PHARMACEUTICAL INDUSTRIES AND PATENTING LAWS WORLDWIDE

Shatruhan Sharma* 1, Veena Sharma2, G.S. Rajpurohit1, Aastha Agarwal2

*1Shatruhan Sharma, Rajasthan High Court, Jaipur India.
2Department of Bioscience and Biotechnology, Banasthali University, Rajasthan India.

ABSTRACT

Intellectual Property Rights offers trails for creating, circulating and executing newer techniques and innovations for human welfare, but patents in the field of life sciences have been a source of many controversies due to changing global health aspects, generic competition, price hikes, finely tuned regulatory analysis, extension into emerging global markets, increasing coalition and gains and a unrelenting economic slowdown. The most controversial patents are related to stem cells, diagnostic tools and rice genes. In present competitive scenario, questions about the impact of patents on access to medicines and health improving devices and on transfer of environmentally friendly technology every rank of society have been always raised. Present review will cover the most contentious patents worldwide to understand the various norms and laws regarding patenting in various countries.


INTRODUCTION

The pharmaceutical and biotechnology industries always have the benefit of a remarkable eminence in Intellectual property rights debates. The patents claimed by this sector always been a matter of great controversies on both national and international platform. The Intellectual Property in India always been in questioned over the way of handling the patent cases. The Indian policy always has been in favor of launching generic drugs in order to warrant the access of underprivileged population to costly life saving drugs. In international market, WTO and TRIPS hold the patenting laws. This agreement attempts to protect the
Intellectual Property Rights around the globe and to bring them under common international rules. TRIPS also raised number of disagreements related to the over expensive drugs and their availability, agriculture chemicals and new variety seeds, patenting of life forms, genetic resources and other biotechnology innovations.

The following examples of patent controversies provide an overview of the patenting scenario worldwide including its major pros and cons.

In 1993, Novartis registered worldwide patent for a drug imatinib, though it did not filed in India because at that time the 1970 patent law of India did not allow patenting of products. In 1995, Novartis applied a mailbox patent in India for the salt form of this drug which was 30% more efficient than the original active molecule reported in the original 1993 patent application. When the patent application was reviewed by the Indian patent in 2006, it was rejected on the grounds that that 1995 Indian application lacked originality and inventiveness compared to the original 1993 patent and because it did not meet the enhanced efficacy requirement of Provision 3(d). Novartis appealed on the grounds that Section 3(d) was not complaint with TRIPS and that it was vague and ambiguous and thus discriminatory against Novartis. The case reviewed by a special tribunal of the Indian Judicial System called the Intellectual Property Appellate Board which suggested the Indian Patenting laws to be clear and reliable in order to effectively advance innovation.[1]

Article 3(d) of Indian Patent Law matters more for particular types of applications, or requires complementary legal strategies to be effective. A number of important HIV-AIDS patent applications have been rejected via 3(d), typically through “opposition” proceedings where third parties (generic firms, HIV activists, and civil society groups) made the case to the patent office that the applications were not patentable on 3(d) grounds. While oppositions were rare as a share of all applications, they do tend to be on 3(d) grounds.[2]

Claims related to methods to recognize tumors which are receptive to the treatment with anti-ErbB2 Abs after determination of the prostate or ovarian cancer in the patient that is positive for HER2 phosphorylation, the patient were given a loading dose of 840 mg of rhuMAb 2C4 on day 1 of cycle 1 of first 21-day treatment period, followed by 420 mg on day 1 of each subsequent 21-day cycle through intravenous infusion. Applicant submitted that improvement lies in new amounts of rhuMAb (420 and 840 mg) The controller refused the application
under section 3(d) (new use of known substance) as being dosage and 3(i) method of treatment that the said MAb are already known as described in the description.[3]

The patenting law decision taken by Supreme court of India was the A.G. v. Controller of Patents, Designs & Trade Marks (in 2002), in which for the very first time utility of a biotech invention was demonstrated. The invention related to a process for preparation of infectious bursitis vaccine. The vaccine was used to protect poultry from Infectious Brusal Disease or IBD. Initially the Patent office disapproved the patent application claiming that it did not constitute an invention. Although this decision was subjected more than twenty years after the U.S. Supreme Court’s decision in Diamond versus Chakrabarty, Indian commentators view it as epoch making as by this decision, the court overturned a long-standing policy of the Indian Patent Office to refuse such process claims, thus opening the door to biotechnology patenting in India much as the Chakrabarty decision did in the United States.[4]

The Indian Parliament passed the Plant Variety Protection and Framers Rights Act, 2001. India has put in place a law to grant Plant Breeders Rights on new varieties of seeds. It has simultaneously provided rights of a farmer. This Legislation was imposed in the form of an agreement by the obligations made by India with trade related intellectual property rights (TRIPS) when it endorsed the Uruguay GATT Round in 1994. Article 27. 3(b) of TRIPS proffered three options for the protection of newer plant varieties settled by a patent of an effective sui generic system or by its combination of two.[5]

In order to diagnose tumorogenicity and resistance effects of anti-neoplastic effects of antineoplastic therapy, a patent was granted for A & G Pharmaceutical, USA, based on the principle in which elevated levels of growth factor – PCDGF (GP88) indicaes of tumorigenicity and resistance to the pharmacological effects of antiestrogen therapy. The methods and kits of the invention were useful for assessing the tumorigency of a biological sample from a patent and determining whether the patient is a candidate for antiestrogen, including tamoxifen therapy.[6]

In late 1997, an American company RiceTec Inc, was granted a patent by the US patent office to call the aromatic rice grown outside India ‘Basmati’. RiceTec Inc, had been trying to enter the International basmati Market with brands like Kasmati and Texmati described as Basmati type rice with minimal success. However, with the basmati patents rights, Rice Tec will now be able to not only call its aromatic rice Basmati within USA but also label it Basmati for its exports. This has grave repercussions for India and Pakistan because not only
will India lose out on the 45,000 tonne US import market, which formed 10% of the total basmati exports. In addition, the patent on Basmati was believed to be a violation of the fundamental fact that the long grain aromatic rice grown only in Punjab, Haryana and Uttar Pradesh and called Basmati. The Government of India reacted immediately after learning of the Basmati patent issued to Rice Tec Inc., stating that it would approach the US patent office and urge them to re-examine the patent to a US firm to grow and sell rice under the Basmati Brand name in order to protect India’s interests, particularly those of growers and exporters. Furthermore, a high level inter-ministerial group comprising of representatives of the ministries and departments of commerce, Biotechnology, All India Rice Exporters Association (AIREA), Apeda, and Indian Council of Agricultural Research (ICAR) were mobilized to begin an in depth examination of the case. The contents and implications of the patents were currently being analyzed. The lawyers planed to challenge this patent on the basis that the above mentioned plant varieties and grains already exist and thus could not be patented. In addition, they encountered some information from the US National Agricultural Statistics Service in its latest Rice Year Book 1997, released in January 1998, which stated that almost 75% of US rice imports are the jasmine rice from Thailand and most of the remainder are from India and Pakistan, varieties that cannot be grown in the US. This interesting fact was further used weapon in opposition to Rice Tec Basmati patent. \[7\]

United State Department of Agriculture and US chemical major W.R. Grace were granted of a patent jointly. The patent gave them right to manufacture the fungicide from seeds of neem. The patent was opposed by the New Delhi based Research Foundation for Science, Technology and Ecology with the assistance of International Federation of Organic Agriculture Movements (IFOAM) and Magda Aelvoet, former green Member of the European Parliament (MEP), who was then was the environmental minister of Belgium before the European Patent Office (EPO). The petition filed had emphatically stated that "the US/Grace patent did not satisfy the basic requirements for a patent." The verdict taken by the EPO has been appreciated by scientists and industrialists across the globe. It attested that the civil society can control its efforts to efficiently avert bio-piracy from developing nations which have rich culture. As Indian farmers and indigenous communities endeavor to better the yields with traditional knowledge, the multinational companies might be there right behind them, ready to "steal" the product or process, introduce a non-existent novelty and then stamp a patent on it. “Without the knowledge of Indian communities of the medicinal and insecticidal properties of Neem, it would just have been another tree to Grace”. \[8\]
The similar happened with the famous Turmeric patent. The news was taken with great incredulity and shock by Indians. Turmeric has been conventionally used in Indian homes for its many special properties as wound-healing. It is used as a blood purifier, in treating common cold and as an anti-parasitic for many skin infections. It is also used as an important ingredient in cooking in almost every Indian kitchen. The prime challenge before India was to prove its stand before US court.

The claimed subject matter was the use of "turmeric powder and its administration", both oral as well as topical, for wound healing. As per the requirements of US law, it was necessary to find adequate evidence in the form of printed and published information that would establish that the manner of use of turmeric as in the claimed invention was known before the patent was claimed and, therefore, the patent was invalid. After an extensive research, 32 references were located, some of which were more than 100 years old, and in the languages of Sanskrit, Urdu and Hindi. The USPTO withdrew the patent, stating that the claims made in the patent were obvious and anticipated, and agreeing that the use of turmeric was an old art of healing wounds. The patent on the "use of turmeric in wound healing" is but one of the many examples of how patents are being sought over various aspects of biological resources and products derived from the same.

Bayer was granted a patent for drug named Nexavar, used in the treatment of hepatic and renal cancers. The company came to know that Cipla had also filed an application for the approval of the generic version of the same drug. Bayer sued to stop Cipla from marketing their drugs. The court directed the Drug Controller General of India not to give marketing authorizations to Cipla. The court appreciated the necessity of protecting patent rights even if the questioned product was not in the Indian markets.

Roche infringed the patented filed by Cipla after the launching Erlotinib. In answer, Cipla also challenged this infringement and filed a counter claim. The Delhi High Court allowed Cipla to continue advertising its generic version though it also directed Cipla to “maintain the accounts of sales, which would be relevant to calculate damage to Roche, in case the latter eventually wins the case”.[9]

Swiss pharmacy Roche applied for the patent of Herceptin on October 11, 2000. After a post grant opposition, the patent granted in 2007. Controllers of the Patent Office gave the opportunity under three applications filed by it “of being heard before the final disposition of
these cases” to the company. But, the request for examination had been filed in 2006 after the prescribed time. The Ministry stated that if the requests were not filed within time they were treated as withdrawn under section 11 B(4) of the Indian Patents Act.[10]

A milestone decision was taken by Supreme Court of India against the company Novartis for the patent of Gleevec in India after a long period of seven years. The Supreme Court defended the decision of rejecting patent application by Indian patent office. In 1993, during the time India did not allow patents on products, Novartis could not patented imatinib in India but patented in many other countries even on not specifying the salts. On examining the patents, this came to the lime light that generic companies are selling Gleevec in India already. The application was rejected by the patent office and by an appeal board on the basis of the Indian Patent Law amended in 2005 stated the patentability of new uses for known drugs and modifications of known drugs. That section, Paragraph 3d, specified that such inventions are patentable only if "they differ significantly in properties with regard to efficacy." Novartis lost the case and then appeal in Supreme Court of India. The Supreme Court decided that the substance that Novartis sought to patent was indeed a modification of a known drug imatinib, which was publicly disclosed in the 1993 patent application and even in research articles. On asking, Novartis did not present any evidence which could prove any subtle differences between the Gleevec’s final form and imatinib’s raw form. On this basis patent application was properly rejected by the patent office and lower courts.[11]

The rosy periwinkle case dates from the 1950s. The rosy periwinkle is native to Madagascar had been widely introduced into other tropical countries around the globe much before the discovery of vincristine, cancer chemotherapy drug. This meant that scientists could obtain this traditional knowledge from one country and plant samples from another to elucidate the anti-diabetic property of this plant. But the results also showed the chemopreventive effects of the same plant. Different countries are reported as having acquired different beliefs about the medical properties of the plant and chemotherapeutic drug vinblastine was also procured from the rosy periwinkles which help in the treatment of Hodgkin’s lymphoma.

The Enola bean, a variety of Mexican yellow bean is famous for its specific shade of yellow. The patent holder subsequently sued a large number of importers of Mexican yellow beans with the following result “export sales immediately dropped over 90% among importers that had been selling these beans for years, causing economic damage to more than 22,000 farmers in northern Mexico who depended on sales of this bean”. A complaint was filed on
behalf of the farmers, and a decision was taken by USPTO in their favor. An appeal was heard on 16 January 2008, and the patent was revoked in May 2008.[12]

A succulent plant named Hoodia which is native to Kalahari Desert and South Africa is used as an appetite suppressant by the people from many generations. South Africa Council for Scientific and Industrial research and companies like Unilever developed a formulation based on this plant to introduce a dietary supplement in markets. The people were not given any advantages from the commercialization of their traditional knowledge, but in 2003 the South African San Council made an agreement with CSIR in which they would be given 6 to 8% of the revenue from the sale of all Hoodia products. In 2008, after having invested 20 million Euros in R&D on hoodia as a potential ingredient in dietary supplements for weight loss, Unilever terminated the project because their clinical studies did not show that hoodia was safe and effective enough to bring to market.[13]

In Europe, a debate on biotechnology patents started in the late 1980s to expounding the difference between patentable and non-patentable and balancing EU member states laws in European countries. This discussion led to the adoption of EU Directive 98/44/EC on the legal protection of biotechnological inventions, known as biopatent directive in 1988. The decree has been executed by all EU member countries. In 1999, the EPC contracting states decided to integrate the directive as secondary legislation into the Implementing Regulations to the European Penal Code. This integrated form of laws endow with a foundation for deciding on the patentability of biotech innovations at the EPO resulted in the greater focus on ethical considerations. For example, the instruction affirmed that isolated biological material is patentable even if it has occurred previously in nature as per the Rule 27(a) EPC. It confirmed that plants or animals are also patentable if the technical feasibility as genetic modification of the invention is not impounded to a particular plant or animal variety as Rule 27(b) of EPC stated. Moreover, an invention relating to genetic sequences can be patented as long as the industrial application disclosed the sequence in the patent applications & fulfill all the patentability standards (Rule 29(3) EPC). These rules strictly inhibit the patenting of entire human body in all its developmental phases, its cloning, processes for modifying the germ-line genetic identity of human beings and the use of human embryos for industrial or commercial purposes. EPC also prohibit patentability of processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical advantage to man or animal and animals resulting from such processes. A landmark ruling on
stem cell cultures was issued in November 2008. In the WARF/Thomson case (G 2/06), the EBoA decided that under the EPC it is not possible to grant a patent for an invention which necessarily involves the use and destruction of human embryos.[14]

In enablement claim between Amgen Inc. and Chugai Pharmaceutical Co, DNA sequences coding for modified proteins having the same function, namely erythropoietin (EPO) which is a therapeutic substance having medicinal value in treating blood disorders was sought to be patented. The disclosure covered certain products of recombinant DNA technology used to produce EPO, but did not cover the product EPO itself, since there were alternate methods to produce EPO without using recombinant DNA technology. It was held that the claim was invalid for lack of adequate disclosure as to how to make other DNA species within the broad genus of EPO. The impact of this decision was that the enablement disclosure must be specific and not unduly broad. Broad claims however be valid if they correspond to the disclosure of the invention.

In the American case of Fiers Vs Revel, Revel had filed for a patent for a DNA coded biotechnology product in Israel and sought to rely on that claim to establish priority over its American competitors. Revel claimed that it had disclosed clearly and adequately how to isolate DNA coding from J-IF (Human fibroblast beta interferon), a protein that had the therapeutic value of promoting viral resistance in human tissue and relied on the affidavits of two scientists who vouched for the fact that it was possible for a person skilled in the art to arrive at that solution without undue experimentation. However Fiers had held that Revel’s disclosure was insufficient since what was required was not just an explanation of how DNA can be isolated from J-IF, but description of the DNA itself. Further, the Court held that a Japanese inventor, Sugano, had established priority because it had legal position, as was re-enunciated in Re Gardner, Roe and Willey, is that the specification must clearly state how to use the invention.

In Indian law, the “how to use” requirement was enshrined in S. 10(4)(a) of the Patents act 1970 wherein it was stated that the specification shall describe the operation or the use of the invention and the method by which it was to be performed.[15]

The claimed invention of Harvard Onco-Mouse T Application referred to all non-human mammalian animals, whereas the invention described in the specification could only be performed on mice. It was assailed on the ground of being too broad, but the Board took the
view that the application should not be refused on the ground that it contained an extrapolation from mice. The logic used was that unsuitability of unspecified variants is irrelevant, as long as the suitable variants were explained sufficient.\textsuperscript{[16]}

U.S. patent on turmeric granted to the University of Mississippi Medical Center in 1995 for the use of turmeric in healing bruises. Who would have thought that brat companies would be allowed to claim age-old knowledge of curative properties of natural resources like turmeric (and Neem) as inventions and discoveries? This patent was successfully contested by India’s Council of Scientific and Industrial Research CSIR, and the patent got revoked in 1997.

US patent granted to Loren Miller on a variety of Ayahuasca or Yage (Banisteriopsis caapi), a plant of hallucinogenic properties held sacred by some 400 indigenous groups in nine countries of South America. This patent was revoked in November 1999.

Lucrative patent grants on life-saving drugs like Cipro (that counters Anthrax) granted to the multinational Bayer AG. Many such drugs can be made available in abundance by cheaper means.

The notorious case of Monsanto Company trying to claim a patent on Chinese Soya just because it discovered that substance’s gene sequence.

US Department of Agriculture attempted to patent Thailand’s Jasmine rice violating a trust agreement on donated seed samples.\textsuperscript{[17]}

The International Treaty on Plant Genetic Resources for Food and Agriculture (PGRFA), well known as the International Seed Treaty got ratified in June 2004, despite heavyweights US and Japan not signing on the dotted line. The treaty complements and supplements the provisions in CBD, and the two aimed at ensuring food security for all through the preserving, conserving, exchanging and prudently using the world’s plant genetic resources for food and agriculture, as well as unbiased benefit sharing. Its other noble intentions included recognition of Farmers’ Rights to have free access to genetic resources without IP regime restrictions and also to participate in policy discussions, and decision making while continuing to use, save, sell or exchange seeds conforming to applicable law.

To realize these intentions, the Treaty incorporated a Multilateral System (MLS) to enable access to and share benefits accruing from 64 important food and forage crops that are
needed to ensure food security through interdependence for all the signatories. Since it included compulsory benefit sharing, one of its funding mechanisms was in place. The Commission on Genetic Resources for Food and Agriculture (CGRFA), acting under UN’s Food and Agriculture Organization is currently administering the Treaty till a dedicated governing body is formed.

In 2009, the American College of Medical Genetics, American Society for Clinical Pathology, College of American Pathologists, three other health care organizations, and several individuals sued the USPTO, Myriad Genetics, and the Directors of the University of Utah Research Foundation in the United States District Court for the Southern District of New York. The suit challenged the validity of the patents on the BRCA1 and BRCA2 breast cancer susceptibility genes, claiming that the patents are overly broad and in conflict with policies that prohibit the patenting of natural phenomena and basic human knowledge and thought. The AMA filed an amicus in support of the plaintiffs.

In 2010, a federal court ruled that several of the BRCA gene patents were invalid. Myriad Genetics appealed the case to the United States Court of Appeals for the Federal Circuit. The AMA again submitted an amicus curiae brief in support of the plaintiffs in the appeals court.18

Genetic engineer Ananda Mohan Chakrabarty, working for General Electric, had developed a bacterium (derived from the *Pseudomonas* genus and now known as *Pseudomonas putida*) capable of breaking down crude oil, which he proposed to use in treating oil spills. General Electric filed a patent application for the bacterium in the United States listing Chakrabarty as the inventor, but the application was rejected by a patent examiner, because under patent law at that time it was generally understood that living things were not patentable subject matter under Section 101 of Title 35 U.S.C. The Board of Patent Appeals and Interferences agreed with the original decision; however, the United States Court of Customs and Patent Appeals overturned the case in Chakrabarty's favor, writing that "the fact that micro-organisms are alive is without legal significance for purposes of the patent law." Sidney A. Diamond, Commissioner of Patents and Trademarks, appealed to the Supreme Court.

The Supreme Court case was argued on March 17, 1980 and decided on June 16, 1980. The patent was granted by the USPTO on Mar 31, 1981.
In 2003, Monsanto filed patent applications with claims on breeding techniques for pigs. Greenpeace claimed that Monsanto was trying to claim ownership on ordinary breeding techniques and the filings became the target for demonstrations in Germany. A UK news article indicated that "the practices it (Monsanto) wants to protect involve identifying genes that result in desirable traits, breeding pigs to achieve those traits and using a specialised device to inseminate sows deeply in a way that uses less sperm than is typically required". In Europe, the EPO rejected some claimed as relating to an essentially biological process excluded from patent protection but an application with claims from this set of filings was granted in 2008 and was later revoked. In 2007, Monsanto sold Monsanto Choice Genetics (the Monsanto entity driving these patent filings) to Newsham Genetics LC of West Des Moines, Iowa. The transaction was completed in November 2007, and Monsanto is no longer in the swine breeding business nor interested in patent filings on pigs and pig breeding.[19]

The U.S. Patent and Trademark Office granted a patent to the Wistar Institute of Philadelphia on a technique for producing monoclonal antibodies against tumor antigens. It was the first patent issued on hybridoma technology in the United States, and the first of several Wistar patents that make broad claims on applications of the technology to the manufacture of antibodies against cancers and viruses. Wistar applications were rejected in the U.K. on the grounds that they constitute obvious extensions of Köhler and Milstein's original invention. The property claim generated a controversy in the scientific community. Milstein had freely distributed the myeloma cell line required for the production of monoclonal antibodies, but had on occasion stipulated that the cells not be commercialized. Hilary Koprowski and colleagues at the Wistar Institute had accepted cells from Milstein, but subsequently insisted that the transfer was unconditional. The Wistar patents were licensed on an exclusive basis in the U.S. to Centocor, Inc., but were mostly ignored and never defended. For all practical purposes, the Köhler and Milstein invention resided in the public domain.[20]

The author argued that there has been a shift from a broader question of whether hESC research should be done at all to more specific concerns over who will own the products of stem cell research. The author then reviewed different arguments for and against property rights before making several recommendations.

The Hagahai are an indigenous group in Papua New Guinea. They lived an isolated existence until 1984, when they sought help because of a disease that was afflicting the community. Researchers found that the members of the tribe carried a gene that predisposes humans to
leukemia, yet they did not themselves manifest symptoms of the illness. Further analysis of blood samples identified a T-lymphotrophic virus, with potential for development into a vaccine for certain types of leukemia. In 1991, the National Institutes of Health in the U.S. sought patent protection for a cell line developed from the DNA of a Hagahai donor (US patent 5397696). The invention related to a cell line infected with a Papua New Guinea Human T-Lymphotropic Virus (HTLV) variant, and to vaccines for humans against infection with and diseases caused by HTLV-I and related viruses.

The patent – which was later abandoned – sparked controversy over whether the Hagahai donor’s consent had, or should have, been obtained before the resulting cell line was patented. Reports of what actually happened vary greatly. But the fact that the genetic material came from an indigenous group made the case particularly sensitive, and gave rise to accusations of biopiracy. Nor was it ever determined whether in this case consent should have been obtained solely from the individual, or from the Hagahai people, or from the state.[21]

CONCLUSION
The biotechnology industry is characterized by rapid growth, complexity and comparative youth. Participants tend to attach a great deal of importance to IP. This is an industry that, collectively, submits a large number of difficult, highly technical patent applications. Patent examiners therefore have difficulty paring down broad claims and weeding out applications that do not meet statutory patentability criteria. There was little evidence that an anti-commons problem had arisen in the biotechnology industry. However, it is an industry in which such a situation might arise in future owing to a growing number of patents and a large number of participations.

From 1975 to 2006 the US Patents and Trademark Office (USPTO) issued over 20,000 patents relating to industrial biotechnology.

The above proposals and case studies offer some guidance as to how the countries might finally implement a procedure of ethical review when faced with biological patents. Even minimal accessory changes to the patent applications would create a heightened system of awareness as to the activities being conducted behind the veil of the patent application. Also, they put a burden on the patent applicant herself. Hopefully, the countries can start to move towards a more active role in curbing ethically-questionable patent applications, so that not
“anything under the sun that is made by man” is patentable, especially when it involves the sacred genetic elements that many indigenous groups believe make up the essence of who they are as people.

REFERENCES


