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Evergreening ï A Controversial Issue in Pharma Milieu*

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A patent is an exclusive right awarded by the intellectual property (IP) authority of a state to an inventor or his assignee for a limited period of time in lieu of disclosure of an invention for the benefit of mankind. In recent times, it has become a practice by a number of innovator companies to extend the patent term of their innovative molecules to maintain market dominance. The extension of monopoly term ôEvergreeningô is a predominant aspect of pharmaceutical patenting. ôEvergreeningô refers to different ways wherein patent owners take undue advantage of the law and associated regulatory processes to extend their IP monopoly particularly over highly lucrative ôblockbusterô drugs by filing disguised/artful patents on an already patent-protected invention shortly before expiry of the óparentô patent. These artful patents tend to protect delivery profiles, packaging, derivatives, and isomeric forms, mechanism of action, dosing regimen, and dosing range, and dosing route, different methods of treatment, combinations, screening methods, biological targets and field of use for the same old molecule. This provides the innovator companies sufficient time to recoup their controversially estimated R&D costs. Patent monopolies thus should be designed to function at an optimum level wherein maximum incentive is accorded to investment in research followed by simultaneous accessibility of the protected inventions to the public. The TRIPS compliance has compelled pharma industries of the developing countries to innovate in order to cater to the requirement of current and future drugs. This paper covers different aspects of ôevergreeningô, its impact in the pharma IP domain and identifies means adopted for limiting evergreening.

Keywords: Evergreening, TRIPS Agreement, Hatch-Waxman Act, market exclusivity, patent strategy, generics, paroxetine

ôEvergreeningô is an aspect of patenting that leads to ópatent life cycle enhancement techniqueô largely employed by the pharmaceutical organizations to develop ôbullet proofô patent portfolios around lucrative drug molecules .This is done in an artful manner by protecting a large number of inventive aspects over the basic invention (viz. NCE, NME, formulations etc.) by avoiding any imminent double patent rejection and eventually leading to extension of patent terms to a further 20 year term for a single drug product. Protection on such family of so called ôlucrative moleculesô can at times act as a jackpot to the multinational pharmaceutical organizations and continue to retain market monopoly. However, ôEvergreeningô perspective leads to the extension of patent terms provided the national patent law allows such flexibilities.[1]

The different methods to cover adjunct possibilities not disclosed in the basic patent are done by filing of continuation patent application, divisional patent application, continuation-in-part patent application, and application for patent of addition. ôEvergreeningô is a clever way of inducing extortion/threats to competitors in the market about an innovatorôs tactical use of patents which results in potential loss to the competitors.[2] Innovators thus erect ópicket fencesô or families of dozens of patents around a single drug product and block a possible entry into the domain of the innovator.

The controversial ôEvergreeningô raises a number of fundamental issues. Unless the later applications disclose independent inventions, though linked to the invention disclosed in the basic application, the allowance of the later application(s) can lead to double patenting. Further, inclusion of multiple inventions (consequently multiple independent claims) in a single application can lead to objection on the grounds of óunity of inventionô.

TRIPS Perspective

The TRIPS Agreement awards a negative monopoly over rivals from using patented invention without consent of the patent holder for a term of 20 years irrespective of the field of technology.

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Article 27.1 of TRIPS stipulates that ó*patents shall be available for any inventions, whether products or processes, in all fields of technology without discrimination, subject to the normal tests of novelty, inventiveness and industrial applicability. It is also required that patents be available and patent rights enjoyable without discrimination as to the place of invention and whether products are imported or locally produced'*. Its features involve maintaining standards, causing enforcement and dispute settlement in varied areas of IP. It has ensured protection of IP of pharmaceutical companiesô thus indirectly enhancing patient compliance by providing access to essential medicines at cost effective price.[3] The signatories to the TRIPS adhere to strict regulations wherein minimum standards are maintained in order to provide product patents for pharmaceuticals and chemicals. This further increases growth of pharmaceutical industries, thus facilitating the birth of a wider range of inventions and subsequently aid in providing affordable medicines for different diseases and disorders.

Although TRIPS has provided stricter standards to provide patents for pharmaceuticals and chemicals and facilitate growth of wider range of inventions, there is still a dilemma which is faced by a number of pharmaceutical companies working in HIV/AIDS programmes in majority of developing and developed countries as they do not have adequate manufacturing capacity which results in compromised access to medicines for treatment of HIV/AIDS. This lead to an uproar in the public which forced WTO member countries to adopt a declaration in the Doha ministerial meeting, ó*The World Trade Organization's Declaration on the TRIPS Agreement and Public Health of 2001'* that affirmed the flexibilities available under the TRIPS Agreement to member states seeking to protect public health.

Although the Doha Declaration supports important principles under the TRIPS Agreement still challenges are being faced with respect to the international trade law regarding protection of public health. Developing and under-developed countries are facing acute pressure on access to export markets in well established industries in developed countries and have to prioritize trade over public health protections. This is disadvantageous to the said developing and under-developed nations which have to compromise public health over trade. Thus, one choice is for the global community to allow the Doha Declaration to follow high politics of trade policy and push access to medicines by the poor even further out of reach ó*OR*ô to give priority to public health protections available within the TRIPS Agreement. Debate is still going on and the Doha rounds have still not been able to deal with this aspect in the international perspective particularly with respect to the developing and the least developed nations.

Evergreening Strategies in Pharma

A number of strategies have been followed by the innovator companies to extend the term of patent, viz. methods of treatment, mechanism of action, packaging, derivatives, isomeric forms, delivery profiles, dosing regimen, dosing range, dosing route, combinations, screening methods, biological targets and field of use. These strategies involve skilled addition of patents to the product by the innovator companies that force the generic manufacturer to maintain forbearance for all the patents to expire and applying for marketing authorization (as and when applicable), bearing the risks of litigation and associated penalties and delays.[4] The innovator companies in the name of ólife-cycle managementô maximize revenues from their so called ó*evergreen*ô products and choke generic competition at the outset of product life-cycles. Although the strategies followed by the innovator companies foray through strictest legal framework, the irony is that still most of these companies represent misuse of pharmaceutical patents and regulations governing authorization.

Evergreening strategies that have been usually followed by the pharmaceutical industries involve: (a) redundant extensions and creation of ónext generation drugsô which result in superfluous variation to a product and then patenting it as a new application, (b) prescription to OTC switch, (c) exclusive partnerships with cream of generic players in the market prior to patent expiry thus significantly enhancing the brand value and interim earning royalties on the product, (d) defensive pricing strategies practice wherein the innovator companies decrease the price of the product in line with the generic players for healthy competition and (e) establishment of subsidiary units by respective innovator companies in generic domain before the advent of rival generic players.[5] Strategies employed find a basis in a classic example on a patent obtained on loratadine (Claritin) by an innovator company, Schering. Schering applied for and obtained 46 months of patent extension owing to regulatory review time and changes in patent laws, giving it nearly 21 years of patent protection, which surpasses the standard 20 year time frame.[6]

Schering sought other probable ways to extend its market exclusivity by patenting the compound desloratadine which metabolizes to loratadine in the body. Patent on desloratadine was challenged in the court and was eventually overturned because desloratadine was ónecessarily and inevitablyô formed in every patient, and generic loratadine was ultimately marketed in 2002.[7]

Patenting and Pharma Research Costs

TRIPS Agreement has laid down the standards wherein the companies under its aegis enjoy monopoly for a guaranteed time frame. Pharmaceutical organizations pour resources into R&D of various molecules for the benefit of mankind. The development of a pharmaceutical goes through a series of permutations and combinations resulting in uncertainties which could be many and substantial. Maximizing the certainty that a research-based manufacturer can obtain, enforce, defend, and make full, legitimate use of IP rights is essential to maintain the cycle of innovation for the benefit of public health. In the absence of strong IP rights at each stage of the innovation cycle, promise of pharmaceutical innovation could be lost.[8]

Pharmaceutical products often rely on substantial amounts of upfront investment and technical knowledge and for the resources involved, companies eventually secure patents for every product they develop. The pharmaceutical companies screen large number of molecules and out of the thousand potential drugs screened, only 4-5 reach clinical trials stage form, of which finally one is approved for marketing. It costs on an average around 800 million dollars to develop and test a new drug before it is approved for use. In the case of pharmaceutical companies, monopolies over the fruits of their R&D efforts are vehicles through which they could recoup huge investments. The costs of research done on screening out the molecule and taking into clinical trial stage are recovered through appropriate pricing mechanisms from the patients who receive the patented drugs. Providing market exclusivity to an inventor through patent protection can encourage the initial outlay of resources needed to develop the product.

Further, capital investment by the innovator companies in the development of new molecules which have reached the stage of marketing also encourage the challenge to invest more in further research, development and refinement of related innovations to expand and improve therapies and cures. Moreover, due to innovation in providing products of medicinal importance, patent protection on the same creates a platform wherein generic companies compete with research oriented innovator companies following the expiration of IP rights. After the patent on a drug expires, any pharmaceutical company can manufacture and sell that drug. Since the drug has already been tested and approved, the cost of simply manufacturing the drug will be a fraction of the original cost of testing and developing that particular drug. e.g. LamictalÊ is an anticonvulsant medication (active ingredient: lamotrigine) sold by GlaxoSmithKline (GSK) for use in the treatment of epilepsy in adults and children. LamictalÊ is indicated as adjunctive therapy for partial seizures, generalized seizures of Lennox-Gastaut syndrome, and primary generalized tonic-clonic seizures in adults and pediatric patients. LamictalÊ is indicated for conversion to monotherapy in adults with partial seizures who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as the single AED. GSK had applied the patent for the active ingredient in 1980 which expired in many countries in 2000. LamictalÊ is marketed as chewable/dispersible tablets which may be swallowed, chewed or dispersed in water or diluted fruit juice (swallowing the resulting liquid dispersion). GSK also applied for a patent in 1992 for the chewable/dispersible tablet formulation of lamotrigine which will expire in most of the countries in 2012. The chewable tablets have the advantage of providing ease of use and compliance to patients. An earlier patent claiming lamotrigine as the active ingredient had already expired in many European countries. This provided the scope of use of the particular patent in European territories. It could be comprehended that any generic manufacturer could make the formulation and compete with the innovator product. Several such generic products are being sold, and it depends on the market that has the option to choose between the original GSK product and a generic version.[9]

Innovator Products or the Generics-Which Stays Ahead?

Patent is a form of insurance policy for inventors, including research-based pharmaceutical companies. It is well comprehended that prescription drug products pose risk, expense, and take time for their development out of which only a small number of prescription drug products actually make it to market.

Prescription products are classified by therapeutic categories. Although patents inhibit other counterparts from entering into the domain of original patent filers, patents do not prevent other counterparts from producing and marketing different medicines to treat the same disease in a given therapeutic category. One of the categories well documented is the COX-2 inhibitors which are generally used in the treatment of arthritis in patients. Varied kinds of prescription and nonprescription treatment options for arthritis are available in the market. NSAIDs which come under COX-2 inhibitors are used to treat the pain and inflammation associated with arthritis. COX-2 inhibitors from the recent past have gained prime importance as they could decrease the side effects of gastric bleeding and ulcers as compared to prescription of more traditional NSAIDs. However, serious cardiac events associated with some of the COX-2 products could not be avoided. Further, COX-2 products are considerably more expensive than the prescription NSAIDs. The cost comparison factor would be taken into account while prescribing the product to the patient. Furthermore, each patient shows a particular response to particular medication and taking this into consideration an older medicine with a generic equivalent may be prescribed as the best treatment option.[10]

Generic applicants for the respective innovator drug products have to be very diligent in filing their applications. Every innovator patent that is set to expire, a prodigious amount of investment is at risk for innovator companies, generic firms and consumers. The Federal Trade Commission (FTC) has been monitoring the patent disputes between innovator and generic companies and is particularly concerned about the possible anticompetitive practices followed by innovator pharmaceutical companies in using the 30-month stay and the 180-day marketing exclusivity provisions of the Hatch-Waxman Act.

The FTC has identified different anticompetitive practices that aid ôEvergreeningô such as Tottered orange book listings, brand migration, unhealthy agreements/trading between innovator and generic companies and unhealthy agreements/trading between generic companies.

Tricky Orange Book Listings

In the United States, a generic company before launching its product in the market has to file paragraph certifications against each and every patent listed in the Orange Book for the innovatorôs product. This gives opportunity to the brand companies to delay listing of some of their patents in the Orange Book. The brand company has the advantage to sue the generic company which thus induces an automatic 30-month stay, regardless of the merits of the new patent. A stay on each patent triggers automatic delay in the corresponding generic approval of the product (until the stay expires or the court resolves the dispute) which helps the innovator companies to extend their market exclusivity indefinitely. This tricky way used by the innovator companies to achieve multiple 30-month stays has led to anticompetitive practices which has drawn the attention. It was argued that Congress was never in favour of more than one 30-month stay on a given product. Finally, the Medicare Modernization Act of 2003 (MMA) brought significant changes in the multiple 30-month stay period wherein single 30-month stay was applied to a particular product.

Brand Migration

Innovator companies use ôbrand migrationô as an alternative in order to extend product life cycles and delay competition wherein when one ôbrand nameô productôs patent and its associated exclusivity is near expiry, innovator companies start directing patientsô attention to the companyôs other product viz. a new branded product that is heavily promoted to both patients and physicians. For example, Astra Zeneca before expiration of the product patent on Prilosec (Omeprazole) started an attempt to move patientsô attention towards its patented successor product , Nexium (Esomeprazole Magnesium). Thus, in a way by ôbrand migrationô these companies extend product life cycles.

Unhealthy Agreements/Trading between Innovator and Generic Companies

This anticompetitive practice is followed widely by innovator companies which try to prevent the entry of corresponding generic product in the market. The innovator companies conspicuously come to an agreement with the generic manufacturers to delay or eliminate specific generic drugs from entering the market.[11] The landmark example is the case of Tamoxifen sold by Zeneca under brand name ôNovaldexô with US sales of $ 265 million in 1992 which rose to $ 442 million in 2001, last full year sales prior to generic entry. Zeneca and first filer Barr reached an agreement in March 1993 wherein Zeneca agreed to pay $ 66.4 million: $ 21 million to Barr, and $ 9.5 million immediately and $ 35.9 million over ten years to Barrôs raw materials supplier , Heumann.

Further, in addition to cash, Barr received compensation through profitable private label sales. Zeneca allowed Barr to sell Zeneca made tamoxifen under Barrôs label. The licensed version sold at 15% discount to Zenecaôs version. Barr soon captured most of the market. Barr also retained potential entitlement to the exclusivity period, without fear of losing it by a patent suit. Barr initially changed its Paragraph IV certification to Paragraph III, thereby certifying that it would wait to enter until patent expiration. Yet Barr later reverted to a Paragraph IV certification, and asserted its continued entitlement to the 180 day exclusivity period when generic firm, Mylan gained FDAôs tentative approval to market a generic product. As per Zeneca, the settlement would have neutralized the first filer threat, by removing from litigation the single firm, Barr, with entitlement to the 180 day exclusivity period. The settlement also created a partial obstruction as Barrôs falling back to a Paragraph IV assertion limited the prospect for approval of later filers. Barr agreed to enter with its own ANDA product until August 2002 after the expiration of Zenecaôs US Pat No 4,536,516. Generic manufacturers entered soon after the expiration of the patent. One further unusual feature of the agreement was that the parties agreed to seek vacatur of the District Courtôs ruling that the relevant patent was invalid. The Federal Circuit granted vacatur.[12]

Unhealthy Agreements/Trading Between Generic Companies

In *FTC* vs *Mylan Laboratories Inc*, the FTC and several states sued Mylan, charging Mylan and other companies with monopolization, attempted monopolization, and conspiracy for elimination of agreements for Mylanôs competition by tying up supplies of the key ingredients for two widely-prescribed anxiety drugsô lorazepam and clorazepate. The FTC posed a penalty of atleast $120 million based on its estimate of Mylan's profit from price increases it had implemented for these drugs. The charges were due to a government assault on the generic pharmaceutical industry. FTC stated that attorneys general from 10 states-Connecticut, Florida, Illinois, Minnesota, New York, North Carolina, Ohio, Pennsylvania, West Virginia and Wisconsin-filed companion complaints in Federal District Court on behalf of consumers and state agencies seeking unspecified damages from Mylan. Private class action suits were filed against the company in Florida and California. As per the FTC, Mylan restrained trade by signing an exclusive deal in 1997 with Profarmaco SRL of Milan, the largest supplier of raw materials for the drugs lorazepam and clorazepate, and conspired to obtain monopoly power in the United States through exclusive licensing arrangements for the supply of those raw materials. The plausible reason for the suit filed by FTC was that in January 1998, the company significantly raised its prices to wholesalers, retail pharmacy chains and other customers which hiked the wholesale price of clorazepate from $ 11.36 to approximately $ 377 per bottle of 500 tablets; and in March, the wholesale price of lorazepam was raised from $ 7.30 for a bottle of 500 tablets to approximately $ 190.[10]

The Indian Perspective

The Patents Act, 1970 allowed patent grants to only processes but not products and further encouraged R & D and domestic competition while protecting interests of the patent holders. In order to create a foothold in the international market, the Patents (Amendments) Act 2005 came into effect from 1 January 2005 which was TRIPS compliant. The TRIPS compliant patent system encouraged third parties interested in the product to file pre -and post- grant oppositions. The definition of patentability was also modified to prevent evergreening and further fresh patents would not be granted for new indications for drug use.

During the ten year period wherein the ómailbox applicationô filings were under progress, myriad pharmaceutical companies filed patent applications containing claims directed at ósubstances capable of being used as food, medicine or drugô. However, it was estimated that, roughly 40-45 new drug molecules were discovered in the last 5-10 years. Taking into the discovery of few molecules, there was a lot of speculation amongst the pharmaceutical sector that a majority of these patent applications were claiming secondary inventive aspects. These secondary inventive aspects could be protected by addition of new claims using effective intelligent routes of continuation patent application, divisional patent application, continuation-in-part patent application, and application for patent of addition. But ôEvergreeningô is still not an easy task. Careless and frivolous filing of patent applications pose the threat of double patenting if the new applications filed for the basic application do not claim or disclose the independent inventions or inventive aspects, though linked to the invention disclosed in the basic

application, the allowance of the later application(s) can lead to double patenting. Other option is to file multiple inventions in a single application. However, such practice may ultimately lead to objection on the grounds of lack of ólunity of inventionô. Thus, the objection on ólunity of inventionô could be bypassed by filing divisional as the effective date of filing of a divisional application is the same as the date of filing of the basic application which may not contribute to patent term extension or óEvergreeningô.[13]

Taking into the amendments in the Patent (Amendments) Act 2005 wherein the scope of patentability was restricted by expounding mandated terms , namely, inventive step and new invention, it could be expected that óevergreeningô of NCEs and NMEs will be restricted in view of negative coverage against patent extensions. Further, as most of the applications filed as mailbox applications related to NCEs and NMEs involved minor improvements, the said applications shall be ineligible for grant of product patents due to lack of inventiveness and thus negating the impact of *'Evergreening'*.

Paroxetine-A Case Perspective

A landmark case exemplifies the judicial support to ólanticipationô and ócevergreeningô. The case study relates to a famous anti-depressant drug:, paroxetine hydrochloride , sold as Paxil® in US. PAXIL (paroxetine hydrochloride) is an orally administered psychotropic drug. It is the hydrochloride salt of a phenylpiperidine compound identified chemically as (-)-trans-4R-(4'-fluorophenyl)-3S-[(3ô,4ô-methylenedioxy-phenoxy) methyl] piperidine hydrochloride hemihydrate and has the empirical formula of $C_{19}H_{20}FNO3.HCl.½H_2O$.

Following a bench trial, the United States District Court for the Northern District of Illinois determined that the generic paroxetine hydrochloride anhydrate product to be produced by Apotex Corp, Apotex Inc, and TorPharm, Inc (collectively Apotex) will not infringe claim 1 of US Pat No 4,721,723 (õ723 patent) owned by SmithKline Beecham Corp and Beecham Group, PLC(collectively SmithKline), *SmithKline Beecham Corp* v *Apotex Corp*, 247 F. Supp. 2d 1011, 1052 (N.D. Ill. 2003). Based on this courtôs revision of the trial courtôs erroneous claim construction, Apotexôs product would infringe claim 1 of the õ723 patent. Nonetheless, because claim 1 of the õ723 patent is invalid as anticipated under 35 U.S.C. § 102(b), this court affirms the District Courtôs judgment in favour of Apotex.

Ferrosan, as inventor obtained US Pat No 4,007,196(the'196 patent) entitled ó4-Phenylpiperidine compoundsô which claimed man-made compounds known as paroxetine and its salts. Ferrosan licensed the ô196 patent to Smithkline Beecham (SKB), who began producing paroxetine hydrochloride (PHC), the crystalline hydrochloride salt of paroxetine. In 1985 during the production of hydrochloride salts of paroxetine, one of the chemists Alan Curzons working in the lab of SmithKlineôs Worthing, England laboratory noticed that PHC molecules in SKBôs laboratory created a different form of PHC on contact with water which was termed as hemihydrate of PHC. It might be emphasized that the original form discovered by Ferrosan was known as an anhydrate. SKB further discovered one of the batches which were produced in December 1984 contained PHC hemihydrate as well. The hemihydrate form proved to be more stable as compared to anhydrate (no water molecules) as the hemihydrate contains one molecule of water for every two molecules of PHC and thus more easily packaged and preserved than PHC anhydrate.

SmithKline filed a patent application in the British Patent Office on 25 October 1985 relating to ócrystalline paroxetine hydrochloride, its preparation and its use as a therapeutic agentô. The application covered both hemihydrate and anhydrate form of PHC, as well as mixtures that contain a major portion of either form. With the discovery of PHC hemihydrate, SKB filed a patent application a year later on 23 October 1986 claiming priority to the British application wherein the said application claimed the crystalline paroxetine hydrochloride hemihydrate, PHC hemihydrate in substantially pure form, in a particular configuration, and related manufacturing and treatment methods for which SKB was issued a US Pat No 4,721,723 on 26 January 1988. The õ723 patent did not claim PHC anhydrate and did not claim mixtures of the two PHC forms. SKB started marketing PHC hemihydrate under the brand name Paxil® after getting the necessary FDA approval in 1993. The õ723 patent that was issued claiming PHC hemihydrate was to expire in December 2006. Way back in 1998, Apotex Incorporation filed Abbreviated New Drug Application (ANDA) in the USFDA to market a generic equivalent of PHC anhydrate claimed in ô196 patent (under 21 U.S.C. § 355(j)(2)(A)(IV)) which stated that Apotexôs generic product would not infringe the õ723 patent listed for SKBôs paroxetine hydrochloride hemihydrate product. The ô196 patent had already expired in 1992.

Apotex was seeking removal of six patents listed in the Orange Book as these patents were serving as delaying the launch of its paroxetine hydrochloride anhydrous drug. Out of the six patents listed in the Orange Book, only one claimed the hemihydrate product and the rest five patents did not claim the drug approved by FDA under the original new drug application.

On receiving the notice from Apotex, SKB filed a complaint in the district court alleging act of infringement under U.S.C. § 271(e)(2) and sued Apotex for act of infringement of the õ723 patent. SKB requested 30 month automatic statutory stay of FDA approval of Apotex's ANDA under the Hatch-Waxman Act. The case was mainly w.r.t claim 1 which claimed ó*Crystalline paroxetine hydrochloride hemihydrate.'* It came into focus that SKB did not allege that the õ723 patent covers PHC anhydrate (Apotex's active ingredient) as the same was claimed in ô196 patent, which would constitute prior art for õ723 patent. SKB contested that Apotexôs antidepressant drug would infringe the õ723 patent because Apotex's PHC anhydrate tablets necessarily contain, by a conversion process, at least trace amounts of PHC hemihydrate. The parties filed various summary judgment motions, including cross motions for summary judgment that claim 1 of the õ723 patent was invalid (or valid) under 35 U.S.C. § 102(b) for an impermissible public use. The district court did not invalidate claim 1 because the ôhemihydrateô was in public use more than 12 months before the US patent application claiming the ôhemihydrateô was filed. The public use was a clinical trial in which the doctors and patients knew what compound was being tested. SKB asserted that the clinical trial was an óexperimental use,ô rather than a public use. However, on a further bench trial, the District Court held that the clinical trial only tested the safety and efficacy of the hemihydrate as an antidepressant, not any claimed feature or limitation of ócrystalline paroxetine hydrochloride hemihydrateô; therefore it was not an óexperimental useô with respect to claim 1. The District Court subsequently invalidated claim 1 as the clinical trial was deemed a public use which occurred more than 12 months before the patent application was filed.

Further claim 1 was also invalidated on grounds of inherent anticipation by the prior art covered by the ô196 patent. 35 U.S.C. 102(b) of the US Patent Law mentions that a patent claim is invalid if ó*the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country more than one year prior to the date of the application for patent in the United States'.*[14] As per SKBôs own argument, Apotexôs anhydrous product, containing the active ingredient PHC anhydrate on conversion produced trace amounts of PHC hemihydrate, which was already claimed in SKBôs õ723 patent. However, the ô196 patent assigned to Ferrosan served as a prior art already covering PHC anhydrate which as per SKBôs argument converted to include at least trace amounts of PHC hemihydrate claimed in the õ723 patent. It could be ascertained that the prior art invention (ô196 patent) ultimately got converted into SKBôs PHC hemihydate invention, unknowingly when the ô196 patent was issued and thus inherently anticipated SKBôs õ723 patent. Thus, the õ723 patent was invalidated and anticipated under 35 U.S.C. 102(b). In other words, the PHC hemihydrate was serendipitously made attempting to make the licensed PHC anhydrate under the ô196 patent. It could be concluded that although the ô196 patent did not literally disclose PHC hemihydrate - it inherently disclosed the compound because the compound was naturally present as a result of the conversion process which SKB mentioned during argument in the District Court. The Federal Circuit in its decision affirmed District Courtôs decision that ó*claim 1 of the '723 patent is invalid for inherent anticipation by the '196 patent under § 102(a). Apotex is, therefore, not liable for infringing claim 1 of the '723 patent.*"[15] Apotex subsequently launched its paroxetine product in September 2003, after receiving final approval from the FDA.[16]

The learnings of Paroxetine case could be summarized as: (i) protection of a new form in the pretext of an earlier known prior art may lead to anticipation and invalidation, and (ii) superfluous patenting by just filing multiple applications in order to extend the patent life might lead to rejection of patents.

Countries like US and Europe have laid down various regulations in order to curb down the menace of ôEvergreeningô which are governed by the statute. In US sections such as *35 U.S.C 102(b)* which states ó(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United Statesô; *35 U.S.C 103(a)* which states that óA patent may not be obtained though the invention is not identically disclosed or described as set forth in

Section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was madeô and *35 U.S.C 271 (e) (2)* which relates to infringement of patent, are various regulations which keep a check on ôEvergreeningô. European regulations are governed by Article 54 which relates to novelty and Article 56 which relates to inventive step. The same can be witnessed by increase in number of such cases of evergreening being addressed by the courts which indicates the aspect that generic manufacturers have successfully used in the provisions of law to counter evergreening methods adopted by innovator companies.

Conclusion

Patent evergreening promotes development of unfair means of competition and related abuse. Enhanced IP scrutiny may remove the curse of these unfair practices which are widely followed by the innovator companies to create a roadblock for generic companies that are trying hard to provide safe and efficacious medicines to the masses at cost effective prices. Landmark case decisions may serve as an aid to understand the complex domain of ôEvergreeningô. There is a need for developing countries to develop and foster effective mechanisms to counter evergreening practices of innovators. It is important to promote innovations of big companies and at the same time honour efforts put down by the generic companies so that with equal balance, cost effective products are launched in the market, thereby benefiting the masses.

References

1 Bakshi G, Pooja Singh S, Section 3 (d) of Indian Patent (Amendment) Act, 2005: A case perspective, *Pharmabioworld*, 7 (7) (2009) 16-22.

2 Temmerman, Michelangelo, The TRIPS Agreement, the Evergreening of Patents and Access to Medicines: *Novartis* v *India* (2008), 1-49.

3 Ragavan Srividhya, A patent restriction on research & development: Infringers or innovators? *Journal of Law, Technology & Policy*, 1(73) (2004) 73-98.

4 Anantharaman M G, Evergreening of patents, http://www.training.iprsupport jpo.jp/en/modules/smartsection/item.php?itemid=56.

5 Hunt M I, Prescription drugs and intellectual property protection, NIHCM Foundation, (2000) 1-12.

6 *Schering* v *Geneva Pharmaceutical*, 339 F3d 1373 (FCCA 2003).

7 Glover Gregory J, The influence of market exclusivity on drug availability and medical innovations, *AAPS Journal*, 9 (3) (2007) E312-316.

8 Andrade C, Shah N, Chandra S, The new patent regime: Implications for patients in India, *Indian Journal of Psychiatry*, 49 (1) (2007) 56-59.

9 GlaxoSmithkline briefings, (2007), (discussing evergreening and basic principles of the patent system), www.gsk.com/policies/GSK-and-evergreening.pdf.

10 Strongin Robin J, Hatch-Waxman, Generics, and Patents: Balancing Prescription Drug Innovation, Competition, and Affordability, *NHPF Background paper*, (2002) 2-19.

11 Scott Hemphill C, Drug Patent Settlements between Rivals: A Survey, 2007, 1-49, http:// papers.ssrn.com/ sol3/ papers.cfm?abstract_id=969492.

12 Mylan Labs denies antitrust charges by FTC, http://findarticles.com/p/articles/mi_m3374/is_/ai_53617533.

13 Analysis of ñMailboxò Applications with special reference to Public Health, 2-110, http://www.whoindia.org/LinkFiles/Trade_Agreement_part2_annexure.pdf.

14 http://www.cafc.uscourts.gov/opinions/03-1285.pdf .

15 http://www.usdoj.gov/osg/briefs/2005/2pet/6invit/2005-0489.pet.ami.inv.pdf.

16 http://www.apotexcorp.com/press/Paxil_generic_04262004.htm.