Pharmaceutical Business Strategy: A Generics Perspective

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Received 2 August 2012

With most blockbuster drug patents facing patent expirations, there is the threat of generic equivalents pervading and diluting the innovator market. This patent cliff is not only making the market more attractive to the established generic drug makers, but is also inviting innovators’ interest in generic expansion. This article discusses the generic product entry routes in different jurisdictions (US, Europe and India) in the light of the nuances in legal provisions. It focuses on the various levels available for the entry of generic drug products such as safe entry, at-risk entry or by exploring licensing options. The article further discusses some strategies employed by innovator companies in order to extend the commercial benefit over a drug even beyond the term of the patent or related exclusivity. It discusses various business tactics employed by innovator companies such as development of follow-on drugs, creation of patent clusters, authorized generics, extensive branding and marketing, which help to delay or disincentivise the generic drug launch.

Keywords: Pharmaceutical business strategy, generic drug launches, patent and exclusivity expiries, generics

In 2010, the global pharmaceutical market was valued at US$ 875 billion.1 The global generic market which was valued at US$ 87 billion in 2008 is estimated to grow to US$ 135 billion by 2013 (ref. 2). The growth rate in the generic sector is observed to be at a faster pace as compared to the overall market.2 Due to the increase in activity in the generic sector, the new drug developers (or innovator companies) are facing immense pressure by the increase in generic companies claiming their market share by producing cheaper and effective duplicates of the innovator company’s drug products. This increase in generic activity and growth can be credited to mainly; the lure of huge revenues from the blockbuster drugs nearing expiry and the ease of generic entry. Blockbuster drugs are drugs that generate sales of at least US$ 1 billion annually for its creator3; examples for the year 2011 being Lipitor, Plavix, Advair, etc.4 The development of blockbuster drugs is an expensive and time consuming process. The time taken to develop a drug generally varies from 7 to 10 years, with the average cost of developing a new drug being around US$ 500 to 800 million.5,6 However, each of these new drugs runs the risk of not being able to be the next blockbuster drug, or even being a failure.

The generic companies, by developing copycat versions of the blockbuster drugs, are able to leverage on the research and development data and investment of the innovator company in order to claim their bit in the innovator company’s market share. The growth rate in the generic sector, over the last decade, has increased as a result of an increase4 in the number of blockbuster drugs.

In addition to the financial advantage available to generics which lures the pharmaceutical companies into developing generic drugs, the fact that most of the blockbuster drugs are now facing patent expiry is also an incentive to generic interest. Generally, post patent expiry, the generics would be able to flood the market to a level that the pharmaceutical innovator sales are reduced up to 20 per cent of pre-expiry level.7

Indian drug companies have evolved to become one of the top players in the global generic market. This evolution is attributed to patent and regulatory changes in the Indian pharmaceutical sector over the last few decades. One of the most important developments was the introduction of the Indian Patent Act, recognising process patents, in 1970. During the process patent regime which prevailed in India for around 35 years, until 2005, India saw an exponential increase in the number of pharmaceutical companies. It is understood that, under the protected environment of the process patent regime, India strengthened its capabilities to reverse engineer and develop generic versions of new drugs. Post 2005,
with the introduction of the product patent regime, the foreign innovator drug industry discovered a market in India. With the advent of the product patent regime, the Indian pharmaceutical companies positioned themselves in a way such that they could portray dominance in the global generic market. India has now emerged as one of the world’s top exporters in generic medicines.8

Witnessing growth in generic drug industry and fearing the possible decline in revenues i.e. consequential to some blockbuster drug patent expiries, innovator companies themselves have turned towards acquisitions to retain their monopoly in the generic drug market. Pharmaceutical majors such as Novartis and Pfizer have agreements with generic giants such as Sandoz and Aurobindo Pharma, respectively, which exemplify the attempts made by the innovator industry to retain a dominant position in the global pharmaceutical market.9

This article specifically focuses on two aspects, namely, the legal procedures for entry of generics and strategies used by innovator companies to extend revenue streams over expired drugs/drugs nearing expiry. The first aspect will investigate the entry of generic drugs into the market, which may be at various points and also easier as compared to new drugs. Generic drug entry could be: (i) safe entry, i.e. at the end of exclusivity and/or patent expiry; (ii) at-risk entry, by trying to challenge the validity of the patent; or (iii) by exploring licensing and compulsory licensing options. The second aspect will focus on the strategies employed by innovator companies such as creating patent clusters, indulging generic companies in extensive patent litigation, authorized generics, developing follow-on drugs, etc., which help to delay or disincentivise generic drug launch.

Options for Launching Generic Drugs

Safe Launches

In cases where entry is by the safe route, the generic manufacturer would be required to await the expiry of exclusivity and patent term. Hence, in the safe entry option, once the innovator’s drug hits the market, the launch of a generic drug generally faces two main roadblocks. Firstly, there are barriers posed by regulatory (non-patent) exclusivities. Secondly, the drug has to surpass the restrictions posed by patent and related term extensions of the innovator’s drug.

Regulatory (Non-patent) Exclusivities

In most countries the launch of a drug is controlled by a national drug regulatory authority (NDRA). It is a general procedure that any pharmaceutical company that is interested in marketing its products has to receive marketing authorization (MA) from the NDRA. The marketing authorization is granted to the company, provided it is able to establish the quality, efficacy and safety of the drug. Unlike the innovator companies, who are required to submit huge amounts of drug testing and clinical trial data, a generic company is required to only establish bioequivalence to the innovator’s drug. Rather, in many cases, the repetition of clinical trials for drugs that are already known to be safe and effective is considered to be unethical.10 This advantage of bypassing the expensive clinical trial stage, available to generics, is one of the main reasons that allows generics to offer their drugs at highly competitive prices.

USA

In US, companies looking at marketing a drug are required to seek marketing authorization from the US Food and Drug Administration (USFDA). In 1984, with the introduction of the Drug Price Competition and Patent Term Restoration Act (also known as Hatch-Waxman Act), separate marketing authorization processes for new drugs and generic drugs were incorporated. Section 505(b)1 (ref. 11) of the Food Drug and Cosmetic Act describes the application, also referred to as new drug application (NDA), which is applicable for drugs that have never before been approved. Depending on the extent of variation in a drug in comparison to the innovator’s drug, also known as reference listed drug (RLD), Section 505 (ref. 12) further includes two types of applications for seeking MA: 505(j)13 application, also known as abbreviated new drug application (ANDA), or 505(b)2 (ref. 14) application.15 Although, the ANDA and 505(b)2 applicants can rely on the RLD data completely or partially for demonstrating safety and efficacy, which would be expected to facilitate early entry, the exclusivities offered for a product by the USFDA contribute towards delaying the launch of generic drugs. In the US, the product exclusivities include a five year data exclusivity and a three year market exclusivity.

Data exclusivity16 for a period of five years is generally granted to a new drug product containing a new chemical entity, beginning from the FDA approval date. Both, the 505(b)1 and the 505(b)2
applications are eligible for the five year data exclusivity. During this period, the second entrants, 505(b)2 and the ANDA applicants, are not allowed to rely upon the data of the originally approved drug for authorisation. Rather, the FDA will not approve any corresponding 505(b)2 or ANDA application during these five years. The generic approval process that generally takes around 1.5 to 2 years will only begin once the five year data exclusivity period lapses, which further stretches the market exclusivity and delays the generic product launch by 6.5 to 7 years.

Further, in cases where the 505(b)2 or ANDA application includes a Paragraph IV certification, the applicant may file for marketing authorization at the end of 4 years. However, if an infringement proceeding begins within a year and the 30 months stay is forced consequential to filing of Paragraph IV certification, it would contribute towards extending the market exclusivity period to around 6.5 to 7.5 years.

On the other hand, the three year market exclusivity is generally granted for a product containing an already approved chemical entity bearing a modification (e.g.: new indication, dosage form, etc.) which requires new clinical investigation to be performed by the applicant. The 505(b)1 application, the 505(b)2 application and any application supplementary to a NDA are eligible for this three year market exclusivity. As opposed to the five year exclusivity, the three year exclusivity period does not pose a hurdle to the authorization of 505(b)2 and the ANDA applicants during the exclusivity period. Hence, the generic drug can enter the market at the end of three years.

Further, there are other exclusivities provided by USFDA that pose a deterrent to the generic entry including orphan drug exclusivity for a period of seven years, paediatric exclusivity for a period of six months; which attach to any existing exclusivity and to the patent term of all patents listed in the Orange book for that drug.

Europe

In Europe, marketing authorization may be obtained by the centralized procedure or the national procedure. The European Medicines Agency (EMA) deals with the centralized procedure wherein a single application enables the applicant to seek marketing authorization in all the EU member states. Alternatively, the national procedure may also be adopted to receive marketing authorization which is generally used to trade the product in the domestic market. The national procedure recognizes two possible routes of receiving marketing authorization: mutual recognition procedure and decentralized procedure. The mutual recognition procedure and the decentralized procedure enable the applicant to seek marketing authorization in the member state (concerned state) by mutual recognition of the authorization already received in another member (reference state). The decentralized procedure and the mutual recognition procedure are generally the routes used by generic entrants. The decentralized procedure, unlike the mutual recognition procedure, brings in the involvement of the concerned member state at a much earlier stage in the authorization process.

The 2001/83/EC Directive describes the particulars and documents that are to be furnished to the NDRA for seeking MA. It spells out (in Article 10) the various levels at which a generic drug could enter the market. Depending on the variation in the generic drug, the various possible ways of a second applicant’s entrance includes essentially similar abridged application [Article 10(1)], hybrid application [Article 10(3)], bio-similar application [Article 10(4)], bibliographic application [Article 10(a)], fixed combination application [Article 10(b)], and informed consent application [Article 10(c)].

Currently, the 2001 directive provides a data exclusivity period of 6 or 10 years in the EU. Countries such as Austria, Denmark, Finland, Greece, Ireland, Portugal, Spain, Norway and Iceland provide the six year term of data exclusivity. Whereas, a 10 year data exclusivity is provided in countries such as Belgium, Germany, France, Italy, Luxembourg, the Netherlands, Sweden and the UK. The entry of generics could thus be delayed by a minimum of 6 to 10 years depending on the country. Additionally, since the generic drug application would generally take around 1.5 or 2 years to receive MA, the innovator would eventually end up with 7.5 to 11.5 years of marketing exclusivity.

For recent applications, the new 2001/83/EC Directive, as amended by the 2004/27/EC would be applicable. The new 2001 Directive provides a 8+2+1 regime in an effort to harmonize the exclusivity system in EU. Under the 8+2+1 regime, the generic drug application seeking marketing authorization would be considered only after the eight year data exclusivity. The regime also provides a two year
market exclusivity. Additionally, one year of market exclusivity may further be granted, provided it receives an authorization for a new therapeutic indication having significant clinical benefit within the eight year data exclusivity period. Consequently, generic entry may be delayed by 10 to 11 years.

In addition to data exclusivity, the non-patent exclusivities in EU include orphan drug exclusivity and paediatric exclusivity. EU provides a 10 year period of orphan drug exclusivity, during which the NDRA shall not grant or accept any generic drug applications for MA. However, this term may be reduced to six years provided it can be established that the drug no longer satisfies the criteria for orphan drug designation. Further, applications including paediatric studies are entitled to a six month extension of the patent term or the Special Protection Certificate (SPC) term.

India

In India, the Drug and Cosmetics Act, 1940, dictates the requisites to import, manufacture, distribute and market a drug. The central regulatory authority, Central Drug Standard Control Organization (CDSCO) also known as Drug Controller General of India (DCGI), is vested with the responsibility of providing authorizations to new drugs. In India, second entrants with new dosage forms, new indication, vaccines, new fixed dose combination, etc., are considered as new drugs and have to be approved by DCGI. A generic drug seeking authorization of an already approved drug within four years of the first authorization will also be considered as a new drug and, hence, require to seek approval from DCGI. However, an applicant seeking authorization for the generic version of an already approved drug can seek permission for manufacturing from the state FDA once the four year time from first authorization expires.

The marketing authorization for new drugs, in India, is obtained through submission of Form 44 to the CDSCO. Once the marketing authorization is granted by the CDSCO, an application to the state FDA is to be made to receive a permission to manufacture the drug. The state FDA then provides a licence to manufacture the drug by way of Form 29. The requirements and guidelines for authorizations are provided in Schedule Y.

The Indian system, unlike US and EU, does not include any exclusivity provision. The need for data exclusivity and orphan drug exclusivity as an incentive to innovation has been debated earlier. However, the impact that exclusivity provisions would have on access of cheaper medicine to public has been discouraging the implementation of any exclusivity provision.

Patent Exclusivity

One of the biggest fears in the launch of a generic drug is the potential infringement of the innovator’s patents. A safe route of generic entry is to launch the product once the patent expires. The US has a specific procedure for indicating the patent status. The ANDA applicants looking at safe launch of their generic products are required to certify their application with Paragraph 1, stating that such patent information has not been filed; Paragraph 2, certifying that such patent has expired; or Paragraph 3, certifying the date on which such patent will expire. In European countries, the requirement varies. Countries such as Portugal and Hungary require that the generic applicant make a regulatory submission including a statement on the patent status of the product. India also has a requirement that the particulars of the patent status be furnished while filing Form 44 for seeking marketing authorization in India. However, it has been observed that the status of patent, whether active or expired, does not impact the approval or rejection of an application for MA.

Patent protection grants the patentee with rights to exclude others from making, using, selling, offering to sale or importing the patented product. Some countries, such as US, India and Canada, have a provision generally referred as regulatory exception or Bolar exemption which exempts the use of the patented product to seek marketing authorization. In India, Section 107(A)(a) of the Patent Act provides such regulatory exemptions. Therefore, a generic company may use the patented product while the patent is still active, to seek marketing authorization. However, commercialization of the generic drug would be possible only after the patent expires.

The patent system works parallel to the drug regulatory system. Corresponding to the regulatory exclusivities that may be provided to a drug product, a patent provides exclusive rights for a standard term of around 20 years. In many countries, this patent term may further be extended or adjusted up to around five years.
Generally, in US, these extensions to the patent term may be granted due to two reasons. Firstly, it may be granted as compensation to the delays by the patent office in the patent approval process (patent term adjustment, PTA). Secondly, it may be granted to remedy the delays incurred during the regulatory approval process (patent term extension, PTE).

Total patent term = Standard patent term + PTA + PTE

Under the Patent Term Guarantee Act of 1999 (ref. 35), the term of patent (PTA) would be adjusted by extending the term by one day for each day delayed by USPTO during prosecution. The PTA is, however, limited to only USPTO delays, any delays from the applicant would be deducted from the USPTO delays. In a situation where applicant delays would exceed PTO delays, the period of PTA would be zero. The PTA would not, in any case, reduce the standard term of a patent. The main purpose of this provision is to ensure that a diligent applicant receives a minimum of 17 years of patent term from the date of issuance. The delays for which patent term may be adjusted include: failure to take action within specified time limit (also known as the 14-4-4-4 rule or ‘A’ delays), failure to issue patent within three years from filing date (also known as three year pendency delays or ‘B’ delays), and delays caused during situations such as interference, secrecy order, and successful appellate review (also known as ‘C’ delays). Under each of these cases, the applicant is credited with one day for every day delayed beyond the deadline, by the patent office.

For example, assume that an applicant files a US patent application on 1 January 2010, and the USPTO issues first office action on 1 June 2011, missing the 14 months deadline of 1 March 2011 by three months. These three months would be ‘A’ delay and, therefore, would be compensated to the applicant by addition of these three months at the end of the standard patent term. Further, assume that the USPTO issues the patent on 1 January 2014 while the issue fee was paid by the applicant on 1 June 2013. In this case, the applicant would be eligible for ‘B’ delay as the three year deadline for issuance of patent would expire on 1 January 2013, and another ‘A’ delay for missing the four months deadline of 1 October 2013 by three months. The total term of adjustment (PTA term) would, ideally, be a sum of all the delays by the patent office. In case of overlapping delays, the total PTA term would be adjusted such that there is no double counting. In this case, the applicant would be eligible for a 1.3 year term of PTA (3 months ‘A’ delay for 14 month deadline + 1 year ‘B’ delay) which would be added to the standard patent term.

In addition to the patent term adjustment, US provides patent term extensions under the Hatch-Waxman Act, to compensate the patent term lost in receiving MA. The patents claiming a product (e.g., medical device, drugs, etc.), a method of manufacturing the product, and method of using the product (wherein, the product would be subjected to regulatory review) are eligible for PTEs. Generally, only one PTE is granted per drug product per patent. Therefore, a patent claiming two drug products would only receive one PTE. Also, in cases where a drug product is claimed in multiple patents, the choice is up to applicant to select the patent for which it would want to receive PTE.

Generally, PTE calculation involves summation of the period of approval phase and half the period of testing phase.

PTE = Approval phase + 1/2 Testing phase

The testing phase is the time starting from the effective date of the investigational new drug (IND) to the date of the NDA. The approval or marketing authorization phase, on the other hand, is the period starting from the NDA date to the marketing authorization date. Here, any time wherein the applicant has not acted with due diligence in any of the phases would be deducted from that phase while calculating PTE. The maximum term of PTE that could be granted to a patent is five years. The PTE is provided such that the total potential exclusive marketing period, i.e. the period from the date of the marketing authorization until the patent expiration date, does not exceed 14 years. Hence, a patent already having a minimum of 14 years of potential exclusive marketing years available, if an applicant receives marketing authorization for a product in 2013, while the patent for that product expires in 2023, the patent would be eligible for PTE of up to four years.

Similar to PTEs in US, EU has a provision of supplementary protection certificate for innovator drug patent holders. SPCs are granted by the patent holder for a maximum period of five years from the date on which marketing authorization is granted. The period of SPC is subject to the number of potential years of marketing period. Similar to PTE, if a patent already has a minimum of 14 years of exclusive marketing period, the patent holder would still be eligible for SPC if the patent expires in 2023 and marketing authorization for the product is granted in 2013.
office to remedy the loss of potential exclusive marketing term by the innovator drug manufacturers in seeking MA. SPCs extend the monopoly period for a maximum of five years, such that the total potential exclusive marketing term including the patent term and SPC does not exceed 15 years. However, the SPC period may further be extended by six months, up to 15.5 years, provided the applicant proceeds with paediatric studies. The term of SPC is generally calculated as the time elapsed between the date of patent filing and the date of first marketing authorization in any EU member which is further deducted by five years.

\[ \text{SPC term}= (1^{\text{st}} \text{MA date} - \text{patent filing date}) - 5 \text{ years} \]

For example, assume, that an applicant receives first marketing authorization in an EU member state on 1 January 2008 for which a patent application was filed on 1 January 2000. The applicant would be eligible to receive an SPC term of three years. With the extension provided by the SPC, the patent term which would have, otherwise, expired on 1 January 2020, would now expire on 1 January 2023. However, in cases where the time elapsed between the date of patent filing and the date of first marketing authorization is less than five years, assuming the date of first marketing authorization was 1 January 2002, instead of 1 January 2008, the applicant would not be eligible for SPC term.

In India, although, the information on patents for a product needs to be furnished to the regulatory authority, the regulatory delays in obtaining marketing authorization does not impact the term of a patent for that product. Unlike the European and the US system, the Indian system, does not provide any patent term extension for regulatory delays.

**At-risk Launches**

Launching a generic drug after the expiry of any patent/non-patent exclusivity is arguably the safest option for the launch of a generic drug in the market. Though, it is arguably the safest option, the time by which a generic drug product is made available in the market is ordinarily the longest. Moreover, any delays in further launching a generic product in the market may lead to more competition from other drug companies and hence less revenues.

Not awaiting the expiry of the patent might seem to be a faster way of launching a generic drug. However, this strategy is associated with risks and delays, stemming from patent infringement and regulatory approvals. Launching a generic drug in a market involves receiving a marketing authorization from NDRAs of their respective countries. Some countries link such marketing authorizations to the patent system prevalent in their countries (known as patent linkage).

In countries following patent linkage system, in order to receive marketing authorization and avoid any form of patent infringement, the generic drug filer has to prove that the patent governing the drug in question is invalid or will not be infringed by the manufacture, use, or sale of the drug product, which is going to be launched by the generic company. Whereas, in countries not following the patent linkage system, the generic drug filers needs to prove bioequivalence as the basis for approving generic copies of drug products and need not provide any patent related information for the drug product. In such systems, marketing authorization may be granted by NDRAs on the basis of scientific criteria concerning the quality, safety and efficacy of the drug product, without involving any patent law related issues.

**USA**

Patent linkage system followed in US is provided under the Hatch Waxman Act, 1984. The Hatch Waxman Act requires FDA to publish ‘Approved drug products with therapeutic equivalence evaluations’, commonly known as the Orange Book. Once a pharmaceutical company is interested in bringing a lower-priced generic version of a previously approved innovator drug, the company is required to file an ANDA application, along with a patent certification. FDA does not provide marketing authorization for an ANDA application that is protected by a patent listed in the Orange book.

Paragraph IV certifications are filed, wherein the ANDA applicant challenges the validity of the patent governing the drug, or confirms non-infringement of the patent governing the drug. Once an ANDA is filed along with a Para IV certification, the FDA has 60 days to accept the same and generic filer is thereafter required to send a notice to each of the patent owner and to the holder of the approved NDA to which the ANDA refers. Once the notice has been served, the patent holder has 45 days to sue the generic manufacturer to automatically trigger the 30 month stay of FDA approval of the ANDA (earliest of the end of 30 months or after court
decision or patent expiration). Once an ANDA applicant prevails in the litigation, the ANDA applicant receives a 180-day period of marketing exclusivity, which is the driving factor in the steady increase of first to file Paragraph IV filings in the US over the years.\(^{47}\)

Patent linkage in US therefore ensures that no marketing authorization of generic drugs is granted till the decision on the validity of the patent is established or the patent covering the drug product or approved use is expired. Patent linkage effectively triggers a 30 month stay which stops the first ANDA filer (and subsequent ANDA filers) from receiving market approval till the time the challenge on the patent is decided, the 30-month stay has ended or the patent term has expired; thereby delaying generic drug launches, when the patent has been challenged.

**Europe**

Under the EU law, no patent linkage system is followed. The EP regulation and directive specifically lays down the grounds on which an application for marketing authorization of a generic drug might be refused, suspended or revoked. Since, the status of a patent (application) is not part of the grounds listed under the regulation and the directive, clearly indicates that no patent linkage exists at the EU level.\(^{48}\) However, the commission identified certain countries within EU which allegedly had patent linkage issues.\(^{30}\)

Any decision to grant a marketing authorization to a generic drug is taken on the basis of scientific criteria alone such as the quality, safety and efficacy of the generic drug. Any issues related to patent law such as the patent (application) status is not dealt by the regulatory authorities but by competent courts, which have to determine whether or not there is any patent infringement.

Although, no patent linkage exists formally in EU, innovator companies have come up with strategies at regulatory levels to delay the launch of generic drugs in EU. The innovator companies use the status of their patent to oppose the marketing authorizations granted to generic companies. Also, they take legal action such as injunction against the decision of the drug regulatory authorities and generic filers regarding their generic application(s).\(^{56}\) Furthermore, innovator companies argue with drug regulatory authorities in most EU member states with regard to the infringement of their exclusive right with regard to their patent(s).\(^{50}\) Though, the outcome of these strategies, depending on the decision of the courts, is not in favour of the innovator companies\(^{49}\), it has definitely helped in delaying the launch of generic drugs.\(^{50}\)

**India**

No patent linkage system has been expressly recognized under any of the Indian laws. A generic entrant is granted a marketing authorization based on the scientific data and does not involve issues related to patent law. However, innovator companies have tried hard to bring in the patent linkage concept through judicial interpretation using harmonious construction of the Patent Act, 1970 and the Drugs and Cosmetic Act, 1940 (ref. 51). Though, this approach proved to be successful to an extent for the innovator companies in the case of *Bristol-Myers Squibb Co v Dr BPS Reddy & Ors (Hetero Drugs Ltd)*\(^{52}\), the courts took the opposite view in the recent case of *Bayer Corporation v Union of India & Ors.*\(^{53}\)

In the former case, Bristol-Myers Squibb Co (BMS) received an *ex parte* ad interim order. Hetero Drugs which had sought a marketing authorization for a generic version of BMS’s patented drug ‘Dasatinib’, was restrained from manufacturing, selling, distributing, advertising, exporting, offering for sale, the said drug in India. Further, the court directed the Drug Controller to take into consideration infringement of any laws in India, thereby, staying the application for drug approval based on BMS’s patent rights. This judgement became an immediate point of concern for generic companies in India as it brought the essence of patent linkage through judicial reasoning.

The Delhi High Court in the latter case (Bayer case) settled the patent linkage controversy. Cipla had applied for a drug licence for its drug ‘Soranib’, a generic version of Bayer’s patented drug ‘Sorafenib tosylate’. Bayer filed a petition before the Delhi High Court seeking directions to restrain the grant of licence to Cipla for the generic version of Bayer’s patented drug. The court rejected that arguments put forth by Bayer and stated that both the statutes (Drugs and Cosmetic Act and Patent Act) have different objectives, thereby, ruling out patent linkage system in India. The court further stated that the Drug Controller did not have the competency and the jurisdiction to deal with patent related matters. Recently, the Supreme Court of India rejected Bayer’s appeal and upheld the High Court judgement.\(^{54}\)
In light of these judgements, it is evident that the innovator companies are actively trying to incorporate the patent linkage system through the courts. Though, patent linkage system ensures the interests of the innovator companies, implementation of such a system in India will impact the interests of both the public health sector and the generic industry.

Licensing – Voluntary and Compulsory

Another approach for a generic company to enter certain markets is by taking licences from innovator companies during the patent term. Voluntary licences are granted by innovator companies, to take advantage of the low cost, high quality production and distribution channels of generic companies; and also to help innovator companies focus on their core business activity of conducting R&D. Voluntary licences are generally granted to multiple generic companies in a non-exclusive manner to provide competitive pricing and better availability of drugs to those in need. Licensing by innovator companies to generic companies is generally limited to certain territories which occupy a relatively small size of the global pharmaceutical market, such as sub-Saharan Africa (SSA) and least developed countries (LDCs).

Voluntary licensing by innovator companies to generic companies is generally favourable for all parties involved. It helps innovator companies reach newer markets and recover some of their R&D costs, helps generic companies to generate revenues, and facilitates competitively priced drugs supply to the public.

Though voluntary licensing is beneficial to generic companies, the terms and conditions are primarily decided by the innovator companies. Also, the innovator companies may use their discretion to deny the possibility of licensing, or do so at unreasonable commercial terms and conditions. Furthermore, this period may also be marked with drugs being sold at exorbitant prices, outside the reach of the common public.

In order to contain the situation and to bring some relief to patients, and for reasons such as public health and public interest; measures such as compulsory licensing were incorporated. Compulsory licensing has been provided under Article 31 of the WTO TRIPS Agreement, and is complied by all major patent systems. The term ‘compulsory licence’ however, does not specifically appear in the TRIPS Agreement. Under the Doha Declaration on the TRIPS Agreement and Public Health (November 2001), member nations have been given the right to grant compulsory licenses and the right to determine the grounds for granting such licences.

Compulsory licences are generally granted to help remedy anti-competitive practices, non-working by patent owner, for reasons of emergency, for public health, or for government use. The grant of compulsory licence allows the compulsory licence holder to sell the drugs alongside the patent holder and its voluntary licensees, if any. Though a royalty is generally granted by the compulsory licensee to the patent owner, compulsory licence is less advantageous to the patent owner than a voluntary licence.

USA

US patent law does not explicitly provide for a compulsory licence, however, compulsory licences have been granted under antitrust law and other special legislations such as US Clean Air Act, 1988 and Atomic Energy Act, 1988. As per Scherer, 1998, more than hundred licences have been granted with licensees required to pay a reasonable royalty or not pay any royalty at all.

Europe

Provisions for compulsory licensing are contained in almost all the European national patent laws. In addition to the concept of compulsory licences, certain countries such as UK and Germany follow what is known as the ‘licence of right’. Compulsory licences are non-voluntary, whereas ‘licence of right’ is voluntary in nature.

National patent laws provide for provisions for the grant of a compulsory licence for public welfare or in public interest. In the interest of public welfare, a national government may allow for the use of the patented invention by everyone in lieu of a user fee being paid to the government. The government in turn pays some or whole of the fee collected to the patent owner. Compulsory licences are also granted in public interest if a dependant patent makes a significant technical advancement over the main patent. Under such situations, compulsory licence is accompanied by counter licences.

India

Provisions for compulsory licensing are contained in the Indian patent laws as well. Provisions containing ‘licence of right’ were omitted in the Patents (Amended) Act, 2002 and provisions for compulsory licence were incorporated.
As per the Patents Act, 1970, compulsory licence is granted in India if reasonable requirements of the public have not been satisfied, or the patented invention is not available to the public at an affordable price, or the patented invention is not worked in the territory of India [Section 84(1)]. A compulsory licence may also be granted for related patents (Section 91) and for exports in certain exceptional circumstances (Section 92A). Compulsory licensing is provided for exports to countries having insufficient or no manufacturing capacity in the pharmaceutical sector to address public health problems [Section 92A(1)]. Compulsory licences may also be granted in case of national emergency, extreme urgency or public non-commercial use by notification of the Central Government in the official gazette [Section 92(1)].

India granted its first compulsory licence on 9 March 2012 to Natco for Bayer’s drug Nexavar, post 2005 amendment, after being convinced that all the factors enumerated under Section 84 of the Patents act were satisfied, i.e. the reasonable requirement of public was not met, the drug was not available to public at reasonably affordable prices, and that the patentee failed to work the invention within the territory of India. The compulsory licence was granted at a royalty rate of 6 per cent.

**Innovator Company Strategies Impacting its Revenue Streams and Generic Company Business**

A patent owner has a right to exclude others from using its patented technology for a particular period only, subsequent to the expiry of which period, the patented technology falls in the public domain. After the expiry of the patent and related exclusivities, innovator drug companies cannot restrain others from manufacturing generic versions of their drugs. As soon as a generic version of an innovator drug enters the market, a decline in the sales of the innovator drugs is generally witnessed. Due to better pricing for generics, the market share of the innovator drug generally reduces drastically in the following years after patent expiry. Therefore, generic drug manufacturers face tremendous opposition from innovator drug manufacturers when they start manufacturing generic versions of the innovators’ breakthrough drugs. The innovators desire to control the phenomenon and aim to prevent generic manufacturers from developing and bringing into market the generic versions of their drugs has led to a mix of strategies which help to delay the launch of generic drugs, thereby prolonging revenue streams of innovator drug companies. These companies adopt various strategies and carve out policies, aimed at extending the commercial life of their drugs in the market and impacting generic company business. These strategies and policies have been referred to as a tool-box of patent strategies. Some of the important ones are highlighted below.

**Patents Rights in Clusters or Divisions**

The most common strategy adopted by innovator companies is to create a bundle of patent rights for a particular drug technology. The innovators, by applying for and obtaining a number of patents (on processes, reformulations, dosage regimes, etc.) intend to create ‘patent clusters’ or ‘patent thickets’, in order to set up a system which can deter/delay the generic companies from developing generic versions. The delaying effect could further be extended by multiplying the number of applications by filing for divisional applications.

This strategy is founded on making several layers of protection and making it difficult for the generic companies to successfully launch a generic drug with complete legal certainty as to not lead to infringement. This legal uncertainty arising out of patent clusters and divisional application filings, leads to delays in launch of generic drugs for a considerable period of time.

**Extensive Patent Litigation**

In case generic drug makers are not deterred by mere patent rights in favour of drug innovators, the innovator companies start enforcing their patent rights by engaging in legal proceedings such as patent litigation. Although a patent holder is entitled to enforce his patent rights in courts of law, yet the extensive patent litigation by drug innovators in this strategy is rested on a different principle, which is to merely delay the launch of generics in the market. An owner of patent over a drug tries to simply persecute a generic manufacturer by seeking enforcement of his rights before courts.

This purpose could also be achieved by merely sending a legal notice or a warning letter with a threat of litigation. As the stakes involved in a patent litigation are quite high, generic manufacturers think several times before launching generic versions of a particular innovator drug.

In case a legal proceeding is initiated by an innovator company, an interim injunction granted to the innovator, serves as an important tool, as the same restrains the generic drug maker from launching the
generic version of the patented drug at least till the final disposal of the proceeding, which again leads to a delay in generic launch.

**Second Generation or Follow-on Drugs**

The innovator companies also aim to formulate follow-on drug compositions. Follow-on drugs are those drugs which are structurally similar to branded drugs, but, different enough from the branded drugs so that they can be patented. Follow-on drugs are developed when exclusivities in the original branded drugs are nearing expiry.

The ideal time for introduction of follow-on drugs in market is a few years before the expiry of the exclusivity on the original branded drugs, so that switching to the follow-on medicine is complete before the introduction of generics into the market. This strategy also involves intensive marketing activities to ensure that patients shift to the new drug prior to the launch of the generic version in the market, thereby impacting the market share of the generic drugs.

Generally, the idea of the drug innovators in bringing follow-on drugs is to keep hold of the market in the therapeutic areas of branded drugs. However, unless a particular follow-on drug has a substantial clinical advantage, either in terms of dose, or mode of administration, over the original branded drug, the follow-on drug is not able to capture the market, in which case generics may be preferred.\(^{50,68}\)

**Own or Authorized Generics**

Another practice observed in the pharmaceutical industry is that the drug innovator companies launch the innovator drug under a generic name, when patent rights over such drugs are approaching expiry. The authorized generics are launched through either the innovator’s generic subsidiary or an independent generic drug company.\(^{69}\)

The generic drugs produced by innovator companies or their subsidiaries, compete with generic drugs produced by other generic companies on price, quality and availability in the market. Such activities lead to lowering of drug prices, thereby impacting the profits made by generic companies and further disincentivising other generic companies.

**Influencing the Medical Fraternity**

In a few instances, drug innovators prefer influencing and getting support from the medical fraternity in order to deal with the generic drug makers. Innovator companies seek favours from pharmaceutical dealers, when they recommend medicines to doctors, giving exorbitant trade margins in return. Medical practitioners are influenced by the innovator drug manufacturer and led to prescribing only branded (and expensive) drugs to patients. At times, the doctors continue with their practice of prescribing expensive drugs merely because of their ignorance regarding new and generic (and cheaper) versions of breakthrough drugs.\(^{70}\)

This strategy of the innovator drug companies, i.e., influencing the medical fraternity and earning their loyalty and support, also plays a vital role in creating an impression that the price of a particular drug is proportional to its quality and efficacy. Thus, less expensive generic versions of over-priced drugs are considered of poor quality and poor efficacy. This leads to poor adoption of generic drugs.

**Branding and Marketing**

Another common strategy followed by drug innovator companies is simply branding their original breakthrough medicines. Although patent rights are granted for a fixed term of 20 years in almost all jurisdictions; the term of trademark protection could be infinite, if it is consistently used by the owner. The appropriate use of branding by the innovator companies at the right period of time helps them in extending the life cycle of their patented products. Due to strong market hold of the innovator drugs maintained through branding and marketing, the generic drug manufactures witness lower adoption of their generic drugs due to better recollection for branded drugs.

**Conclusion**

Thus, there are several options, both systematic and complicated, by which generic drug companies can launch generic versions of patented drugs. The discussed options primarily include, launching generics after patent and exclusivity expiry in the regular course, taking risks and challenging the validity of the patent in the drug, obtaining licences from the patent holder and lastly, obtaining compulsory licences from the authorities.

After assessing the pros and cons of each option, when the generic companies are ready to launch generic versions of patented drugs in market, they face an indirect, but strong opposition from the lobby of innovator drug companies, so as to delay and disincentivise, as much as possible, the launch of generic drugs in market. A tool-box of strategies is created and employed by almost each of the innovator
drug companies so as to achieve their goal of extending their revenue streams and in turn making it difficult for the generic drug companies to do their business. Delay in generic launch also causes serious prejudices to the public at large, as needy patients are forced to resort to expensive branded drugs for a longer duration, when they can have easy access to generic and cheaper versions of such drugs.

It is quite obvious that even generic drug makers, in order to sustain in market, must keep their guard in place and adopt effective counter practices, which would help them successfully deal with the strategies adopted by innovator drug companies. These counter practices generally vary from activities such as patent monitoring and watch of innovator drug patents, to conducting marketing campaigns to build own generic brands, etc. Though countering strategies of innovator companies is possible in certain cases to a certain extent, some of the innovators’ strategies like patent litigation are beyond the control of generic companies. Hence, development of an effective counter practice should be gauged on a case to case basis.

References
9 Gaining market share in the generic drug industry through acquisitions and partnerships, thomsonreuters.com/content/science/pdf/ls/newport-deals.pdf (20 June 2012).
11 A 505(b)(1) application is an application that contains full reports of investigations of safety and effectiveness. The investigations the applicant relied on for approval are conducted by or for the applicant or the applicant has obtained a right of reference or use for the investigations, www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069943.htm (7 April 2012).
14 A 505(b)(2) application is an application for which the investigations that the applicant relied on for approval were not conducted by or for the applicant, and the applicant has not obtained a right of reference or use for the investigations [21 USC 355(b)(2)]. Section 505(b)(2) expressly permits FDA to rely, for approval of an NDA, on data not developed by the applicant - such as published literature or the agency's finding of safety and/or effectiveness of a previously approved drug product.
15 The drugs which are identical or almost identical to the originally approved drug generally take the 505(j) route to receive MA. The ANDA applicants are required to establish bioequivalence with the RLD, but can rely on the RLD's safety and efficacy data. A 505(b)2 application, on the other hand, is for drugs which are similar to RLD with modifications, such as: new dosage form, new use, new formulation, new combination, new route of administration, new dosage strength, new active ingredient-salt or ester or complex, etc., which require support data that is not available/accessible from the RLD. In such a case, the support data may be published literature or FDA’s findings from a previously approved drug.
16 Article 39.3, Section 7, Part II, TRIPS.
17 ‘...the applicant shall provide the patent number and certify, in its opinion and to the best of its knowledge, ...that the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the abbreviated application is submitted. The applicant shall entitle such a certification ‘Paragraph IV certification’, CFR 314.94(a)(12)(i)(A)(4), www.fda.gov/AboutFDA/Centers/Offices/CenterforDrugsandBiologics/ucm134444.htm (3 April 2012).
19 The publication Approved Drug Products with Therapeutic Equivalence Evaluations (the List, commonly known as the Orange Book) identifies drug products approved on the basis of safety and effectiveness by the Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (the Act), www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079068.htm (2 April 2012).
22 EU members had time until 2005 to incorporate the new regime. Recent applications include applications filed post 2005.


33 35 USC § 154(b), 37 CFR §§ 1.702 - 1.705, MPEP §§ 2730 - 2736.


36 Applicant of original applications filed on or before 29 May 2000.

37 Portfolio Media Inc patent term adjustment after Wyeth v Kappos, http://www.dechet.com/Publisher/Publication/fc554844-10cb-47b4-b178-8359ad291b9c/Presentation/Publication Attachment/46fb22e8-6086-400e-86f2-884e164a423/Law 360_01-28-10.pdf (20 April 2012).

38 35 USC § 154(b)(1)(A); 37 CFR §§ 1.702(a), 1.703(a).

39 35 USC § 154(b)(1)(B); 37 CFR §§ 1.702(b), 1.703(b).

40 35 USC § 154(b)(1)(C); 37 CFR §§ 1.702(c)-(e), 1.703(c)-(e).

41 USPTO’s interpretation of the PTA provision was affected by the Wyeth v Kappos case. Under the old calculation, prior to the Wyeth’s case, the applicant would have been eligible for a 1 year extension, as opposed to 1.3 years, www.cafc.uscourts.gov/images/stories/opinions-orders/09-1120.pdf (20 April 2012).


44 A generic drug product is one that is comparable to an innovator drug product in dosage form, strength, route of administration, quality, performance characteristics and intended use.

45 As per Section 505(j)(2)(A)(vii) of the Act, the patent certifications are: (I) no patent information on the drug product that is the subject of the ANDA has been submitted to FDA; (II) such patent has expired; (III) the date on which such patent expires; or (IV) such patent is invalid or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted.


52 Bristol-Myers Squibb Company & Ors v Dr. Bps Reddy & Ors, CS(OS) No 2680/2008 (Delhi High Court).

53 Bayer Corporation v Union of India & Ors, 2009 (41) PTC 634 (Del).


Article 31, TRIPS mentions ‘Other use without authorization of the right holder’.


Carlos Correa, Compulsory licensing: How to gain access to patented technology (Chapter No 3.10), www.iphandbook.org/handbook/ch03/p10/ (6 July 2012).


The voluntary nature of ‘licence of right’ has blurred in the case of Switzerland, wherein provisions have been incorporated to provide what is known as a ‘licence of right for research tools’ in situations, wherein an applicant has failed to secure a licence from the patent owner for essential research tools such as polymerase chain reaction (PCR), etc.