

IMPLEMENTATION OF TRIPS UNDER WTO IN INDIAN LAW WITH SPECIAL REFERENCE TO PHARMACEUTICALS INDUSTRIES

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“Whether a new drug that merely modifies an existing patented molecule deserves its own patent depends on the therapeutic advantages it offers”

The first week of April produced two landmark judgments for multinational pharmaceutical companies trying to make their mark in India. On April 1, the Indian Supreme Court denied patent protection for Glivec¹. On April 5, the Delhi High Court dismissed a claim by Merck's Indian subsidiary², that Mumbai-based Glenmark Pharmaceuticals should be barred from marketing generic versions of the hit diabetes drugs Januvia and Janumet. By allowing generic versions of these three drugs to flood its market, India seems to be sending a strong message that pharmaceutical manufacturers outside its borders will not have unlimited pricing power over its market of 1.2 billion people. India's denial of patent protection, therefore, raises questions about the pharmaceutical industry's ability to make a profit in the world's second-most populous country -- and it adds fire to the debate over whether the industry's obligation to provide access to life-saving drugs should outweigh its drive for profits.

The decision of the Indian Supreme Court to deny Novartis' application for patent protection for an improved version of its Glivec drug - the culmination of a seven-year battle - has certainly made world headlines and put the spotlight on generic drugs and the practice of evergreening, which could have a significant impact on the local pharmaceutical industry

The key issue is a practice known as "evergreening"³ & “generic drugs”: making small changes to a drug, often about to come off patent, in order to gain a new patent that extends its manufacturer's control over it. It's a way of cheating on the implicit bargain of patents: that a government-backed monopoly is granted in exchange for the invention entering the public domain at the end of the patent's lifetime is called evergreening⁴. According to the U.S. Food and Drug Administration (FDA), generic drugs are identical or within an acceptable bioequivalent range to the brand-name counterpart with respect to pharmacokinetic and pharmacodynamic properties. In most cases, generic products are available once

¹ (spelled Gleevec in the U.S.), a cancer drug made by Novartis that is patented in nearly 40 other countries.

² Merck Sharp and Dohme,

³ "Faunce TA The awful truth about evergreening". The Age. 2005-12-20. Retrieved 2007-09-21.

⁴ "Evergreening of Pharmaceutical Market Protection". European Generic Medicines Association. Retrieved 2007-10-19.

the patent protections afforded to the original developer have expired. When generic products become available, the market competition often leads to substantially lower prices for both the original brand name product and the generic forms

'The judgment is significant as it sends out a strong message to the world that while we respect international agreements, we also have a responsibility towards the poor and will not support any measure to extend patents beyond their normal lives,'

Earlier days when the three words 'Drug Patents in India' didn't have much chance of appearing together in a sentence, but that all changed in 2005, when the country changed its laws to recognize *chemical substances* as well as *process patents*. Before 2005, only *manufacturing processes* could be patented in India, not *molecules*. The result was a very strong generics industry, built on the skills of chemists who developed new ways to make drugs without infringing Pharma companies' process patents.

World Trade Organization (WTO) Trade-Related Aspects of Intellectual Property Rights Agreement (TRIPS) set out for the minimum standards for the protection of intellectual property, including patents for pharmaceuticals. It focuses on India's concerns about the impact of TRIPS on prices for pharmaceuticals and other healthcare inventions. It traces how the TRIPS aids low-income consumers in developing countries from obtaining life-saving medications and equipment. Also the article explores how these concerns are responded by the WTO by issuing a Declaration at the Ministerial Meeting in Doha, Qatar in 2001 in which measures to protect public health were taken. It explores how public health is reaffirmed by the right of governments to use compulsory licenses to override the exclusive rights conferred by patents.

Improved efficacy is the basis for granting Patent, can turn out to be in the eye of the beholder. In India Glivec, Tarceva, Viread, and (most recently) Nexavar are drugs that have fallen into this particular pothole.

In its decision to dismiss Bayer's appeal, the Delhi High Court made a blistering attack on the company's efforts to block copies of its cancer medicine Nexavar. Calling the appeal "a speculative foray," the court added that "the petitioner, no doubt, is possessed of vast resources and can engage in such pursuits."

What, exactly, is Indian drug patent law supposed to accomplish in terms of evergreening and generic drugs? And why would any drug-inventing company be so foolish as to rely on it?

Because generics pose a threat to pharmaceutical companies, the issue of evergreening has become very important. Indian patent law is known to be hostile to evergreening, but it's been reported that there are patents for the new Glivec in a number of countries, including the US, China, Russia and South Africa.

India has had lax patent laws compared with other countries. They allow Indian companies to produce generic versions of drugs that are under patent elsewhere. The competition between manufacturers drives down the price of the drug for many years; India did not recognize drug patents at all. The establishment of the World Trade Organization (WTO) has led to a tremendous paradigm shift in world trade. The agreement on Trade-Related (Aspects of) Intellectual Property Rights (TRIPS) was negotiated during the Uruguay round trade negotiations of the General Agreement on Tariffs and Trade (GATT) and “one of the primary reasons for incorporating intellectual property issues into the GATT framework was the pharmaceutical industry”.⁵ India signed the GATT on 15 April 1994, thereby making it mandatory to comply with the requirements of GATT, including the agreement on TRIPS. An international law that gives drug companies a 20 year patent on the production of drugs. TRIPS required India to introduce patents on medicines in 2005.

In contrast to other countries in the TRIPS agreement, India also introduced laws that prohibited an industry tactic called “evergreening.” Evergreening is where a company extends its patent on a drug by repatenting slightly modified versions of the drug. For example, they might release the original drug in its salt form, even if this does not bring a therapeutic improvement.

India—alongside Brazil, Thailand, and South Africa—is one of the few countries with laws against evergreening. The Indian Patent Act, as amended by the Patents (Amendment) Act 2005, states that drugs cannot be patented if they result from “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.” This has allowed the continued production of cheap generic versions of drugs by Indian companies.

Data exclusivity provides exclusive rights to technical data generated by innovator companies through clinical trials and prevents competitors from producing low-cost generic versions of the drug during the period of exclusivity. The TRIPs Agreement already provides for data protection. However, data protection is different from data exclusivity. “Article 39(3) of TRIPs prevents unfair commercial use or marketing by generic companies of the data generated by clinical trials from innovator companies and submitted to the drug regulator. However, this is not the same as data exclusivity. As of now, Indian firms that make generic versions of innovator medicines get their approvals after proving that their product is bio-equivalent to the original drug. The drug regulator uses the data submitted by the innovator to decide the safety and efficacy of the generic drug. Data exclusivity will prevent this. The regulator will not be able to use the innovator’s data to make decision. This will in turn oblige generic companies to undertake clinical trials and delay the entry [into the market] of generic drugs.”

⁵ Zafar Mirza, *WTO/TRIPs, Pharmaceuticals and Health: Impacts and strategies*, The Society for International Development, SAGE Publications.

Compulsory licensing -- the granting of a license to produce a generic version of a product -- is explicitly protected by WTO treaties to help countries improve public health and ensure access to medicines.

When India finally adopted its expanded patent law, it was widely hailed and multinational firms began expanding with gusto. They now sell their latest branded medicines here, expecting the burgeoning middle class and slowly growing health insurance system will pay for them. Pharmaceutical manufacturing has boomed, as has the clinical trial industry.

The Indian Supreme Court has rejected Novartis' appeal for patent protection for Glivec in a judgment delivered on April 1 2013, & held that Glivec was an example of "incremental innovation" under Section 3(d) of the Indian Patents Act and, as such, not liable for protection. This controversial section deals with "ever-greening," a term used to describe creating a new version of a drug with only incremental modification and no innovation in order to extend the life of a patent.

What constitutes an "incremental" change is, of course, a matter of judgment and the ruling brings back into the spotlight the patent wars that have been fought in India over the past few years.

"There has been a lot of debate about a judgment given by the Supreme Court. It's not an issue of law because section 3(d) is embedded in the Indian Patent Acts, which is TRIPS compliant".

In 2006 the drug company Novartis applied to the Indian government for a patent on their cancer drug imatinib mesylate (marketed as Glivec), which was rejected as contravening anti-evergreening laws because it was based on a compound that already existed. Imatinib mesylate is used to treat several forms of cancer including chronic myelogenous leukaemia and is the salt form of its precursor imatinib. Novartis showed that imatinib mesylate had a 30% increase in bioavailability (the proportion of the drug absorbed into the bloodstream) compared with imatinib. However, the Patent Office didn't consider this sufficient to meet the "enhanced efficacy" requirement of the Indian Patent Act.

Novartis challenged the decision, taking their case to the Supreme Court stating that the judgement violated World Trade Organisation (WTO) rules on intellectual property set in 2005 that India had adopted, but its request was rejected by Chennai's court in 2007.

However, numerous western pharmaceutical companies have struggled to patent their drug molecules in the country; for example, Pfizer was granted a patent for anticancer agent Sutent (sunitinib) in 2007, but this was revoked last year. Merck & Co is currently also suing Indian firm Glenmark over generic versions of its diabetes treatment Januvia (sitagliptin) and Janumet (sitagliptin plus metformin). The high court in Delhi has allowed the suit to proceed, but denied Merck an injunction to prevent Glenmark from selling its generic

versions in the meantime. And even when patents are granted, India's government can override them by issuing a 'compulsory license', as happened with Bayer's anticancer drug Nexavar (sorafenib) last year.

Indian law requires certain pharmaceutical inventions to show 'enhanced efficacy', thus greatly limiting pharma companies' ability to obtain patents on molecules, especially those that were already patented elsewhere before India introduced product patents. 'Not only is this term unclear, but it goes far beyond the specific requirements of patents under TRIPs,' 'Moreover, by discriminating against a particular field of technology, it may be inconsistent with TRIPs, which sets one standard for all patents and does not allow different patent requirements for different industries.'

The Swiss firm, however, did not give up and appealed to the Supreme Court of India in 2009, arguing that Glivec was a "new product" under section 3(2) of the Act, attributed to beta crystalline form of Imatinib Mesylate.

For this reason, the drug in question, they claimed, had much better properties: it was easier to absorb, had better thermodynamic stability and lower hygroscopicity and therefore qualified for a fresh patent.

However, the court discovered that the package of the drug described its product as Imatinib Mesylate and not the beta crystalline form of the compound.

As a result, they rejected the plea based on a law aimed at preventing companies from getting fresh patents, making only minor changes to existing drugs, a practice known as "evergreening".

The bench also explained the meaning of the word "invention" when it ruled out the plea, as "something different from a recent previous or one regarded as better than what went before or in addition to another or others of the same kind" and Glivec failed to fulfill any such features and certainly did not qualify enough to warrant a patent.

Evergreening has been a hot topic of late because of the recent ruling by India's Supreme Court to refuse to grant in the above case the companies claims the drug is more easily absorbed into the blood and, considering it is used to fight leukemia, that is enough of an improvement to warrant patent protection. This decision was defended by Indian Govt. on the ground that it was absolutely justified under the law and that India's patent law does not accept evergreening. The counterparts argues that There can be no evergreening in India because there have never been any patents for Gleevec.

Furthermore, India's concept of evergreening is somewhat overreaching. According to its patent law, a new version of an old drug must demonstrate improved efficacy to merit a patent monopoly. But what if the new product improves patient safety? Or reduces adverse effects? Or increases adherence? Anything done to a molecule which results in a clear medical advantage for patients, then it should be protected.

The problem is, these modified drugs don't offer enough of an advantage over generic versions of the original molecules. So the sophisticated lifecycle plans brand-name companies have for their products — rolling out new versions when patents near expiry — are created primarily to help bottom lines rather than patients. And the argument that this is necessary to earn enough money to reinvest in new R&D doesn't hold much weight, if that research only results in more "me-too" drugs.

They have to recoup R&D costs, yes, but the question is: Is it useful R&D? If the R&D is just to tweak a product to get more monopoly protection without really providing an improved medication, then maybe it doesn't deserve a patent.

Generic drugs are equivalent to brand-name drugs. They have the same medicinal ingredients. A me-too drug, in some ways, is just a sophisticated generic drug. It is just tweaked a bit to claim it as a new invention. Should they get patents?

Well, if that tweak advances medical science in any way, then the answer to that question is yes. Bringing a new drug to market carries Vegas-like odds and putting up barriers to protecting intellectual property will only discourage innovators from taking those risks.

In near future we may find company's drug got wiped out in a phase-3 clinical trial, and by that time they had already sunk 800 to 900 million bucks into that drug.

There are extremely high risk involved to develop new therapies and compounds. Some are going to be revolutionary. Some are going to be incremental. The patent system, all the way back to the Statute of Monopolies⁶ recognizes that it is good for the economy to encourage people to take these risks and to bring new things forward.

A recent Indian Supreme Court decision prohibited pharmaceutical companies from extending patents through "evergreening." Evergreening delays availability of more affordable generic drugs through minor changes to the existing drug. Evergreening is a strategy with a great return on investment⁷.

⁶ [a British act passed in 1624],

⁷ That's because pharmaceutical companies spend \$19 for promotion and marketing to every \$1 spent on basic research.

Conclusion: The new financial year began with above landmark judgment by the Supreme Court on Novartis which will have far reaching effects on the patentability of therapeutic drugs. Though it is seen as a triumph of generic drug companies over pharmaceutical giants, of hope for the common man, a socio-legal fairytale, its actual legal implications are lost in the excitement.

At the core of the judgment is whether a patent should be given to an invention comprising a new form of a known drug, which does not enhance the efficacy of the drug - and, in this context, what is the efficacy of the drug.

The judgment has analyzed the Indian Patents Act, specifically the provisions relating to what are patentable inventions as far as chemical or pharmaceutical substances are concerned. It has laid down standards for patentable inventions relating to medicines. The judgment has interpreted those provisions and has curbed attempts at repetitive patenting of known medicines. The apex court has held that for grant of patent the subject must satisfy two distinct tests at the heart of the Patents Act, namely of "invention" and "patentability".

The test of patentability sets up a second and higher tier of qualifying standards, especially for chemical substances/medicines, in order to leave the door open for true and genuine inventions, but, at the same time, check any attempt at extension of patent term on spurious grounds. Under the scheme of patent, a monopoly is granted to an individual in exchange of the invention being made public so that, at the end of the patent term, the invention will belong to the people at large who may benefit from it. The apex court has observed that a patent should not be traded as a commodity, especially for making high profits and filing infringement actions. In the case of a new form of a known medicine, it must possess therapeutic efficacy that is the ability to produce a desired result, which must be judged strictly and narrowly. The court also discussed bio-availability (the degree to which a drug becomes available to the target tissue after administration) and held that increased bio-availability does not necessarily imply increased therapeutic efficacy.

What does this mean for future patents in this arena ? A patentee will think twice about evergreening patents. A drug merely passing the test of inventive step that is a technical advance as compared to the existing knowledge, and not obvious to a person skilled in the art, is not enough. It must clear the test of enhanced therapeutic efficacy. Future patentees would do well to remember that evidence of enhanced therapeutic efficacy must be shown.

The judgment is not meant to deter patenting inventions but rather to exclude claims to patents on spurious grounds. It is not a strike against the pharmaceutical industry, nor is it a ruling meant to appease the masses. It will be a grave mistake to read the judgment to mean that the Act bars patents for all incremental inventions

of chemical and pharmaceutical substances. *The judgment attempts to strike a balance between public interest and inventor interest.*

