COVER STORY

Patent to plunder

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India's efforts to produce and supply life-saving drugs at affordable prices face challenges from multinational companies trying to “evergreen” their patents.

Demonstrators outside the offices of Novartis in New York City on February 22 demanding that the Swiss pharmaceutical giant withdraw its appeal in the Supreme Court of India against the Madras High Court verdict in favour of the rejection of its patent application. The hearing in the case will begin in July.

THE average life expectancy across the globe has increased from around 30 years a century ago to over 65 years today. This has been made possible in large part by modern medicine. Never before in history have humans had access to such an array of medicines and
devices to treat and ameliorate illness. These advances have also created a new terrain of conflict. While the knowledge required to promote health has expanded enormously, paradoxically, so have the attempts to restrict access to such knowledge.

The current regime of intellectual property rights (IPR) seeks to exercise monopoly control over the production and reproduction of knowledge. Consequently, products to treat a range of diseases are denied to those who need them the most merely because they cannot pay for them. It is denied to them not because these medicines cannot be produced at a reasonable cost but because a few corporations treat the knowledge as their property and sell these medicines at exorbitant prices. They also use the monopoly created by patents to prevent other companies from producing and selling these drugs at much lower prices.

Nothing illustrates this better than the impact of the human immunodeficiency virus/acquired immune deficiency syndrome epidemic in Africa. In 2001, the annual cost of treating one HIV/AIDS patient was $10,000. Some African countries would have had to spend more than half their gross domestic product to procure these medicines for those who needed them. The tragedy is that these medicines need not have been so expensive. In 2003, the Indian company Cipla finally started selling the same medicines at $250 per annum – at 1/40th the earlier cost. Even this price was high, and the same drugs can be bought today at less than $100 for a year's supply.

Between 1972 and 2005, India had one of the most progressive patent laws in the world. It was precisely in this period that the domestic drug industry became a global force and is now the third largest (by volume) producer of drugs in the world. The signing in 1994 of the World Trade Agreement [Uruguay Round] – which became the World Trade Organisation (WTO) in January 1995 – marked India's accession to a global patent regime. India's earlier law, the Patents Act, 1970, worked on a very simple principle. It argued that patents (a monopoly over the manufacture and distribution of a product) would not be allowed in the two most vital areas of human existence – food and health. New medicines could be manufactured by Indian companies without hindrance. This is why Cipla was able to manufacture and supply HIV/AIDS medicines at a fraction of the earlier prices. Much of this enabling environment for Indian companies changed when India amended its Patents Act in 2005 – after completing the 10-year transition period allowed when India signed the WTO agreement.

However, Parliament, while amending the Patents Act to conform to the obligations set by the WTO agreement, introduced a number of “health safeguards”. These were designed to mitigate the impact of a patent regime that denied Indian companies free access to available knowledge. Two recent developments are now poised to test the ability of the domestic law on patents after the 2005 amendments to actually secure access to medicines.

The Indian law faces a challenge from the Swiss drug maker Novartis. At the heart of the challenge lies the vital anti-leukaemia (blood cancer) drug called imatinib mesylate. The drug was introduced in 2001 and has quickly become the key drug used to treat a form of leukaemia called chronic myeloid leukaemia (CML). For patients suffering from CML, the drug is the difference between a healthy life and a death sentence.

Imatinib mesylate has been patented in many countries by Novartis, which sells the drug under the brand name Glivec (or Gleevec). The
patent application for Glivec was rejected in 2006 by the Indian patent office, which upheld the contention of Indian generic companies and of the Cancer Patients Aid Association (CPAA) that Glivec was not a new drug and did not merit grant of a patent.

Novartis persisted in its efforts and appealed to the Intellectual Property Appellate Board (IPAB). In June 2009, the IPAB upheld the decision of the patent office. Simultaneously, Novartis filed two writ petitions in the Madras High Court, one challenging the decision of the patent office and the other challenging Section 3(d) of the Patents Act. In the latter case, Novartis claimed that the section was in violation of India's obligations to the WTO. The Madras High Court rejected both these appeals. It pointed out that domestic courts could not be asked to give an opinion regarding international treaties and obligations and that Novartis should take its complaint to the disputes settlement mechanism in the WTO. Novartis has never done so, and clearly Section 3(d) does not violate international obligations.

It is important to understand why courts and the patent office have repeatedly turned down Novartis' request for a patent. The original patent on Glivec was filed by Novartis in 1993 for the amorphous molecule of the chemical imatinib mesylate. An amorphous salt is what exists in nature and is a mixture of different variants. In the late 1990s, Novartis filed a fresh patent for the beta variant of the molecule, which is already present in the amorphous salt patented earlier. It also claimed that the beta variety was better absorbed in the body and was more stable. The 1993 patent was not recognised in India as at that time Indian law did not allow the patenting of medicines.

When the law was changed in 2005, Novartis applied for a patent for the beta variety of the salt. The patent office refused a patent on a number of grounds. It said that under Section 3(d) a slightly modified version of a known molecule could not be patented. Section 3(d) stipulates that trivial changes in existing molecules cannot be candidates for fresh patenting. Such trivial patenting (known as “evergreening”) is an old ploy used by drug companies to extend their monopoly. Companies first apply for a patent for the basic molecule and then attempt to extend the life of their monopoly by applying for fresh patents after a few years on a slightly different version of the original molecule.

The patent office also said that the patent application did not fulfill two necessary criteria for patenting – novelty (that is, it should be a new compound) and inventive step (that is, it should involve an inventive state that is not anticipated by someone well versed with the technology). Both the patent office and the IPAB invoked Section 3(d) to deny Novartis' appeal.

Novartis is now arguing its case in the Supreme Court through a special leave petition challenging the IPAB's interpretation and application of Section 3(d) to its patent application, and final arguments on the case are to commence on July 10, 2012. Instead of challenging Section 3(d), Novartis now argues that the section has not been properly interpreted. The section says that minor variations in an existing molecule cannot be patented unless there is a “significant” enhancement in the “efficacy” of the medicine. Now Novartis claims that since the beta variant is better absorbed (by about 30 per cent) it constitutes a significant enhancement. Novartis' panel of expensive lawyers is led by Gopal Subramaniam, who was the Solicitor General of India (and hence technically responsible for leading the government's defence) when Novartis first approached the Supreme Court.

Claims of altruism
How much would Novartis gain if its patent were to be upheld? The arithmetic speaks for itself. A month's supply of Glivec costs Rs.1,20,000 – way beyond the means of more than 99 per cent of Indians. Remember that the drug has to be taken lifelong. Yet the same drug is sold by several Indian companies at Rs.8,000 for a month's supply – 1/15th of what Novartis charges. At the heart of Novartis' battle is a $4-billion-plus global market for Glivec – about Rs.20,000 crore, which is equal to the entire Union health budget of India for 2010-11.

Novartis claims that price is not an issue in India because “eligible” patients are covered by a programme called GIPAP – Glivec International Patient Assistance Programme. The only problem with Novartis' spin on the issue is wrong arithmetic. Novartis claims that it supplies the drug free of cost to about 11,000 leukaemia patients in India. The CPAA estimates that there are over 100,000 patients in India who suffer from CML and that 20,000-odd new patients are added every year (the disease has an annual incidence of 1-2/100,000 population a year). Studies also show that the disease strikes earlier in life in India – in a younger age group – than in Europe and North America.

Novartis has regularly claimed credit for its GIPAP programme. How altruistic is the GIPAP programme? The programme was launched in 2002, and Novartis claims that it reaches 35,000 patients in 80 countries. In 2003, The New York Times carried an investigative report that blew the lid off the claims of altruism. The report (as well as another report from Argentina) documents how GIPAP has been used by Novartis to first create a demand for Glivec and then to pressure governments and health management organisations to reimburse its cost. The report stated: “In wealthier countries like South Korea, Hong Kong and New Zealand, Novartis, meanwhile, has encouraged patients who have received free drugs to become advocates, pressing public health systems to pay high prices for the drug. One company document declared that drug donations along with media campaigns and legal tactics were part of a concerted plan to win reimbursement.
Novartis says that it is not fighting the case to make money but to uphold the principle that it deserves credit for the investment it made in research to develop the drug. What Novartis does not tell us is that Glivec was granted “orphan drug” status in the U.S. and was therefore eligible for tax rebates equal to half the cost of clinical testing (the major cost of drug development).

Brian Druker, one of the scientists involved in developing imatinib while working in Oregon Health and Science University Knight Cancer Institute, commented in a signed article in Livemint in 2007: “My work in Oregon on a therapy for CML was primarily funded by public sources, particularly the National Cancer Institute. My persistence with scientists at Ciba-Geigy (now Novartis) helped to keep the development of imatinib on their agenda despite uncertainty from product managers. As imatinib progressed through early and late clinical trials and demonstrated outstanding results, scientific and media interest in our discovery increased. The approval of imatinib by the FDA [the U.S. Food and Drug Administration] in May 2001 for use in CML was the culmination of a 10-year project for me, something I had dreamed of since medical school.” And yet, Novartis laments that it is not being given due credit for its “original” research.

**India breaks a patent**

In March 2012, the Indian patent office issued a compulsory licence (CL) to the Indian generic drug company Natco Pharma Ltd for Bayer's anti-cancer drug sorafenib. The licence was issued under Section 84 of the Patents Act. It breaks Bayer's monopoly over the drug, and Natco can now manufacture and sell the drug in India.
Section 3(d)

Section 3 of the Indian Patents Act, 1970, lists “what are not inventions”. The relevant subsection (d) after it was amended in 2005 reads:

“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”.

Before 2005, subsection (d) read thus:

“the mere detection of a new ...
Sorafenib has been shown to extend survival rates among those suffering from hepatocellular carcinoma (liver cancer) and renal cell carcinoma (a form of kidney cancer). At present, Bayer's version of the drug costs Rs.2,80,000 a patient a month. Natco will make the drug available at a cost of Rs.8,800 a month, a 97 per cent reduction on Bayer's price.

The decision has been followed by reverberations across the world. A range of people working on public health and access to medicines issues have welcomed the decision of the Indian patent office. The fact that this is the first CL issued in India is in itself a major step and can be a precedent for many more CLs in the future.

The CL on sorafenib not only helps cancer patients who require the drug but is also a step towards building domestic manufacturing capacity and knowhow in a new range of anti-cancer drugs. Sorafenib is one of the first in a group of new drugs that specifically target cancer cells. Similar drugs with better results are likely to be available over time, and it is important that generic manufacturers develop capacity to manufacture these.

Patents are supposed to represent a balance between the rights and obligations of a patent holder. Patent laws are required to ensure that the products of new research are available to the largest number of people, while providing a fair return to the innovator. Compulsory licensing is a key instrument incorporated in patent laws to maintain this balance. It allows regulators to break the monopoly of a patent holder by allowing a third party to use the patent in situations where the patent holder abuses the monopoly right to deny access to its innovation to a very large number of people.

The 2005 Patents Act provided broad grounds for issuing a CL, including (a) the reasonable requirements of the public with respect to the patented invention have not been satisfied, or (b) it is not available to the public at a reasonably affordable price, or (c) the patent is not being worked. By pricing its drug at almost Rs.3 lakh for a month's treatment, Bayer was denying access to the drug to thousands of cancer patients in the country.

**Decisive battle?**

The two developments have several long-term implications for India's domestic drug industry. Novartis is challenging the very heart of the Indian Patents Act and its attempt to balance the rights of patent holders with the needs of the Indian people for access to treatment that is affordable. Section 3(d) of the Act has been used several times by the Indian patent office to deny patents for other similar trivial inventions, especially in the case of HIV/AIDS medicines. If the section is diluted or overturned, all these cases will be reopened. Not just that, it will open the door for a flood of applications, many of which were not filed by companies because of the existence of Section 3(d).

The case has implications not just for leukaemia patients but for a whole range of patients who are today able to access cheaper drugs made by Indian companies. These patients are located not just in India but in over a hundred countries in Asia, Latin America and Africa. For example, over 80 per cent of all patients in developing countries who consume HIV/AIDS medicines are able to do so because Indian companies supply them these medicines at affordable rates. This is a case that Novartis must not win because it is not about corporate pride. It is a case that sets corporate greed against the lives of millions across the world.
It is useful to recall that the Madras High Court, while rejecting Novartis' appeal, had said: “We have borne in mind the object which the Amending Act wanted to achieve, namely, to prevent evergreening; to provide easy access to the citizens of this country to life-saving drugs and to discharge their constitutional obligation of providing good health care to its citizens.”

The first grant of a CL in India has clear implications for the availability of new drugs at affordable costs, not just in India but in many developing countries. Compulsory licence provisions exist in the laws of most countries, but they are rarely used. As a result, only a few countries have issued CLs since 1995. Most of these have been for HIV/AIDS medicines and almost all have been for use by the government or in situations where a government has declared a national emergency (as in the case of the HIV/AIDS epidemics in Africa). The U.S. and the European Union, acting at the behest of their pharmaceutical industries, have brought extreme pressure to bear upon developing country governments to dissuade them from issuing CLs.

What is extremely significant in the case of the sorafenib CL in India is that it is a rare instance when a general CL has been issued, not bound by “government use” provisions or provisions allowed only in cases of “extreme urgency” or “national emergency”. This has the potential to expand the scope of CLs vastly, in terms of both the kind of drugs for which they can be issued in the future and the conditions under which they are issued.

Further developments in both these areas will be closely watched as they will determine whether India can continue to be known as the “pharmacy of the South” – with the ability to produce and market new drugs at prices people in most countries in the developing world can afford. We may well be watching the decisive battle against patent monopolies that have, for too long, erased the benefits of scientific advances in health care across the world.

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