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Concept of Substantial Similarity In Pharmaceutical Patent Infringement Cases and the Implications of Section 3d of Indian Patent Act

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ABSTRACT

The research paper discusses the main aspects of Section 3(d) of the Indian Patent Act 1970 with respect to the Indian pharmaceutical industry. Three cases viz. the Novartis Glivec, Pfizer's Sutent and GSK's Tykerb have been discussed that explicitly demonstrate, pharmaceutical inventions rarely relate to new chemical entities or novel active ingredients that have never before been available for therapeutic use, thus encouraging pharmaceutical companies to prolong patent protection by obtaining separate patents on multiple attributes of a single product. Section 3(d), whereby, regulates the granting of pharmaceutical product patents by limiting the scope of protection available for derivatives and new uses of a known substance, thereby preventing patents on trivial modifications of known substances. Thus, India's Section 3(d) should be viewed as a "public health safeguard" that aims to prevent "evergreening," and not a radical departure from international practices.

Key-words: Section 3d, Evergreening, Efficacy, Indian Patent act

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Introduction:

The history of patent law in India dates back to year 1856 with the introduction of the Act for protection of inventions based on the British law. However the main Patent Act was passed in the year 1970. This Patent Act came into force from 20th April 1972 and was further amended in years 1999, 2002 and 2005. [1]

The Salient features of The Indian Patent Act are as follows:

- Both product and process patent provided
- Term of patent – 20 years
- Examination on request
- Both pre-grant and post-grant opposition
- Fast track mechanism for disposal of appeals
- Provision for protection of bio-diversity and traditional knowledge.
- Publication of applications after 18 months with facility for early publication.
- Substantially reduced time-lines.

Section 3(d):

Section 3(d), as introduced in April 2005 into the Indian patent law, represents a unique requirement to be fulfilled for patentability of certain types of pharmaceutical inventions. According to Section 3(d), in order for a new form of a known substance to be patentable, it must show an enhanced efficacy with respect to the known efficacy of the substance concerned. [2]

Section 3 (d) reads as follows:

"The mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant." [1, 2]

Explanation: For purposes of this clause, salts, esters, ethers, polymorphs, metabolites, pure form, particle size, isomers, mixtures of isomers, complexes, combinations and other derivatives of known substance shall be considered to be the same substance, unless they differ significantly in properties with regard to efficacy.

Therefore, inventions which are mere discovery of a new form of a known substance and which does not result in increased efficacy of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such process results in a new product or employs at least one new reactant are not patentable. This, in other words meant that India does not support inventions which are minor modifications and thus prevent undue monopoly during the extended period of patent protection by the inventor/company.

The main aim of introducing Section 3(d) is to prevent evergreening of patents. It clarifies what products/technologies are not patentable as well as intents to balance pharmaceutical patent protection with the need to provide access to affordable medicines and healthcare services to the common man at large. The real intent of section 3(d) is that the inventions that are mere "*discovery*" of a "*new form*" of a "*known substance*" and do not result in "*increased efficacy*" of that substance are not patentable. By making the "new form" of a "known substance" with enhanced efficacy patentable, section 3(d) encourages the research and development of existing products or technologies to facilitate and get pharmaceutical products of better therapeutic efficacy in the market, that address the unmet needs of the healthcare sector.[2]

It was addressed at the Federation of Indian Chambers of Commerce and Industry (FICCI) round table on 29th March 2010 that removal of section 3(d) would result in 'ever greening' and delays in the entry of generics, thereby affecting public health. This was especially to keep a check on patenting of trivial modifications of current patented inventions to extend its monopoly regime. This section sought to prevent ever-greening by disallowing the patenting of a known substance unless it results in an 'enhancement of the efficacy of that substance'. By making derivatives with added

efficacy patentable, section 3(d) encourages sequential developments of existing products or technologies that help bring in improved products to the market. [3]

Premise:

In essence, section 3(d) states that:

1. Unless a new form of an existing substance depicted increased efficacy, it is patentable. If it does demonstrate increased efficacy, then it is treated as an altogether 'new substance'.

2. The 'mere new use' of a known compound cannot be patented.

OBJECTIVE & RESEARCH METHODOLOGY

The research paper is based on a case study approach. The objective of the study was to analyse the impact of Section 3(d) on the Pharmaceutical Industry patents and how Section 3(d) helps in checking ever greening of patents which is useful for the growth of generic drug market as well as the poor class of patients.

CASE STUDIES:

1. The Novartis Glivec case:

In 2002, Novartis started its Glivec donation program in India to provide Glivec to patients, who were unable to afford the medicine, but halted that program after Indian drug manufacturers like Natco, began to produce a generic version of Glivec. In 2003, the Patent Office granted Novartis, Exclusive Marketing Rights (EMR) in India, which allowed Novartis to enjoy Glivec manufacturing and raise the price of Glivec almost ten-fold. In January 2006, with the introduction of the Product patent regime, the Madras Patent Office refused to grant Novartis a patent for imatinib mesylate. [4, 5]

Glivec (imatinibmesylate) film-coated tablets contain imatinibmesylate equivalent to 100 mg or 400 mg of imatinib free base. Imatinib mesylate is designated chemically as 4-[(4-Methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino] phenyl] benzamide methanesulfonate, Imatinib mesylate is a white to off-white to brownish or yellowish tinged crystalline powder. Its molecular formula is C29H31N7O • CH4SO3 and its molecular weight is 589.7. Imatinib mesylate is soluble in aqueous buffers of pH 5.5 but is very slightly soluble to insoluble in neutral/alkaline aqueous buffers. In non-aqueous solvents, the drug substance is freely soluble to very slightly soluble in dimethyl sulfoxide, methanol and ethanol, but is insoluble in n-octanol and acetone.

The first major ground for rejection was that because imatinib mesylate was a salt form of the free base imatinib, the Indian application therefore lacked novelty and inventiveness. The second major ground for rejection was based on Section 3(d) of the 2005 Amendment, which required that new forms of a known substance could only be patented as a product if they demonstrated "enhanced efficacy."

Therapeutic efficacy:

Although Novartis disclosed information that imatinib mesylate had a 30% increase in bioavailability (the percentage of the drug absorbed into the bloodstream) as compared with imatinib, the Patent Office found this insufficient to meet the "enhanced efficacy" requirement of Section 3(d).

Novartis filed petitions before the High Court at Madras, challenging the legal validity of section 3(d) of the Act 2005. Novartis challenged this provision when Indian Patents Office (IPO) rejected patent application of its drug called 'Glivec'. While deciding on the issue, the Court upheld that section 3(d) is neither vague nor arbitrary and therefore is not violative of Article14 of the Indian Constitution. [5]

It is submitted that the judgment of the Madras High Court in the Novartis case is in the right direction. Patent law is emerging in India and the Indian courts have followed a strict interpretation of an Indian statute which involves compliance with an international agreement. In history, every monopoly power has been abused and patent monopoly is not an exception. The interests of cancer patients are more important than monopoly rights. However, the ambiguities raised in the case should

be filled by appropriate amendments to the patent law in India. The Patent Controller's decision to reject the claim is fully justified on the following grounds:
(i) Novartis had not satisfied the pre-requisites for patenting, *viz*., novelty, inventive step and non-obviousness.
(ii) There is prior publication of the invention through patent applications filed in many countries, including Canada and U.S., in 1993, by taking priority from the Swiss applications filed in 1992.
(iii) The patent application does not claim any added therapeutic efficacy from the alpha-crystal form disclosed in the earlier applications. Hence, the patent application cannot satisfy the scrutiny of Section 3(d) of the Indian Patents Act, 2005.

The Novartis case, therefore, raised the question of rationality of patenting and pricing of medicines. It is an open secret that the pharmaceutical companies always try to continue the protection through ever-greening of their patents by incremental innovations. Despite new drug inventions and life expectancy ratios, most of the people in the developing countries do not have access to these medicines mainly due to price barriers. This decision will definitely go down in the annals of history as representing a milestone in patent jurisprudence in India.

2. Pfizer's Sutent case:

In Sep 2012, India's Patent Office revoked pharmaceutical company Sugen and licensee Pfizer's patent for the cancer drug Sutent, agreeing with Indian drugs maker Cipla that it lacks inventive step. An injunction stopping Cipla from launching a generic version of the drug, Sunitinib, was also been lifted. Sugen was granted a patent by Indian patent office for Sutent in 2007. Cipla filed a post-grant opposition in 2008, stating that the invention of the active compound in Sutent is obvious to person skilled in medicinal chemistry, based on previous publication on previous compounds used in anti-cancer treatments. Cipla also argued that Sugen had not disclosed information required under section 8 of India's Patent Act. Sugen attributed Cipla's lack of inventive step claim to hindsight bias, but the claim was upheld and the patent revoked in September 2012. [6, 7]

Sugen appealed against this decision at Delhi's High Court, and was granted a writ preventing Cipla from launching Sunitinib. Cipla appealed against the injunction at India's Supreme Court and in November, the case was referred to the assistant controller of patents.

3. Case of GSK's breast cancer drug Tykerb

India's Intellectual Property Appeal Board (IPAB) revoked a patent containing GlaxoSmithKline's (GSK) breast cancer drug Tykerb. [8] The IPAB supported GSK's basic patent for lapatinib, a compound which blocks signals within cancer cells that make them grow and divide, but they rejected a second patent directed to the salt form of the original compound. GSK markets lapatinib as Tykerb in countries including the US and India. Generic drug company Fresenius Kabi Oncology challenged the patents, prompting two separate IPAB rulings on July 27, published on August 1. Fresenius tried to revoke both patents by citing obviousness, non-disclosure and section 3(d), a provision in Indian patent law preventing the patenting of new forms of known substances that fail to enhance the substance's efficacy. IPAB rejected all parts of the challenge to the basic patent, which contains lapatinib as its active ingredient and is set to expire in 2019.

However, for the salt form of the original compound, GSK had claimed it absorbs much lower amounts of water "when exposed to a broad range of humidity's, and can be prepared in a stable crystal form", and therefore had greater therapeutic efficiency. But the IPAB said that while the properties of the salt may have more advantages over those in the original compound, it "do not result in therapeutic efficacy."[9] But the equivalent European patent was granted by the EPO, which acknowledged that the ditosylate salt absorbed significantly lower amounts of water when exposed to humidity, and that this could not have been predicted by the skilled person. So, the salt was non-obvious. Therefore, the concept of increased efficacy as recognized in Indian Patent act differs from other nations such as EU and may further impact the research and development in India.

Analysis of the cases:

Western pharmaceutical companies, looking to emerging markets such as India to help drive growth, have run into various obstacles recently, ranging from corruption and pricing probes in China to stock management problems in Brazil. But, while the move by Indian courts strengthens the country's burgeoning generics industry, big Western pharmaceutical firms will not make their formulae easy to copy.

If Novartis had won the case, it would have been granted a monopoly on Glivec, and denied Indian companies the right to make the drug. This would obviously have allowed Novartis to sell the medicine at a much higher price. Already, there is a huge differential with generic versions by Indian companies costing Rs 5,000-9,000 for a month's treatment, compared to Glivec's cost of around Rs 1.2 lakh a month. The order is also likely to encourage existing Indian manufacturers to step up production and perhaps new players to enter the market. This should lead to a further fall in prices.

The multinational drug companies are worried that this could be a trendsetter and are even threatening to block supplies of new patented medicines to India. But this is unlikely to deter Indian industry from developing "copycat" versions that would sell at a lower price. In short, while this is bad news for Big Pharma, it is as much good news for domestic manufacturers as it is for consumers. Big Pharma could also be worried that the Indian example may be emulated by others.

While the inclusion of section 3(d) by the way of an amendment in 2005 of the Indian Patent Act supports humanitarian aspect like affordable drug prices but is not very encouraging from business perspective. The very objective of having Section 3(d) as an amendment clause to Indian Patent Act was to prevent the "ever-greening" of patents ….removal of section 3(d) would result in "ever greening" and delays in the entry of generics, thereby affecting public health.

Importantly, major R&D investments in any case have moved to China with seven global companies having invested billions of dollars after the patent law was promulgated in India. The decision against patent rights in India today may negatively impact businesses' ability to invest in tomorrow's medical and technological advancements. However, Indian market is too important and lucrative and Big Pharma may not carry out the threats it has been making. And even if that were to happen, the Indian generics would have the capability to manufacture these newer drugs, especially as … many re-tinker existing compounds.

We should, therefore, be more worried about what impact this will have on patient's well-being and the ability to address the challenge of unmet medical needs. It is a huge relief for the millions of patients and doctors in developing countries who depend on affordable medicines from India, and for treatment. Though India has been under fire from multinational pharma companies for a public interest safeguard like Section 3(d) in its patent law, which leaves you to think to what extent can global intellectual property rules address in an effective manner the needs of the most vulnerable members of society.

In this respect, governments can improve access to patented pharmaceuticals in three ways. First, they can utilize the flexibilities which are already embedded in the TRIPs Agreement and Doha Declaration on public health, such as making it mandatory to have a compulsory license issued in order to manufacture generic drugs. Second, they can adopt some mechanisms, such as price information, price competition and price negotiation with public procurement and an insurance scheme, which will enhance the affordability of the drugs.[10-12] Third, governments can negotiate for a lower price with the pharmaceutical companies, as an incentive extended period of more than 20 years, which is the minimum stipulated under the TRIPs Agreement, can be allowed. The WHO can create a global database of the prices of drugs and the expiry of patent period so that there will be readily available data on the competitiveness of prices of medicines all over the world. Developing countries need cheaper medicines for fighting endemics like HIV/AIDS, Malaria etc. [13]

Conclusion:

Section 3 (d) of Indian Patent Law, April 2005, has helped to curb and bring to light, instances of substantial similarity in Patent infringement cases and thus reduce the ever greening of patents. The implications of scrapping the section 3(d) of the Indian Patents Act would prove serious and might endanger the Indian pharmaceuticals sector, comprising 20,000 plus pharma companies, besides, undermining the R&D and education in the field of Pharmacy in India. Indeed, section 3(d) of the Indian Patents Act in its present form and if interpreted firmly can prevent ever greening of existing patents as it does not consider any new form of a substance as invention if it does not result in the marked increase in efficacy of that substance. Therefore, this section is vital to stop frivolous patents and evergreening of patents. By virtue of this, the generic manufacturers can introduce cheap generic versions, on the expiry of the original patents, as derivatives based on incremental research do not qualify for patents. The generic sector is the ray of hope for all those patients who cannot afford costly patented molecules. India being a leader in the area of manufacturing of generic drugs, is considered to be the provider of the life line for chronic patients spread world over and dependent upon affordable generics of Indian origin. Developing country governments, international agencies like UNICEF or foundations like Medicines Sans Frontiers (MSF) and Clinton Foundation, rely heavily on importing affordable drugs from India. Almost 84% of the anti-retrovirals that MSF prescribes its patents worldwide come from Indian generic companies. Thus, Section 3d aims to promote the inventor for sequential developments of existing products or technologies, thus helping to bring in improved products and not redundant ones, to the market.

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