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Review Article

Regulatory Strategies for API going off-patent

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Abstract

Pharmaceutical industries are one of the most developing industries having enormous profit margins. Today the pharmaceutical companies are challenged with increased costs of drug discovery and development and intrusive competition from generic drug companies. The pharmaceutical companies have begun the process of drug development and in the same period also begin to espouse the various schemes to expand the duration of patent-holding. So, increasing patent term for the already patented products is an effective strategy for withstanding generic competition. Pharmaceutical industries can use various ways to optimize the patent protection on large products, optimizing the market lifecycles and the strategies for API going off-patent in pharmaceutical industries in India are outlined below to provide the significant pharmaceutical patenting information.

Keywords: Patent, types, norms, submission requirements, exclusivity, strategies.

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1. Introduction

A patent is an exclusive right granted by the United States patent and trademark office (USPTO) by the government, or a set of specified rights, to an innovator or a person who claim to be the true and first innovator or the discoverer of a new process to make, use, or sell an resourceful process and are adequate for the industrial application. A patent for an invention is the grant of a property right to the innovator, issued by the patent and trademark office (PTO). Generally, the period of a new patent in the United State is 20 years from the date on which the patent application is applied or registered. The innovation must contain practical purpose. They are imposed by court proceedings. Independent of human ramification, the patent safeguard feasibly makes a monopoly for the pharmaceutical industry. Patent is not an inherent or statutory right, but a rational option by the governing bodies to allow innovators to have sole ownership of patients, based, as stated, on what is best for all national people. Patenting, thus offers a mechanism to safeguard invention without keeping the innovation secret. A single patent application through which patent can be registered in huge number of countries and this method was given by the Patent Cooperation Treaty (PCT). Nevertheless, only under the diameter of the individual patent office rests after filing the PCT application patent permit. Furthermore, the Supplement Protection Certificates Regulation (SPCS) grants up to 5 years of "patent extensions" to pharmaceuticals and plant products that provide up to 25 years of patent life for inventor innovations. (1)

Types of Patent in India (2)

According to the pharmaceutical patent list provided on its website in the Indian patent office there are 7 types of patent. They are given below:

- **Drug Compound Patent:** It is a Markush type claim. It generally claims a drug compound by its structure per se. Here, Markush type claim referred as a claim with multiple "functionally equivalent" chemical entities permitted in one or more parts of the drug compound. In this patent, other industries are not permitted to formulate any products using this composition containing the similar drug compound before the expiry of the specified patent.
- **Formulation Patent:** These patent target the particular technology for the preparation of formulation or its essential components.(3)
- **Synergistic Competent Patent:** These patents can be acquired on new synergistic combination of the drug. Synergy drug take place when two or more drug are interacting with each other in a way that increases the effects of those drugs.

- **Technical Patent:** These patent are focused on the methods used to solve particular problems allied to methodology like taste masking, stabilization, etc.
- **Polymorph Patent:** Polymorphs are various physical shapes or crystal structure of a substance that is existing. Generally, they are able to diminish impurities or enhance the compound stability.
- **Biotechnology Patent:** In the preparation of pharmaceutical product, biotechnology includes the utility of living organism or biological materials.
- **Process Patent:** These patents don't assert the product per se, but only protects the development of a particular product through a new and innovative process.

Norms or Principles of Patent (4)

Patent are permitted to those invention which fulfill all the expectations of patentability criteria. According to the Indian Patent Act, a patentable invention is referred to as a "new outcome or process that demands a new innovative operation and is responsible for industrial application". Therefore, the basic ground for any innovation to be patentable is given below. They are:

- **Newness:** The subject matter of the invention must not be identified before the patient filing date. The innovation shall be appraised unique if it is not published in any document or is not used in the country or anywhere else in the world.
- **Novelty:** The invention must be new, original, or unusual.
- **Inventive Step:** Inventive step is the attribute of an invention that implies technical progress relative to current or economically significant information or both.
- **Industrial Applicability:** The technology has to be made or used effectively in the industry.

Submission Requirements (5)

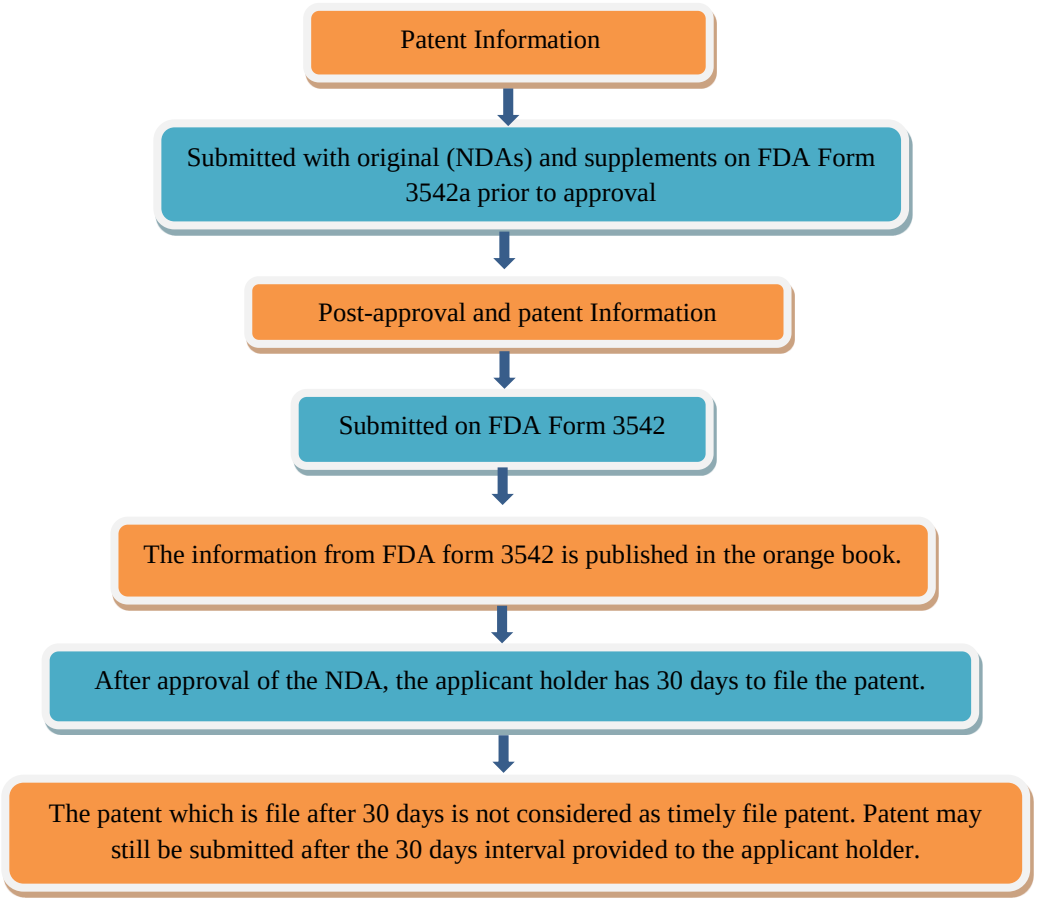

Figure 1. Submission requirements

If the generic application is submitted before the patent is issued the Abbreviated New Drug (ANDA) holders are not needed to issue an early-filed patent waiver. The patent deemed by the FDA to be protected by the legal guidelines of patent information is as follows:

- Patent alleging the active ingredients,
- Some other patent as detailed on Form 3542 of the FDA,
- Drug product patent,
- Use patent for a specific approved sign or method of use.

The API Going Off-patent in the Year 2019-2022 are listed below (6)

Table 1 Drug of 2020

Brand Name	Generic Name
Atrovent HFA	Ipratropium HFA
Byduredon	Exenatide
Chantix	Varenicline
Dexilant	Dexlansoprazole
Inlyta	Axitinib
Namenda XR	Memantine er
Safyral	Drospirenone/ethinyl estradiol/levomefolate
Saphris	Asenaphine
Silenor	Doxepin
Sprycel	Dasatinib
Tykerb	Lapatinib
Vigamox	Moxifloxacin

Table 2 Drug of 2021

Brand Name	Generic Name
Crixivan	Indinavir
Emtriva	Emtrisitabine
Hysingla Er	Hydrocodone Er
Perforomist	Formoterol
Sutent	Sunitinib
Veramyst	Fluticasone, Fuoroate
Xarelto	Rivaroxaben
Zomig ns	Zolmitriptan

Table 3 Drug of 2022

Brand Name	Generic Name
Januvia	Sitagliptin
Oxecta	Oxycodone
Prestiq	Desvenlafaxin
Selzentry	Maraviroc
Victrelis	Boceprevir
Vimpat	Lacosamide

Exclusivity (5)

The FDA permitted sole marketing rights after approval of a drug and may or may not run at the same time as patent. It prohibits ANDAs or applications defined in section 505(b)(2) of the act from being submitted or accepted effectively and was intended to encourage an equilibrium between new drug development and generic drug competitor.

When the legislative essentials/demand is fulfilled, exclusivity is permitted upon pharmaceutical product approval. The duration of time the FDA offers exclusivity to a new drug rely on the type of exclusivity. Note exclusivity period is not given to the patent life.

Regulatory Strategies of Pharmaceutical Industries for API going off-patent

Pharmaceutical industries can use a various strategies to optimize the patent protection on large products, optimizing the market lifecycles. Once a composite or pharmaceutical ingredient is patented, the patent becomes a preliminary art guide that must be taken into account when seeking for an additional patent safeguard for the composite or pharmaceutical. Consequently the new patent defense generally includes limited enhancement or new uses for the non-disclosed or proposed drug in the original patent. (7) Some of the strategies to protect or prolong the drug patents are given and explained below (8):

- Orphan drug exclusivity periods
- Stereo selectivity/Chiral switches
- Hatch-Waxman Act
- New Formulation, Route Of Administration Technique or uses
- Pediatric Exclusivity(PED)

Orphan drug exclusivity periods

This act encourages the establishment of drugs for treating rare diseases. Under this act, the drug formulated for rare diseases earn 7 years of further exclusivity of sales of drugs and during this period the FDA is prevented from authorizing any challenging generics. The aim of this law is to support to the drug developers in recovering the significant development and drugs marketing costs that have never expected to have large markets. But very few drug manufacturers can gain advantages of this act. (5)

- **Stereo selectivity/ chiral switches**

Currently there are only two third of the drugs present in the market which are chiral, meaning that one is good in both forms, and the other is inefficient or even life-threatening. Most medicines are compounds consisting of various stereoisomer mixtures, and these combination can be comprises of either enantiomers or isomers. A combination of an equal mixture of pairs of enantiomers is known as 'racemate' or 'racemic'. Many industries possessing a patent close to expiry for a racemic drug select to highlight enantiomer under another patent. This "switching of racemic" process permit drug industries to appeal for the enantiomer's FDA consent before the racemic patent expires, while supporting the drug as an overall market exclusivity.

- **The Hatch Waxman Act**

The Hatch Waxman Act comes to protect the patent the manufacturer of drugs, patent new ingredients in the beginning of the process of drug research. In 1984, Hatch waxman act was approved to permit the patent extensions for 5 years to account for the duration of the FDA consent process. If a drug takes 5-6 years from formulation to market, it is great. But normally FDA approval takes a longer duration, so Hatch Waxman act permit 5 years, no matter how long FDA consent requires.

- **New formulation, Route of administration technique or uses**

A drug companies can elongate a patent by redeveloping a drug-frequently to ease dosing or how to administered. The most common ways is extended release versions of drugs. Under the regulation of FDA, when a new application of drug is known or developed, it can gain a further 3 years of protection. For example: A drug which treated clinical depression also treated attention deficit hyperactivity disorder (ADHD). In such cases, the drug can earn 3 years of patent.

- **Pediatric Exclusivity(PED)**(9)

When the sponsor has organized and submitted pediatric research on the active moiety in respect to a written request from FDA, it permits an additional 6 months safeguard at the end of patents or exclusivity for sponsor's drug products containing the active moiety.

Conclusion

The strategies must be established before the pharmaceutical of patent and entry of generic drugs in prior to the imminent market. It is extremely crucial to concoct strategies for expanding patent protection and lifecycle of product in the early stage in the process of development in order to extend patent. Also the competition between the scientists and attorneys should be must. In order to create more effective patents and ultimately secure their intellectual rights, pharmaceutical researchers and patent lawyers need to work closely during the drug's lifecycle to prolong their patent existence along with apprehension the underlying belief and values of the others patent-related disc.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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