

# Patent term extension strategies in the pharmaceutical industry

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The purpose of this paper is to discuss patent term extension strategies for pharmaceutical companies in the United States. Market exclusivity acquired through patents can yield higher prices and profits for pharmaceutical products. Therefore, pharmaceutical companies use a variety of strategies to increase market exclusivity of their products. Some of the strategies discussed in this paper include one-year extension of time to file for patent under the Paris convention, patent term restoration allowed by the Waxman-Hatch Act, orphan drug exclusivity, pediatric exclusivity, the 30-month stay provision and so on. Even though, the strategies discussed in this paper are for the United States, they may be applicable to most European countries, Australia, New Zealand, Japan, and Canada with minor modifications as similar pharmaceutical regulations exist in these countries.

Keywords: Patents, generics, pharmaceuticals, market exclusivity, Paris convention

## 1. Introduction

Intellectual property rights have emerged as an important policy issue for pharmaceutical companies. The average gross sales margins of the US pharmaceutical companies during the past few years are nearly twice those of the semiconductor companies. Such significant differences in gross margins are primarily attributed to the better track records of pharmaceutical companies in protecting their innovations [24]. Therefore, the protection and dissemination of innovations are of paramount concern to the pharmaceutical companies.

R&D costs of developing new drugs are very high. The costs of reproducing pharmaceutical drugs are very low. Therefore, very few companies will be willing to make huge investments in pharmaceutical R&D without patent protection. Patents also support higher economic growth as the pharmaceutical industry provides high paying jobs which in turn lead to higher economic growth. Patents are needed for technology transfer. Since no company possesses all technologies needed to carry out its business, no company can survive without technology transfer. The technology transfer will occur only if both parties to the transaction can benefit. The owner wants to make sure that transfer will not jeopardize his existing and potential business and at the same time transfer is profitable. The buyer of the technology wants to ensure

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that he can reap benefits from the technology. If the technology is protected as a trade secret, then there is no guarantee that it will remain that way. One way the technology owner can ensure that he will not lose control of his technology is through patents. The patent system will help the owner to exclude others from using his technology during the term of the patent. The owner of the technology can also ensure that he will continue to receive royalty as he can put an end to the use of the technology if he has the patent. Strong intellectual property rights are also found to attract foreign direct investments [15]. They are also found to expand trade [11]. In spite of significant advantages, the patent systems in many countries suffer from serious shortcomings.

The Agreement on Trade-Related Aspects of Intellectual Property (TRIPs Agreement) Rights, a component of Uruguay Round of GATT negotiations that tries to overcome major deficiencies in intellectual property rights, has significant impact on the pharmaceutical industry.

TRIPs Agreement achieves several intellectual property protections the pharmaceutical companies want. By requiring the signatories to have patent protection for pharmaceutical products, TRIPs Agreement extends process and product patent protections in many developed and developing countries. TRIPs agreement also makes process patents as strong as product patents by requiring protection of products manufactured by a patented process. Nondiscrimination features of TRIPs Agreement require its signatories to treat their own citizens and others equally. Treating import of a product equivalent to domestic production makes working requirement feature in statutes of many developing countries invalid. The validity of patent rights should be at least twenty years from the date of filing. This extends the life of pharmaceutical patents in many countries thus motivating companies to invest more in R&D.

The average prescription price of a brand name drug is \$65.29 compared to only \$19.33 for a generic drug in 2000. Net profit margin before taxes of ten brand name pharmaceutical manufacturers was 23.6 percent compared to only 17.2 percent for ten generic pharmaceutical manufacturers [8]. Therefore, the market exclusivity provided by patents yields higher prices and profit margins to brand-name drugs. In addition, the longer is the market exclusivity, higher are the profits. The profits are typically much higher at the end of the market exclusivity as drugs need minimal advertising and promotion. The brand-name drugs with total sales of \$40 billion are expected to lose patent protection during 2002–2006. Some drugs that will lose or lost patent protection include Prilosec (\$3.7 billion in sales), Claritin (\$2.5 billion in sales), Glucophage (\$2.0 billion in sales), Augmentin (\$1.8 billion in sales), Paxil (\$1.8 billion in sales), and Cipro (\$1.3 billion in sales) (sales 1999). It is therefore natural for brand-name pharmaceutical companies to develop strategies to maintain their market exclusivity. The purpose of this paper is to discuss various strategies to extend patent terms with a view to maintain market exclusivity of drugs in the United States. This paper is organized into four sections. In the next section, we briefly describe the Waxman-Hatch Act of 1984 followed by the patent-term extension strategies. We close this paper with conclusions.

## 2. Background

The Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Waxman-Hatch Act, was enacted to facilitate faster introduction of generic drugs. It made significant changes to the patent laws as they relate to the pharmaceutical industry. It provided patent extensions for pharmaceutical companies, exemption to generic manufacturers from patent infringement for work related to regulatory marketing approval, and procedures for generic manufacturers for challenging the validity, enforceability, or infringement of pharmaceutical patents. This act encourages performance of R&D for new drugs and introduction of generic drugs. The Congressional Research Service Report for Congress and references contained therein describe the Waxman-Hatch Act in more detail [14]. The Waxman-Hatch Act is not applicable to antibiotics and biotechnology products.

Before a drug can be marketed in the United States, it needs to be approved by the US Food and Drug Administration (FDA) as safe and effective. Patents that grant exclusive rights to their owners are issued for compounds that make up the drug and also for making and using drugs. Patent ownership by itself does not provide right to market patented drugs in the United States. In other words, granting of patents and approval of drugs are done on different criteria. Still, both patent ownership and drug approval are necessary for a company to sell drugs without civil or criminal liability in the United States. If a company gets a marketing approval for a drug whose patent is not owned by the company, it could be subjected to liability for patent infringement. The Waxman-Hatch Act simplifies and provides procedures to introduce generic drugs immediately upon the expiry of the patents on the drug.

### 2.1. The generic drug approval process

Before 1984, generic drugs were subjected to the almost the same approval procedures as those of the new drugs including the performance of expensive clinical trials. As a result, few companies introduced generic drugs prior to 1984. In addition, the Federal Circuit Court decision that clinical trials and other procedures that need to be done to obtain marketing approval constitute patent infringement also forced potential manufacturers to wait until the expiry of patents before they could start working on the introduction of a generic drug. The Waxman-Hatch Act remedied this situation by allowing generic manufacturers to rely on safety and efficacy data of the original brand-name manufacturer. This saved generic manufacturers substantial costs of conducting clinical trials and other procedures needed to prove that the drug is safe and effective. Still, generic manufacturers have to prove that their drug is bioequivalent or performs in the same manner as the branded drug. One method which scientists show the bioequivalence is by measuring the rate and the extent of absorption of the drug in the blood stream in 24 to 35 healthy normal volunteers and comparing them against those of the branded drugs.

The Waxman-Hatch Act also introduced a simple application for the approval of generic drugs called Abbreviated New Drug Application (ANDA) for filing with the FDA. This helped a generic manufacturer to introduce its drug as soon as the patents on the original drug expired. To encourage pharmaceutical manufacturers to do R&D, the term of pharmaceutical patents were extended by a fraction of the time lost because of clinical testing and the FDA approval. This time includes the time elapsed from the effective date of the Investigative New Drug Application until New Drug Application is filed and the time taken for approval of New Drug Application (NDA) by the FDA. However, this time may not exceed five years. In addition, the patent term from the time of approval of the New Drug Application may not exceed 14 years. If a patent for a drug had been granted and human clinical trials had started at the time of the enactment of the Act, then the patent extension is only for 2 years. The Waxman-Hatch Act also allows the FDA to confer market exclusivity for certain FDA-approved drugs. If the approved drug is a new chemical entity, then a generic manufacturer cannot submit an ANDA for the generic version for five years after the approval of the New Drug Application. The drug consisting of active ingredients including the ester or salt which have not been approved in any other full New Drug Application is defined as a New Chemical Entity. If the approved drug is not a new chemical entity, then the generic manufacturer has to wait three years before an ANDA for the generic version can be submitted.

The Waxman-Hatch Act allowed generic manufacturers to perform functions needed to obtain approval of generic version of a patented drug during the life of a patent without charge of patent infringement. However, the submission of an ANDA is considered as an act of patent infringement so that the questions relating to the validity, enforceability and infringement of patents can be resolved before a generic drug is introduced. This Act requires the listing of patents relating to each approved New Drug Application in the "Orange Book" maintained by the FDA. The potential generic manufacturer should indicate in the ANDA any of the following four intents (called certifications) relating to each patent in the Orange Book that:

- I patent information on the drug has not been filed;
- II the patent has already expired;
- III the date on which the patent will expire; or
- IV the patent is invalid or use or sale of the drug will not infringe the patent.

The FDA will approve the ANDA filed with paragraphs I and II certifications. For paragraph III certification, the FDA will approve the ANDA only after the listed patents expire. When the potential generic manufacturer indicates paragraph IV certification, the FDA should send the copy of the ANDA to the patent owner. The patent owner has 45 days from the date of the receipt of the ANDA to execute patent infringement suit. If the patent owner executes the patent infringement suit in the timely manner, the patent owner immediately gets a 30 month stay from the FDA from approving the generic version of the drug. The FDA should then wait until:

- Court finds that the listed patent is either invalid or not infringed;

- The listed patent expires if the court finds the listed patent is valid;
- Court orders or thirty months from the date on which the patent owner received the copy of the ANDA elapse.

Every time a new patent is added in the Orange Book, the brand manufacturer gets a 30-month stay from approving the ANDA. However, the 30-month stay obtained for each patent runs concurrently. Currently, the brand manufacturer can only get one 30-month extension. The first generic manufacturer who files ANDA with paragraph IV certification is rewarded with 180-day market exclusivity, if its generic drug is approved.

To sum up, the Waxman-Hatch Act

- extended the life of the pharmaceutical patents up to 14 years from the time the New Drug Application is approved by the FDA,
- provided additional market exclusivity for the new uses or new formulations,
- allowed potential generic manufacturers to conduct work related to marketing approval of the drug without the charge of patent infringement,
- permitted generic manufacturers to use safety and effectiveness research performed by the brand-name pharmaceutical companies,
- introduced the concept of bioequivalence to obtain the approval of generic drug, and simplified generic drug approval process by introducing ANDA, and
- encouraged patent challenges by providing 180-day market exclusivity for the first generic manufacturer who files ANDA.

In the next section, we will discuss various patent term extension strategies that could be applied by the pharmaceutical companies.

### **3. Patent-term extension strategies**

#### *3.1. The Paris Convention*

The Paris Convention allows an inventor who files for a patent in any member nation one year to file patent in any other member nation. For example, if an inventor in the US files for a patent in Japan, a Paris convention signatory country, the inventor has one year to file for a patent in the US. Since 20 year validity of patent in the US is from the date of filing, this can provide an inventor one year of extra patent term in the US. So the strategy is to file for patent in a country which is a signatory to the Paris convention and also with low sales potential.

#### *3.2. Take advantage of regulations*

Strategies that exploit regulations to maintain market share or delay the introduction of generic drugs involve identification of regulations to increase market exclusivity.

The use of such strategies is pervasive in the pharmaceutical industry. An analysis of 24 HIV/AIDS drugs produced by 26 patent owners indicates that 11 patents received some extensions in the United States [2]. The Waxman-Hatch Act provides a time extension for patents to make up drug testing and approval time. The extension of time may not exceed five years, and the time between the approval of the drug and the expiry of the patent may not exceed 14 years. This strategy was used to increase the market exclusivity time period of Celexa. A copy of the notice published in the Federal Register describes this strategy:

“Determination of Regulatory Review Period for Purposes of Patent

Extension; Celexa,” Federal Register, February 25, 2002, (Volume 67, Number 37): 8546-8547

“A regulatory review period consists of two periods of time: A testing phase and an approval phase. For human drug products, the testing phase begins when the exemption to permit the clinical investigations of the drug becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human drug product and continues until FDA grants permission to market the drug product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Commissioner of Patents and Trademarks may award (for example, half the testing phase must be subtracted, as well as any time that may have occurred before the patent was issued), FDA’s determination of the length of a regulatory review period for a human drug product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA recently approved for marketing the human drug product Celexa (citalopram hydrobromide). Celexa is indicated for the treatment of depression. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for Celexa (US Patent No. 4,650,884) from H. Lundbeck A/S, and the Patent and Trademark Office requested FDA’s assistance in determining this patent’s eligibility for patent term restoration. In a letter dated December 19, 2000, FDA advised the Patent and Trademark Office that this human drug product had undergone a regulatory review period and that the approval of Celexa represented the first permitted commercial marketing or use of the product. Shortly thereafter, the Patent and Trademark Office requested that FDA determine the product’s regulatory review period.

FDA has determined that the applicable regulatory review period for Celexa is 5,498 days. Of this time, 5,061 days occurred during the testing phase of the regulatory review period, while 437 days occurred during the approval phase. These periods of time were derived from the following dates:

1. The date an exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(i)) became effective: July 30, 1983. The applicant claims August 4, 1983, as the date the investigational new drug application (IND) became effective. However, FDA records indicate that the

IND effective date was July 30, 1983, which was 30 days after FDA receipt of the IND.

2. The date the application was initially submitted with respect to the human drug product under section 505(b) of the act: May 7, 1997. FDA has verified the applicant's claim that the new drug application (NDA) for Celexa (NDA 20-822) was initially submitted on May 7, 1997.
3. The date the application was approved: July 17, 1998. FDA has verified the applicant's claim that NDA 20-822 was approved on July 17, 1998.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the US Patent and Trademark Office applies several statutory limitations in its calculations of the actual period for patent extension. In its application for patent extension, this applicant seeks 1,826 days of patent term extension."

#### **4. New product exclusivity for clinical testing**

The Waxman-Hatch Act provides three additional years of "market exclusivity" for new uses of drugs that requires clinical testing. This data exclusivity is for five years for new chemical entities. Since a potential generic manufacturer can file an ANDA only after these data exclusivity periods have elapsed, the actual time during which there is no generic competition include a market exclusivity period and the ANDA approval time, the median of which was 18.1 months in 2001. For new chemical entities, an ANDA can be filed after 4 years if patent invalidity or non-infringement is involved. Even though, identification of new uses of a drug is a good strategy, this strategy cannot protect against generic competition for the original indication. However, this strategy can help companies to retain patients who otherwise might choose the cheaper generic version manufactured by someone else. In 2001 alone, 172 new indications for previously approved medicines were approved by the FDA. Unlike consumer products, development phase of a drug rarely ends. Valium, for example, when it was first introduced in 1963 was for the relief of anxiety and sedation. However, by 1974, the number of indications had increased to 18 including surgery, alcoholism, dermatology, gastrointestinal disorders, obstetrics, coronary thrombosis, stress, thyroid disorders, anesthesia, rheumatism, urology, poisoning, asthma, tetanus, convulsions, and narcotic poisoning [5]. Developing new dosage forms can provide advantages to certain patient groups thus convincing physicians to prescribe these drugs. Product extensions with slight modifications such as extended release capsules can get at least 3 years of market exclusivity if their developments involve clinical research. Such modifications can be done just before the patent on the original drug is about to expire. By doing so, the manufacturers can hold on to their patients which they would have otherwise lost. Combining two different drugs sold separately into a single one is another strategy to thwart generic competition.

Development of combination drugs may involve expensive clinical and other studies. Even though this strategy may not be liked by physicians and regulators, useful combinations may be able to add life to a drug whose market exclusivity would otherwise expire. For example, Wyeth-Ayerst created Ziac by combining zhydrochlorothiazide and the cardioselective beta-blocker bisoprolol [12]. This combined drug with 80 percent efficacy and placebo-like side effects can provide greater efficacy than any single hypertensive agent can offer [18]. Claritin D-24 a combination of decongestant and antihistamine in a once-daily dosage form, launched by Schering-Plough is another example of combination medicine [1].

## 5. Pediatric exclusivity

With a view to encourage pharmaceutical companies to conduct research about the effectiveness of their drugs in children, pediatric exclusivity extends existing “market exclusivity” by six months. All exclusivities granted by the Waxman-Hatch Act, orphan exclusivity and patent exclusivity run concurrently. However, pediatric exclusivity is added to the existing exclusivity periods. Pediatric exclusivity is not available for drugs without any exclusivity. Therefore, this exclusivity should be taken advantage of before any other exclusivity runs out [21]. In order to obtain pediatric exclusivity, the studies of the product on a pediatric population must be requested by the FDA. The study need not be successful in order to receive pediatric exclusivity. An industry survey estimates that pediatric tests cost an average of \$3.87 million per drug. Based on 188 tests for which the FDA has requested tests, pediatric testing would cost the industry about \$727 million. However, this exclusivity is estimated to be worth \$29.6 billion to the patent holding companies [13]. On October 17, 2002, the US District Court for the District of Columbia has barred the FDA from enforcing pediatric exclusivity holding that the FDA did not have the authority to issue Pediatric Rule [21]. However, the US Congress reinstated the exclusivity and extended to “off-patents” drugs also. As of July 23, 2004, 100 approved drugs have been granted pediatric exclusivity [20].

## 6. The orphan exclusivity

The Orphan Drug Act of 1983 provides market exclusivity for drugs that treat diseases or conditions that affect fewer than 200,000 people in the US There are about 5000 rare diseases that afflict 20 million Americans. Orphan drug products receive seven years of marketing exclusivity after the approval of the drug. This market exclusivity is offered to compounds not patented and also compounds with expired patents. The FDA can approve the same drug for the same indication with the approval of the sponsor or for insufficient supply of the drug [22]. In addition sponsors can receive tax incentives for clinical research, grants for clinical testing

and waiver of user fees. Patients can be added to studies on an ongoing basis thus allowing open protocols.

Initially, manufacturers did not pay much attention to the Orphan Drug Act. However, orphan drug exclusivity was attractive to compounds without patents. There are no price restrictions on orphan drugs. Ten years before the Orphan Drug Act was enacted, only 10 orphan drugs were approved. However, during 1983 to 1994, the FDA designated 600 orphan drugs and approved 111 drugs [16]. More than 200 drugs have been approved under orphan drugs statute.

### **7. The 30-month stay provision**

The FDA cannot approve an ANDA with a paragraph IV certification if brand-name company that receives notice files a patent infringement suit within 45 days of the notice. The FDA needs to wait until the patent expires, a court invalidates the patent, or 30 months elapse. This strategy has helped companies to delay the introduction of generic drugs. According to an US Federal Trade Commission [19]'s analysis, all brand name companies do not take advantage of this stay. About 72 percent of brand-name companies out of 104 NDA's took advantage of this provision. The median sale of drugs for which patent infringement suits were filed was about \$190 million per year. On the other hand, the products involving no patent infringement suit had net sales of less than \$100 million per year.

### **8. Patenting strategies**

Generics can significantly reduce the market share of brand-name products. Within six months of the introduction of generics for Zantac, its market share plummeted to 7 percent from 24 percent. The sales of Capoten fell from \$146 million to \$25 million within 12 months of patent expiration in the US [3]. With the help from Pharmacy Benefit Manager's and managed care organizations, the market share of brand name companies can fall by one-half in four to six weeks of patent expiration [23]. When Prozac went generic in August 2001, Express Script Inc., a Pharmacy Benefit Manager, converted three-fourths of its prescription for Prozac to generic within 12 weeks. Within 2 months of going generic in late January 2002, more than 80 percent of prescriptions for the oral antidiabetic agent Glucophage were captured by the generics and within six months, that percentage was 90 percent [4]. It is therefore important for every company to have a patenting strategy.

Filing a vast number of patents relating to a drug is a common strategy to delay generics. Traditionally, the pharmaceutical companies filed only a few patents for a drug. They primarily patented the active compound, medical use, formulation, and processes. However, because of effects of patents on market exclusivity and increased profits, the pharmaceutical companies have significantly increased patents

filed for a pharmaceutical product. It is therefore not unusual to patent packaging, dosing, methods of treatment, delivery systems, combinations, biological targets, and screening methods.

Body converts the active ingredient of a drug into a metabolite which in turn creates therapeutic effect. Patents have been filed for metabolite with a view to delay the introduction of generic drugs. Polymorph represents different crystalline structure of the same compound. Brand-name companies have used patents of polymorph compounds to delay the introduction of generic drugs. A study by the US Federal Trade Commission [19] indicates that brand-name companies currently file more patents to protect market exclusivity of their products. However, a few companies are using these frivolous patenting to obtain market exclusivity to such an extent that these strategies may be referred to as “abuses”. For example, a patent was obtained for a new dosing schedule involving taking a quarter of the pill at a time and slowly building up to taking the whole pill. This patent was used to delay the generic version of Ultram. A kit in which the pills of Fosamax can be rearranged is used to obtain patent and delay its generic introduction. A container for Pulmicort, an asthma medication, is patented to delay generic introduction. A computer program that could be used to dispense Thalomid, a cancer drug, was patented to delay its generic introduction [17].

Patenting strategy should be formulated as soon as a novel lead compound is patented. The first product to replace new compound could be an incremental product. This incremental product may belong to the same chemical class with a chemical structure with similar mechanism of action. This incremental product must be patentable. For example, Nexium, the new antiulcerant drug, is made from a purified form of the active ingredient of Priloses [9] Some strategies to increase the attractiveness of the product include reducing dosages per day, making smaller capsules, improving safety, increasing dosages and so on.

The next step is to introduce second generation drugs with significant improvements. The second generation drugs could focus on improved safety, fewer side effects, better quality of life, fewer doses and so on. Bristol-Myers Squibb’s strategy of introducing Monopril as an incremental drug to Capoten followed by Irbesartan, and Eli Lilly’s strategy of introducing Ceclor as an incremental drug to Keflex followed by Lorabid are examples of this strategy [12].

Changing formulation is another strategy to add life into product with expiring patents. Changing formulation may require new processes which could be patented. Even though the process patent is a weak form of patenting and is hard to enforce, it could act as a deterrent to introducing generic versions. New formulation strategy is considered to be the best alternative as it produces the highest return with ten more years of market exclusivity and expanded market. The cost of introducing new formulation is estimated to be between \$10 million to \$50 million [10].

The introduction of new delivery methods can improve performance and attractiveness of drugs. The new drug delivery methods are useful to expand market, identify new indications, extend product life cycle, and produce new opportunities.

Table 1  
Summary of Market Exclusivities

Description	Description	Duration	ANDA Filing
Patents	Compound, medical use, process, formulation	20 years from the date of filing.	Before patent expires.
Patent Term Restoration	To make up for time lost in clinical testing and FDA approval time	Maximum 5 years for the lost time. Time from NDA approval until patent expiry may not exceed 14 years.	Before patent expires.
The Paris Convention	Patents	Allows an inventor who files for patent in any member nation one year to file patent in any other member nation	
Waxman-Hatch Exclusivity	Drug (new chemical Entity) approved by the FDA	5 years from the date of drug approval (plus ANDA approval time).	Only after market exclusivity time expires.
Waxman-Hatch Exclusivity	Drug (Not a new chemical entity) approved by the FDA	3 years from the date of drug approval (plus ANDA approval time).	Only after market exclusivity time expires
Orphan Drug	Drugs with indications with less than 200,000 US patients.	No approval of same drug for same indication for 7 years	
Pediatric Exclusivity	Granted for studies done for drugs requested by the FDA. Not available to drugs without any exclusivities.	6 months added to existing exclusivity periods (more than one exclusivities are possible).	
First-to-challenge exclusivity for generics	First company to file ANDA with paragraph IV certification.	180 days from the date of first commercial marketing or court decision favorable to generic company.	No other ANDA will be approved for generic introduction during 180 day exclusivity
The 30 month stay provision	Brand-name drug manufacturer against whose drug ANDA with paragraph IV certification has been filed and brand-name company sues for patent infringement.	Until (1) the date patent expires, (2) court decision, (3) 30 months from the date of receipt of notice of the paragraph IV certification	Currently, only one stay is allowed.

ANDA – ANDA, NDA – New Drug Application.

The new drug delivery systems are so important to the pharmaceutical industry that drugs incorporating them account for about 13 percent of the global pharmaceutical market [7]. A typical way to go to incorporate new delivery methods is to form collaboration with drug delivery companies. A variety of new delivery including through lungs and skin are currently available [6].

## 9. Litigation

Evergreening is a patenting strategy which involves repeated use of 30-month stay provision to delay the generic introduction for many years. The goal is to list more patents in the Orange Book which in turn forces generic applicant to file paragraph IV certifications. This strategy has helped companies to delay generic competition for several years. The US Federal Trade Commission [19] report describes this strategy in great detail. The report presents 8 drugs with multiple stays. The total sales during these delays would be between \$16 billion and \$22 billion. Paxil with a sales over \$1 billion had 5 stays and delayed generic introduction by 65 months. The Federal Trade Commission report analyzed all ANDAs with paragraph IV certifications from 1992. The brand-name companies did not sue 1 in 4 applications with paragraph IV certifications. Most of these products had sales less than \$100 million per year compared to median sales of \$190 million per year for products for which brand-name companies sued. Out of 75 suits filed by the brand-name companies, 22 suits were pending at the time of the study. Out of 53 cases, 20 were settled. The settlements involved license agreement, supply agreements, agreement with brand payments, and other provisions. Twenty-two out of 53 lawsuits, the generic manufacturers prevailed. In 9 of these 22 cases, court held that the ANDAs did not infringe and other 9 brand name company's patents to be invalid. Out of 40 cases involving patent infringement, the generic companies won 29 cases. In 11 cases out of 40 at least one patent was held to be invalid. The Medicare Prescription Drug, Improvement and Modernization Act (MMA) of 2003 does not any more allow more than one 30 month stay.

## 10. Conclusions

Market exclusivity acquired through patents can yield higher prices and profits for pharmaceutical products. Therefore, the pharmaceutical companies use a variety of strategies of to increase market exclusivity of their products. Table 1 summarizes various strategies pharmaceutical companies use to extend patent-terms. The Paris convention, patent term restoration allowed by the Waxman-Hatch Act, orphan drug exclusivity, pediatric exclusivity, and the 30-month stay provision represent some strategies to maintain market exclusivity and delay introduction of generics. Even though, the strategies discussed in this paper are for the United States, they may be applicable to most European countries, Australia, New Zealand, Japan, and Canada with minor modifications as similar pharmaceutical regulations exist in these countries.

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