, the *monopoly power conferred to patent holders is counterbalanced ex-ante through price regulation which limits the effectiveness of the diffusion of generics* as a way to induce price competition in the market, after patent expiration.

This heterogeneity in price dynamics and generic diffusion between the US and the EU countries is, therefore mainly the result of the different regulatory environments. Because higher price-cost margins encourage generic penetration as mentioned above, *price regulation, which offsets the power of monopoly prior to patent expiration – can be an obstacle to the creation of a competitive environment in the off-patent sector of the pharmaceutical market*¹⁴⁶.

*The regulation of pharmaceutical industry pricing in the EU can also be seen as seriously impairing the industry's incentives for investment in new products or infringing upon the dynamic efficiencies*¹⁴⁷. The reason for that is that governmental bodies regulating prices and profits are said to have a “myopic” view and may recapture profits of relatively new highly profitable products, without taking into account failures experienced on a much larger scale in the pharmaceutical industry. The regulation of profits hence causes *cumulative profits to be insufficient* to sustain a high rate of technological progress. Assuming that important new drugs yield substantial consumers' surplus, consumers may also lose, along with the drug companies.

IV.2.2. An EU ‘Single Market’ for Pharmaceuticals

The enlargement of the EU brought with it the potential of a considerably larger market for pharmaceuticals and an increased generic industry. However, due to the fact that the average per-capita income in the central and eastern European (CEE) countries is much lower than the average income in older MS, the citizens of the CEEs may be faced

¹⁴⁶ Another factor slowing down generic entry is the high presence of licensed products on the market.

¹⁴⁷ F. M. Scherer, “Pricing, Profits and Technological Progress in the Pharmaceutical Industry”, *Journal of Economic Perspectives*, Volume 7, Number 3, Summer 1993, pg. 97-115.

with difficulties in *accessing affordable pharmaceuticals in prices realistic in the single market context*. PT of medicines may alleviate this problem.

Some of the recommendations of the Commission for the advancement of the single market in the year 1998¹⁴⁸ were the relaxation of price controls for generic drugs, the encouragement of prescribing doctors to dispense more generic products, and the *moving from a mechanism whereby prices are fixed by public authorities to a dialogue between these parties allowing for price negotiation*. These recommendations have already been adopted and implemented in the EU, as it is well documented in the AstraZeneca case.

*However, the different functioning of pharmaceutical markets and national health care systems across European MS, as well as their different financing and organization, may still constitute an impediment to the creation of a unified European market with all its consequences in terms of market size, economies of scale and higher competition*¹⁴⁹.

IV.2.3. The Codification of a ‘Generic’ and ‘Biosimilars’ in the EU Legislation

The recent reform to the EU legislation brought about it an explicit and codified definition of a ‘generic’ product and introduced a new policy and legal framework for ‘biosimilars’, which do not always fulfill the conventional generic requisites. Absence of

¹⁴⁸ See *supra* note 116.

¹⁴⁹ Laura Magazzini, Fabio Pammolli and Massimo Riccaboni, “Dynamic Competition in Pharmaceuticals, Patent Expiry, Generic Penetration and Industry Structure”, *Eur. J. Health Econom* 2004, Vol. 5, pg. 175-182.

such regulation in the US may lead to a *competitive advantage* for the EU biosimilars¹⁵⁰ and generics' industry and to *a benefit in static efficiencies*.

IV.2.4. Data Exclusivity Periods

Data exclusivity periods granted to the originators product differ between the EU, which currently allows for a period of *up to eleven years* of data exclusivity in case there is *a significant benefit to a new therapeutic indication* and the US, which allows for *five years of data protection*. Awarding more time of data exclusivity may have positive implications on the 'dynamic' incentives to innovate.

IV.3. Different Delaying Tactics and Their Solutions

In the US, *the grant of FDA approval or marketing authorization is linked to the non-infringement of the patent*, in a manner giving the patentee advance notice of generic entry, so as to allow him/her the opportunity to vindicate its patent in court *before the generic competitor is approved*. This brought about some of the most common abuses, such as the stacking of several thirty-month stays pending approval or outcome of litigation.

Conversely, in the EU context, *no such condition is required to be fulfilled prior to the approval*, albeit the different MS allow for the issuance of interim injunctions

¹⁵⁰ EuractivNews, "First biosimilar drug gets EU market authorization", 21 April 2006.

The European Generic Medicines Agency (EGA) has welcomed the new legal framework and believes the EU is now set to become "the global center for R&D and production of this new generation of affordable, biotech pharmaceuticals, giving the EU a huge competitive advantage over other countries like the United States and Japan"

against generic marketing pending the approval, in case of infringement of European patents.

In addition, the distinct frameworks of legislation and case-law bring about different generic delaying stratagems as well as different proposed solutions in the US and EU spheres.

In the US, it seems that the revisions in the Medicare Act have covered the most flagrant abuses delaying market entry of generic competition, such as the triggering of successive thirty-months stays or the creation of a bottleneck through the ‘parking’ of the 180-day exclusivity period for the first filer of an ANDA.

The matter of *settlement agreements* entered into by generic and brand-name drug manufacturers has not yet been resolved in a conclusive manner and there still appear to be differences of opinion between the FTC’s clear opposing approach and US courts and the Department of Justice views, as voiced by the Solicitor General in the Schering-Plough case. The final word in this matter will most probably be given by the Appellate Court’s decision regarding the cert petition in the Schering case, a decision still awaited for.

Another important issue which has not been settled completely is that of the regulatory abuse by *the ‘trend’ of listing any patent*, however marginally related to the pioneer brand drug, in the US “Orange Book”. This practice may still lead to the delay of

generic entry, as seen in the recent case of *Abbott v. Teva*¹⁵¹. As case law demonstrates, *this trend has been made possible by the Orange Book listing system in the US, which permits the brand companies to list patents without accountability or adverse consequence*¹⁵². Although the courts have recognized that the FDA's role as a gatekeeper in this sense is limited and have described it as 'strictly ministerial' (due to its lack of power, resources or expertise to compel or remove listings) – there is some indication in the case-law that they may require FDA scrutiny of listings in the future.

Nevertheless, this matter is still unaccounted for. There are no screening procedures in place yet to ensure that only patents within the scope of the legislation are listed.

In the European context, the question of whether there was an abuse of a dominant position via restrictions to PT remained unsettled as a matter of EU law. Nevertheless, the opinion of AG Jacobs may give an indication to the point of balance found, *preferring the dynamic efficiencies over the static competitive efficiencies* as well as over the free movement of trade as part of the EU single market¹⁵³.

Additionally, the new reform of legislation allowing for the Bolar amendment solved what was one of the major setbacks for generic competition in the EU setting. Another element which was settled was that which allows a generic producer to apply for

¹⁵¹ Abbott registered with the FDA a new tablet form instead of its capsule form drug. Once approved, it ceased to produce the capsule form and changed the code for the capsules in the National Drug Data File to "obsolete", preventing pharmacies from filling prescriptions.

¹⁵² See Stephanie Greene, "A Prescription for Change: How the Medicare Act Revises Hatch-Waxman to Speed Market Entry of Generic Drugs", *The Journal of Corporation Law*, Winter 2005, pg. 309-355.

¹⁵³ It remains to be seen whether the ECJ will follow the Advocate General opinion. If it does, the volume of lower-priced parallel imports (and corresponding pressure on prices) can be expected to fall.

an abridged procedure even in a MS where the reference product was withdrawn, an abuse seen in the case of AstraZeneca.

In the case of the extension of the data protection period, it is important to note that the new regulation allows for the extension of up to 11 years *only if a new therapeutic indication* of the drug brings to it a *significant* benefit.

*Yet the EU institutions did not address the matter of the filing of “secondary” or frivolous patents*¹⁵⁴ (not just *indications*) at the EC centralized level. At the MS’ level, the filing of frivolous new patents lacking a significant benefit can freeze the *original patent* and as a consequence still halt generic competition. Most recent examples are particularly provided in UK case-law. Such is the case of *Abbott v. Ranbaxy*¹⁵⁵ where the UK High Court refused to issue interim injunctions against a generic firm alleged to infringe European patents “*on the basis of the manifest weakness of the patent*”, which was a crystalline form of the basic patent. In another UK case, a combination of the basic GSK patent for an asthma product was held to be invalid *on the basis of lack of inventive step*¹⁵⁶, and in the case of *Mayne v. Teva*¹⁵⁷, the trial judge concluded¹⁵⁸ that the patent had been infringed yet is invalid due to *lack of obviousness*.

The lack of a viable solution to clearly target the tendency of patent-holders to list secondary, minor patents, in a way likely to be manipulated to retard generic competition,

¹⁵⁴ As mentioned, secondary patents are not just patents on the product per se or the process used to manufacture it but may also include those which cover crystalline forms, dosing regimes *or a second medicinal use*, i.e. - indication.

¹⁵⁵ Unreported, Decision of Pumfrey J. given on 19 November 2004.

¹⁵⁶ *R. v Glaxo Group Ltd's Patent*, [2004] R.P.C. 43.

¹⁵⁷ *Mayne Pharma (USA) Inc & Anor v. Teva UK Ltd & Anor* [2005] EWHC 2141 (Pat) (12 October 2005), available at: <http://www.bailii.org/ew/cases/EWHC/Patents/2005/2141.html>.

¹⁵⁸ It is the same trial judge who ruled in the *Abbott* case (supra note 53), Mr. Justice Pumfrey.

is therefore what I find to be the common ground between the EU and the US regulatory and case-law framework.

IV.4. Concluding Remarks

To sum, I did not find there to be a significant distinct approach to the matter of generic delay and the tension between dynamic and static efficiencies stemming from it on part of the US and the EU systems. In the past, there was more divergence between these two international markets in their relation to the importance of *generic competition*, observed in the absence of Bolar exception in EU legislation. However, the current trend is that of *convergence, attempting to strike the optimal balance by compensating either generic or brand manufacturers for infringement upon their dynamic or static efficiencies*. Thus, in the US context – a reform to the legislation curtailing the most significant generic delays – strikes a better balance in favor of the static efficiencies that have long been harmed by practices of delay. In the EU, the latest reform balanced between the static efficiencies – allowing for the bolar provision and for faster generic entry – and the dynamic efficiencies – allowing for longer data exclusivity protection in case of a new indication.

The US is characterized by a myriad of cases relating to generic delay and issues of antitrust, be it merger control or monopoly and anti-competitive effects, whereas the EU has only addressed the specific issues of abuse of monopoly position due to generic delay in one case, as mentioned.

It may be persuasive to link this with the Hatch-Waxman Act, which encouraged generic entry into the US market many years before it was allowed in the EU, yet it is also possible that it is linked to the nature of the US system, which places greater emphasis on litigation, be it public or private.

The multitude of cases dealing with generic delay in the US does not leave room to claim that there is a conclusive approach of US authorities or academia to generic delaying tactics. Some assert that they should be regarded as illegal per se (in the case of ‘pay for stay’ settlement agreements) while others claim they should be subject to the rule of reason. In the EU context, the only case that tackled these practices found them to be an abuse of a dominant position. However, much criticism has been made regarding this decision and the CFI will still have to express its own view on it. Therefore, I can not conclude that the EU institutions have had a ‘tougher’ stance towards generic delay.

Inherent differences between the regimes that I have tried to point to bear different implications on generic delay, yet the prevailing phenomena is that of convergence, and not of overall differing ‘policies’.

However, while most of the main delaying tactics relating to generic delays have been somehow settled or are under such an attempt, the form of delay carried out through improper listing of patents remains unresolved – in both environments.

It is for that reason that I will concentrate on offering a policy solution to this specific tactic for delay embodying the tension between the static and dynamic efficiencies, i.e., the elimination of generic competition due to frivolous patents that lack dynamic efficiency on their face – yet may have dynamic purposes, if R&D for other failed products is to be reimbursed through further patent extension.

V. Common Policy Recommendation

V.1. The Listing of Secondary Patents

Under the European Patent Convention of 1973, to which all EEA Contracting Parties are also parties, in order to obtain a European or national patent, the applicant has to fulfill certain substantive conditions such as *industrial applicability*, *novelty* and *inventive step*.

Similarly, Section 101 of the U.S. Patent Act states that for a patent to be granted by statute it must be *useful*, *novel* and *not obvious*¹⁵⁹.

In the past two decades, however, the above three standards interpreted in a similar way by both the EU and US regulatory regimes have been considerably relaxed, so that *new uses* (AKA new ‘indications’), new dosage forms and even the *coating* or *color* of pills have been patented¹⁶⁰. Such was AstraZeneca’s strategy in relation to its switch from *capsule* to *tablet* formulations of its patented drug. Such was also the tactic of improper Orange Book listings in the US, which received a great deal of attention from the FTC, the courts, the Bush administration¹⁶¹, health institutes and academia¹⁶², mainly due to the trigger of a thirty-month stay (albeit with the new reform, only *one* such stay per applicant) with the filing of an ANDA. A report by the non-profit US National

¹⁵⁹ See 35 U.S.C. § 101.

¹⁶⁰ Another recent example was seen in the SmithKline v. Apotex case, in which the Federal Circuit held that the product-by-process claim was anticipated based on an earlier patent for the drug, and was therefore invalid. The decision is available at: <http://www.fedcir.gov/opinions/03-1285.pdf>.

¹⁶¹ In this matter, US President, George W. Bush, stated in 2002: “*Our message to brand-name manufacturers is clear: you deserve the fair rewards of your research and development; you do not have the right to keep generic drugs off the market for frivolous reasons*”.

¹⁶² See section above “FDA Listing Requirements and the Right of Generic ANDA Applicants to have a Private Cause of Action to Delist a Patent”.

Institute for Health Care Management found in the year 2002 that the FDA approved 1035 drugs during 1989-2000, yet *only 361 were new molecular entities*, the remaining 65% contained active ingredients available in drugs that were already approved¹⁶³. Thus, with a new listing of the *color* of the pill as a patent, for instance, the thirty months stay would be triggered despite the fact that there is *no reasonable claim of patent infringement* and no reason to accept the new color as falling within the scope of the legislative requirements from a new patent¹⁶⁴.

While the main issue dealt with in the AstraZeneca case was the withdrawal of a European reference product (currently an action which cannot prevent generic entry to any national authority), the underling question was also the attempt to delay generic entry as well as obstruct parallel trade through a new registration of a *'tablet' form, with essentially no significant benefit over that of the capsule form*.

However, the value of secondary patents was not only raised in AstraZeneca, known as the main EU case in this matter, but also in case-law of MS within the EU, as aforementioned.

The arguments raised by the brand companies making the so-called improvements have been essentially the same in the EU and US context. It has been claimed with respect to the AstraZeneca case, that it is the pharmaceutical companies' *right* to withdraw marketing authorizations or register new formulations of the patented drug, if

¹⁶³ Anonymous, "An Innovative Challenge to the Pharmaceutical Industry", *The Lancet*, Nov. 2, 2002, 360, 9343; Research Library, pg. 1341.

¹⁶⁴ Devesh Srivastava, "The Food and Drug Administration and Patent Law at a Crossroads: The Listing of Polymorph Patents as a Barrier to Generic Drug Entry", *Food and Drug Law Journal*, Vol. 59, pp. 339-354, 2004.

they have developed *an improved version of the drug* and that it is *questionable whether the competition authorities should intervene in their actions*.

In the recent US case of Abbott Laboratories¹⁶⁵, the brand companies claimed that *any product change that produces an improvement, however minor, can not violate antitrust laws*. Furthermore, they claimed that the success of the new products on an open market demonstrates that consumers have a preference for them¹⁶⁶.

The court, however, rejected these claims asserting that *in the case of the market for prescription drugs, the FDA approval and pharmacies' required use of the National Drug Data File does not permit unrestricted consumer choice*.

Furthermore¹⁶⁷, the court stipulated that *the value of the 'improvement' should be weighed against the damage inflicted on the generic competition*.

In another very recent case, the US Supreme Court, following the Solicitor General's advice, established that: *"What patent applicants cannot do is to receive patent protection for a substance that was inevitably produced by the practice of prior art and thereby withdraw that prior art from public domain and make the exploitation of expired patents difficult or impossible"*¹⁶⁸.

Empirical evidence indicates that the speed with which the original brand *loses revenue due to generic entry is directly proportional to how successful the brand is*.

¹⁶⁵ See *supra* note 99. Abbott also changed Tricor, its patented drug, from a capsule to a tablet and then again to another form of tablet differing from the old one in that it could also be taken with food, but otherwise identical.

¹⁶⁶ In making this argument, the companies relied on the Second Circuit decision in *Berkey Photo, Inc. v. Eastman Kodak Co.*, 603 F. 2d (2d Cir. 1979), which indicated that courts should generally not inquire into alleged anticompetitive effects of new products.

¹⁶⁷ Basing its balancing test on that used by the court in the *United States v. Microsoft Corp.* case (See *supra* note 144).

¹⁶⁸ *SmithKline Beecham v. Apotex Corp.*, U.S., No. 05-489, review denied June 19th, 2006. .

Under the same line of logic, unsuccessful drugs may provide “a safety device” for a firm, for it is less likely to meet generic competition, and may thus maintain profits for a longer time.

The listing of secondary patents must thus be brought about in cases of *successful drugs*, that cannot enjoy the said “safety device” and must therefore concoct an artificial means by which to prolong their profits – such as the production of drugs that do not provide patients with significant qualities.

This, inter alia, may also lead to a ‘*moral hazard*’ problem, because the patients do not have the ability to estimate the quality of change or improvement in the case of secondary patents, a problem which may be exasperated by *the inherent asymmetric information*¹⁶⁹ between drug manufacturers and final patients.

The question of the *value of improvement or innovation* of a patent is also intertwined in the cost and benefit analysis of settlement agreements, supporting opponents of these agreements.

It was claimed that because the Hatch-Waxman Act allows the issuance of an entry injunction against potential entrants for the so-called infringement of *frivolous patents*, substantial deterrent for patent-infringement settlements is required¹⁷⁰.

Additionally it was argued that because some innovations are held valid by the court while others are held invalid due to their estimated ‘improvement’ value – there is a ‘probabilistic’ nature to patent property rights¹⁷¹. This *probabilistic nature* demonstrates

¹⁶⁹ Moral hazard describes a situation whereby the quality of a product cannot be objectively estimated by either the seller or the buyer. Asymmetric information describes a situation in which either the producer or consumer is in a better state of knowledge or of acquisition or access to knowledge.

¹⁷⁰ Richard S. Higgins, “Short-Run Welfare Analysis of FTC Antitrust Oversight of Patent Litigation Settlements Under the Hatch-Waxman Act”, *The Antitrust Bulletin*, Winter 2002, 47, 4 pp. 661-676.

¹⁷¹ Alden F. Abbott and Suzanne Michel, “Exclusion Payments in Patent Settlements: A Legal and Economic Perspective”, *Journal of Intellectual Property Law & Practice* 2006 1(3): 207-223.

that exclusion payments which exclude at times in an absolute way, fall *outside the scope of a patent's exclusionary scope* and should thus be subject to antitrust scrutiny.

The value of the improvement of the drug may also shed light on the claim that branded-drug manufacturers enjoy 'persisting abnormal profits' because of their '*innovative propensity*' and not due to monopoly power. Total welfare will no doubt enhance, however, with the measurement of such propensity through *technological or other novelty which is important to society* rather than by *economically successful innovations, which may be less valuable to society* and unnecessarily abused¹⁷².

The listing of improper secondary patents has resulted in a call to strengthen the patent listing/declaration process and to a change in legislation¹⁷³. This was one of the only difficulties not addressed by the Medicare Act reform, perhaps also after case-law has justified the FDA's passive role in this context.

Case law suggests that despite several district court opinions, recognizing the difficulty of the ANDA applicants, the circuit courts of appeal have been unwilling or unable to "stretch" the Hatch-Waxman provisions to answer to the interests of the generic drug manufacturers.

In the case of *Mylan Pharmaceuticals v. Thompson*¹⁷⁴, the Federal Circuit established that an ANDA applicant has no private cause of action to delist a patent. In the case of *Andrx*

¹⁷² A firm might therefore be persistently profitable although it lacks any underlying, valuable capabilities.

¹⁷³ *Generic Drugs: GPha says FTC settlement reinforces need for legislative "fix" for Hatch-Waxman*, Drug Week, Atlanta, Apr. 11, 2003.

¹⁷⁴ *Mylan Pharmaceuticals v. Thompson*, 268 F. 3d 1323, 1323 (Fed, Cir, 2001).

Pharmaceuticals v. Biovail¹⁷⁵, the Federal Circuit did suggest, in dicta, that an ANDA applicant may bring an action under the Administrative Procedure Act¹⁷⁶ to compel the FDA to approve the ANDA if its denial was “*arbitrary, capricious, or not in accordance with law*”. However, the FDA’s acknowledged passive role in administering the Orange Book leaves little room for interpreting its conduct as such, a fact further emphasized in the case of aaiPharma, Inc. v. Thompson¹⁷⁷, where the Fourth Circuit established that the FDA’s role is “*purely ministerial*”.

This matter is therefore still considered to be one of the loopholes of US legislation¹⁷⁸, allowing listings in the Orange Book to be conducted without any scrutiny.

The new EU reform allowing for an eleven-year data exclusivity period, at least rewards a *significant “indication”*, which is considered a secondary patent. This in itself may curtail some abuse portrayed in new ‘repurposing’ of known therapeutics¹⁷⁹, yet the legislation should provide *more specific guidance* with regards to the listing of *any* secondary patents (not just indications). This can be done, I believe, by explicitly establishing in legislation that *only significant patents* should be listed and that screening processes of these patents will be conducted. More so if an EU community patent will be instituted¹⁸⁰ ensuring a unitary form of EU-wide protection.

¹⁷⁵ Andrx Pharmaceuticals, Inc. v. Biovail, 276 F. 3d 1368(Fed. Cir. 2002).

¹⁷⁶ See 5 U.S.C.S. §§ 702-706 (Law. Co-op. 1989)

¹⁷⁷ aaiPharma, Inc. v. Thompson , 296 F, 3d 227 (4th Cir, 2002).

¹⁷⁸ Annual Report of Retail Pharmacy, Drug Store News, August 28, 2000, pp. 44-46.

¹⁷⁹ Melissa Hunter-Ensor, George W. Neuner, Peter F. Corless, “Exploiting Newly Discovered Indications of Known Therapeutics”, Edwards Angell Palmer & Dodge LLP, *available at: <http://www.ltd.jhu.edu/whatsnew/Exploiting%20Newly%20Discovered%20Indications%20of%20Known%20Therapeutics.pdf>*.

¹⁸⁰ Arthur Rogers, “EC Will Take Up Patent Reform in July”, Patent, Trademark & Copyright Journal, Volume 72, Number 1774, Friday, June 16, 2006.

I also find it to be easier for the FDA or national medicinal offices in European MS, already having to establish the *safety, efficacy and quality of the product* to inspect new patents. In lieu of suffering the consequences of improper listing *ex-post*, i.e. – the costs of a thirty-month generic stay in the US, the costs of litigation for patent infringement suits both in European MS and US contexts – it may be more efficient to incur the costs *ex-ante* of a selective investigation of the ‘new patent’, especially as the FDA and MS’ national medicinal authorities or the EMEA are already supposed to be doing so.

Although this is not a tort case, the tort examinations may be inspirational in this situation, if the damage is considered: The *ex-ante* procedure will comply with Holmes and Coase assertion with regards to the “*cheaper cost avoider*”, for the screening procedure conducted by either the FDA or the EMEA and MS national medicinal offices will be *cheaper than the infringement litigation procedure* which will be unnecessary if the new patent listed has no added-value to it.

Furthermore, in accordance with the *Learned-Hand formula* ($B < p \times L$), the burden (B) that both the FDA or EMEA will be faced with by screening new approvals will be less than the probability (p) of harm, multiplied by the degree of loss (L) because the probability of harm will be large in the case of secondary, invaluable patents – and the competitive harm will also be great, more so when it is due to a non-novel innovation.

Moreover, costs of litigation will become a sunk loss in these cases, in which the initial assumption to be made is that the *patent will not be held valid* in court due to lack of novelty or improvement.

*Prevention of the improper listing of patents may also actually promote funding of new innovative research*¹⁸¹, thereby benefiting *dynamic efficiencies* – due to the fact that the restriction of generic delay and the lower generic prices¹⁸² allow for significant savings. Be it via health plans in Europe or HMOs and PBMs in the US encouraging generic substitution – generics could save consumers losses¹⁸³.

It therefore seems that a sound cost & benefit analysis of secondary patent listing should take into account *not only the benefit of the improvement versus the harm to competition*, as mentioned above, but also *the affect on the dynamic efficiencies* that a decision to invalidate a patent may have.

In many of the cases discussed hitherto, the ‘improvement’ as such did not present a *significant novelty* or a “*real innovation*” and therefore a verdict in favor of the generic applicants invalidating the secondary patent should not be conceived as *likely to infringe upon potential future incentives to innovate*. Where no therapeutic advantages or innovation result from the new patent – *there is no apparent increase in dynamic efficiency warranting the extension of monopoly power in any case*.

With this very straightforward model I try to show that settlement agreements of patent infringement suits which occur both in the European MS and US context in the case of secondary ‘invaluable’ patents will be unprofitable from a social standpoint:

¹⁸¹ “EU Review Threatens Generics”, *Chemist & Druggist*, London, Feb. 8, 2003, pg. 6. John Beighton, chairman of the British Generic Manufacturers Association, has warned: “Research has consistently shown that protecting innovative industries causes them to wither and die”.

¹⁸² Sustainable, Fair and Pro-Generic, *Chemist & Druggist*, London, Dec. 9, 2000, pg. 26.

¹⁸³ Diane West & James Frederick, “BCBS Study: Generic Delays Could Cost Consumers Billions”, *Drug Store News*, May 20, 2002; *Research Library*, pg. 21.

(1)

As long as: $p[\pi(T - t') \leq Paym.$

=> A settlement will be profitable for the generic applicant.

The profits for the duopolist generic (I assume that no other generic entrant enters the market, for the sake of simplicity) which is the first ANDA or abridged procedure applicant, is denoted π , and the monopoly brand-name profit is denoted π_m .

The profits that a generic may receive are conditional on his winning the patent infringement suit, both under the US thirty-month delay trigger and under European MS patent litigation. p denotes the generic's probability of winning the litigation. The assumption I am making is that because the secondary patent is of no real value, the generic will have a very high probability of winning the infringement lawsuit.

Litigation costs, as well as other fixed and marginal costs of production for the generic applicant (FC + MC), will be subtracted from his total revenue (TR) subsequent to his entry into the market, so that the profits of the generic applicant will 'include' them. $\pi = TR - (FC + MC)$, where the litigation costs, denoted L , may be considered as fixed costs under the assumption that the generic will challenge a frivolous patent in almost any case, due to his expectation to win the infringement suit.

$Paym.$ denotes the payment that the monopolist will pay the generic applicant in order not to enter the market at a certain period prior to the expiry of his secondary patent.

T denotes the time until patent expiry, whereas t' denotes the time of litigation. $T - t'$ is therefore the time left after litigation, for the generic to enjoy profits.

To conclude:

Where the payment that the monopolist brand-name pays the generic is at least as big or equal to his expected profits from entering the market – a payment settlement will be profitable for the generic.

(2)

As long as: $Paym. \leq (1-p)\Pi_m \cdot t'$

=> A settlement will be profitable for the brand-name manufacturer.

Because both the monopolist brand company and the generic applicant are competing in the same setting of the lawsuit – the probability that the monopolist will win the suit is exactly inverse to that of the generic winning.

The payment is the same payment the monopolist will pay under (1).

However, because of my assumption that the court will hold the secondary patent invalid due to lack of evident improvement – i.e., that the monopolist will lose in any case under these specific circumstances – he will only be able to enjoy monopoly profits for the remaining time of the litigation, denoted by t' .

(3)

The combination of the two terms will yield a situation in which a settlement may be profitable for both:

$$p\Pi(T-t') \leq (1-p)\Pi_m \cdot t'$$

The expression $(T - t')$ is positive, because it is assumed that the time until patent expiry is longer than the period of time of the litigation. The probabilities of winning are of course positive as well.

This overall expression therefore expresses that monopoly profits during the time of the litigation only, must be greater or equal to the profits of a duopolist generic during the *whole term until patent expiration*. For this to be true the profits of the monopoly must be particularly supra-competitive and high for the period of time of litigation alone is usually shorter than the period between litigation and patent expiry, i.e., for the expression on the right to be greater than that on the left the profits of the monopoly will have to compensate for the smaller time expression on the right (t' instead of $(T - t')$). The conclusion may therefore be that such particularly high monopoly profits, causing significant deadweight losses during the monopoly period and its extension, are not efficient from a social standpoint.

With regards to the *value of improvement* of the secondary patents filed, it may be argued that as long as the *expected social welfare* rising from the 'improvement' is *greater or equal to social costs of the deadweight loss rising from the monopoly extension* (due to new filing), *as well as the already lost sunk fixed costs of the generic applicant* (assuming that he was already ready to enter, and then discovered the new filing, as is usually the case because filing a new color for a pill as a patent does not take the brand-name company much time or other efforts) and the *costs incurred by the brand manufacturer for the new patent* (which are assumed to be minor, due to the minor

development to the original innovation), *delaying of generic competition* through the finding that the second patent is valid, *may be allowed*. However, albeit hard to measure, most of the secondary patents filed do not amount to a *significant* social welfare, taking into account that they are generally a new form or dosage in a better-case-scenario and a pattern on a pill or the pill's color in a worse-case-scenario – the probability that the delay ought to be allowed should be very small.

Social welfare will represent consumer welfare¹⁸⁴ from the new secondary patent, which will be a hard value to measure, as well as encouraging incentives for innovation, through the finding that the secondary patent is valid and taking into account the “dry holes” incurred by innovators and a low 25% of patent approval, generally speaking.

¹⁸⁴ Consumer welfare is usually represented by the difference between consumers' willingness to pay for a certain product and the price they actually pay. However, in the case of life saving drugs, a willingness to pay may not be the right criteria to measure the consumers' welfare, if consumers do not have much paying power.

VI. Final Conclusions

Although there are different regulatory frameworks, as well as judiciary systems and traditions in the EU and the US, the generic delaying tactics used in both settings are in general quite similar, albeit the Hatch-Waxman Act in the US has invited more ‘creative’ methods of advancing the delaying stratagems used by brand-name manufacturers.

The EU background and its unique features, such as the emphasis on the creation of a single market of pharmaceuticals across the European MS, as well as the price regulation of pharmaceuticals, create some distinctive dilemmas within the EU settings with respect to competition in the pharmaceuticals’ market – such as the example of parallel trade, which on the one hand allows for a single market and for cost-containment and on the other may infringe on the research-based industry’s interests to recoup their R&D and risk costs.

However, I have not found a significant divergence in the *policy* of the US and the EU towards generic competition delay. This is mainly due to a trend of reform, both in the US with the Medicare Act and in the EU with the ‘Pharma Review’, which both tackled some of the most blatant previous forms of abuse allowing for generic entry deferral eventually leading to a closer harmonization of the regimes.

The principal tactic that remained to be resolved, both in the EU and the US is that of ‘improper listing/registration of patents’ also known as listing of ‘secondary patents’, which may serve to delay generic entry.

It is for that reason that I suggested a policy recommendation with respect to this particular delaying method, which constitutes of a legislative modification – *requiring the prior screening of the secondary patent* to be filed, so as to ensure that it complies with the requirements from an ‘innovation’ and awards *a significant benefit*. I also suggest, albeit less strongly, that the FDA or national medicinal authorities and EMEA in the EU context will be in charge of this selection process, due to the fact that these bodies already normally examine the safety, efficacy and quality of the product and may be better suited than patent offices to do so, which usually assume a more technical-formalistic role.

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