No patent to artful claims: "Incremental innovation" versus "therapeutic efficacy"

Introduction

The Supreme Court of India (**"SC"**) on April 1, 2013 rejected Novartis' appeal[1] for patent protection for its blood-cancer treatment drug "Glivec", which was held an "incremental innovation" not liable for protection. This judgment has again raised the issue on the contentious section 3(d) of the Patents (Amendment) Act, 2005 (**"Act"**) that aims to prevent "ever-greening"[2] by prohibiting the patenting of new forms of existing pharmaceutical substances that do not demonstrate considerably improved "efficacy." Making substances with enhanced efficacy patentable, section 3(d) encourages the sequential development of products to address the health care requirements more efficiently.

Section 3(d) also provides a test for patentability and, therefore, any pharmaceutical invention that does not comply with section 3(d) is not patentable. Patentability demands novelty, inventive step (non-obviousness), utility (industrial applicability), and sufficient description. It refers to those set of requirements that must be satisfied for a patent eligible subject-matter, i.e. an invention, to be granted a valid patent. The Novartis case highlighted the challenge which the provision against ever-greening poses to pharmaceutical companies in India. In light of the above, this e-newsline will trace the history of the Novartis patent application, discuss the legal basis, the crucial arguments raised before the various forums and assess the impact on the pharmaceutical sector in general.

1.0 Tracing the history of the case

In 1997, Novartis filed an application for a patent for the beta-crystalline form of Imatinib Mesylate with the name Glivec. This application was taken into consideration in 2005, under a "mail box" scheme. The Chennai Patent Office (**"CPO"**) refused patent to the invention of Novartis on the following grounds: **(i)** The subject compound did not differ significantly in properties with regard to efficacy as compared to the known compound despite recording that there was a 30% increase in bio-availability[3] of the subject compound over the known substance; **(ii)** Anticipation by prior publication, *i.e.*, the subject compound was already discussed in public documents, thereby, destroying the novelty of the invention; and **(iii)** The subject compound was in an obviously naturally occurring form and there was no inventive step involved. Based on these reasons, the CPO concluded that the beta-crystalline form of

[1] Novartis AG vs Union of India; Civil Appeal Nos. 2706-2716 of 2013 (Arising out of SLP(C) Nos. 20539-20549 OF 2009); Natco Pharma Ltd vs Union of India; Civil Appeal No. 2728 OF 2013 (Arising out of SLP(C) No. 32706 of 2009); and Cancer Patients Aid Association vs Union of India; Civil Appeal Nos. 2717-2727 of 2013 (Arising out of SLP(C) Nos. 12984-12994 OF 2013) SLP(C)……../2011 CC Nos.6667-6677)

[2] Ever-greening refers the strategy of taking new patents by creating a small variation in the existing patent and extend the term of high earning patents

[3] Bio-availability is the increased ability of the drug to dissolve into the bloodstream of the patient

Imatinib Mesylate was not an invention under the Act and rejected the Glivec patent application.

Novartis appealed against this rejection before the Chennai High Court (**"HC"**) and challenged section 3(d) of the Act, which, it said, was in violation of India's obligations under TRIPS.[4] After the formation of the Intellectual Property Appellate Board (**"IPAB"**), the petition challenging the order of the CPO was transferred to IPAB by order dated April 4, 2007, where these cases were registered as appeals. The petition challenging section 3(d) was heard by the HC. Though HC ruled that it had no jurisdiction to decide on the issue whether Indian patent laws comply with TRIPS, it however, held that section 3(d) of the Act does not suffer from ambiguity and arbitrariness and contains reasonable in-built protection for patent applicants and, accordingly, dismissed the petition. The HC explained that it casts a duty on the patent applicant to prove that the discovery had resulted in "*enhancement of a known efficacy of that substance*". The HC added that the explanation creates a "*deeming fiction that all derivatives of a known substance would be deemed to be the same substance unless it differs significantly in properties with regard to efficacy*". IPAB also rejected the appeals transferred to it from HC. Novartis preferred an appeal against IPAB's order to the SC in 2009.

2.0 Legal basis

There are two legal aspects central to this case; first, the prerequisites of section 3(d) and second, if India is really violating its obligations under TRIPS. The requirements under section 3(d) of the Act are described below –

"***3. What are not inventions*** *–The following are not inventions within the meaning of this Act –*

(d) *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.*

Explanation – For the 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;"

The above clearly provides that a new form of a known substance which does not result in enhancement of the known efficacy shall not be considered as an invention. In addition, the derivatives or other forms of a known substance would be considered as a new substance only when it differs significantly in properties with regard to efficacy. So, prominence is put on the significant increase in the efficacy of the product while considering a new form of a known substance for granting patent.

[4] Prior to 2005, Indian patent law provided for process patents but with the 2005 amendment, the Act retrospectively allowed for product patents. This was done to meet TRIPS obligations under the WTO

Regarding the TRIPS Agreement, it does not prevent members from taking measures to protect public health. The Doha Declaration[5] has been instrumental in interpreting the provisions of TRIPS Agreement as incorporated in the Act and states that the TRIPS Agreement "*can and should be interpreted and implemented in a manner supportive of WTO member's right to protect public health and, in particular, to promote access to medicines for all*". The dichotomy of safeguarding the rights of the patent holders while protecting public health as well still prevails.

3.0 Discussion before the SC

The primary contention raised by Novartis before the SC was that section 3(d) of the Act would not apply. The SC rejected this contention and analyzed if the product for which Novartis claims patent qualifies as a "*new product*" and involves technical advancement over the existing knowledge and that makes the invention "*not obvious*" to a person skilled in the art. The SC found that Imatinib Mesylate was a known substance from the Zimmermann patent.[6] Accordingly, the SC held that the chemical compound did not qualify as an "invention" within the meaning of sections 2(1)(j)[7] and 2(1)(ja)[8] of the Act. Even the therapeutic qualities of the beta-crystalline form of Imatinib Mesylate were the same as those possessed by Imatinib in free base. The SC clarified that chemical properties like solubility or thermodynamic stability may help in processing and/or storing the substance, but not enhance the "therapeutic efficacy". The SC noted that section 3(d) provides for a second level of qualifying standards for pharmaceutical products in order to leave the door open for genuine inventions. It simultaneously keeps a check on repetitive patenting or extension of the patent term on spurious grounds. The SC further clarified that the term efficacy relates to "therapeutic efficacy" and rejected its broader interpretation, which would have included even non-therapeutic efficacy such as properties which contribute to better storage and ease of administration.

The other contention raised by Novartis was if the 30% increase in bio-availability of the beta-crystalline form of Imatinib Mesylate will qualify as an increase in therapeutic "efficacy." Efficacy means "*the ability to produce a desired or intended result*". Hence, the test of efficacy in the context of section 3(d) would be different. It would depend upon the result that such a product will produce. In other words, the test of efficacy would depend upon the function, utility or the purpose of the product under consideration. Therefore, in the case of a medicine that claims to cure a disease, the test of efficacy can only be "therapeutic efficacy". The SC held that there is a need to establish a link between the increased bio-availability with the increase in therapeutic efficacy of a drug and when Novartis could not establish it, the SC rejected this argument as well. According to the SC, the concept of "therapeutic efficacy" is to be judged both strictly and narrowly. From this perspective, "efficacy" does not extend to the change of form of a substance, and the change of the chemical properties characteristics of that form.

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[5] WTO Ministerial Conference, Fourth Session, Doha, November 9-14, 2001, Declaration on the TRIPS Agreement and Public health

[6] Patent previously granted in US to Zimmerman in 1993, which included the substance Imatinib Mesylate

[7] "Invention" means "*a new product or process involving an inventive step and capable of industrial application*"

[8] "Inventive step" means "*a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in the art*"

In light of the above, the SC dismissed the appeal filed by Novartis for its cancer drug Glivec. The SC not only considered the above contentions but also a number of factors before giving this judgment, like, striking a balance between promoting R&D in science and technology and minimizing the abuse of patent monopoly and give prominence to the accessibility to health care.

4.0 Impact

The concept of "efficacy" sets the balance between the conflicting interests at stake, as the threshold of patentability. The Act also provides a new definition for a pharmaceutical substance as "*any new entity*[9] *involving one or more inventive steps.*"[10] The above definition is quite broad, and definitely has a bearing on determining patentability for pharmaceuticals. The judgment made it clear that though the interpretation of efficacy is now a settled topic as SC unequivocally interpreted it to mean "therapeutic efficacy", it has left open the question of how exactly to interpret "therapeutic efficacy".

Indeed, ever-greening would become more difficult in India and the applicants would have to show the enhanced efficacy of the new substance over the existing. Therapeutic efficacy has become as an additional condition for patent registration. Interestingly, this judgment does not say that new forms of known compound can never be patented or improving the bioavailability characteristics of the drug will never result in enhanced efficacy. The focus should be on therapeutic enhancement rather its physical properties. Definitely the improved safety profile and reduced toxicity will have an impact on the efficacy of the drug but its therapeutic effect will be separately analyzed. The SC has confirmed that the Act discourages and prevents ever-greening of patents and provides for stricter standards of patentability for medicines, which section 3(d) encapsulates.

Following this judgment, the primary question that is being widely discussed is the impact on foreign investment in the pharmaceutical sector in India. Currently, the Indian pharma market is estimated to be of $30 billion a year and the patented products make up barely 1% of that. McKinsey & Company's report, "India Pharma 2020"[11] predicts that the market could grow to $70 billion by 2020 and grow annually at 21%. Given this kind of growth predictions, the business opportunities will grow tremendously in this sector, so it is safe to assume that the impact of this case could be limited but will definitely compel pharmaceutical companies to re-think their strategies in India. Affordability is on one side of the debate and IP protection on the other. The well-known assumption that greater levels of IP protection necessarily lead to higher rates of innovation has not been empirically proved. The reasoning of SC, essentially emanating from the interpretation of section 3(d), sets a higher threshold for patentability, which seems reasonable. The strict interpretation of section 3(d) by the SC should force the pharmaceutical industry to invest more in R&D and actually come up with more efficacious drugs having real enhanced therapeutic value.

[9] Ideally, "new entity" is required to be stated clearly as a "new drug molecule" for specificity
[10] Section 2(1)(ta) of the Act
[11] Please see http://www.mckinsey.com/locations/india/mckinseyonindia/pdf/India_Pharma_2020.pdf for details, viewed on May 17, 2013

Conclusion

In India, this litigation has been pitched as a battle between big pharma and health aid groups. In 2012, the Indian Patent Office granted compulsory license[12] to the Indian drug company Natco to manufacture Bayer's patented cancer drug, Nexavar. These steps have compelled the pharmaceutical companies to re-think their approach on conducting R&D in India, obtain patents in India and secure their patented products or processes. The primary aspect of the pharmaceutical industry is the perpetual advance in creating new knowledge through R&D and providing proprietary safeguard to it. Without effective patent protection, the incentives for multinationals to invest in R&D in India would be minimal.

Indeed, the success of the pharmaceutical industry requires not only the ability to frequently come out with new drugs but also the feasibility of obtaining patent protection for them. India is slowly moving into global markets and competing with international quality standards and prices. Although R&D is an important factor to ensure a competitive edge in the international arena, the future of the Indian pharmaceutical industry hinges on patent protection of products with optimal patentability threshold.

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[12] Section 84 of the Act provides for this option wherein an individual or company seeking to use another's patent can approach Patent Controller if the following three conditions are satisfied: **(i)** reasonable requirements of the public with respect to the patented invention have not been satisfied; **(ii)** the patented invention is not available to the public at a reasonably affordable price; and **(iii)** the patented invention is not worked/developed in the territory of India