

Section 3(d): Implications and Key Concerns For Pharmaceutical Sector

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TRIPS has granted certain flexibilities to the member nations in framing their Patent Laws considering their social and economic needs. Flexibility provided in TRIPS has been utilized by member countries as a safeguard to mitigate the potential adverse effects that drug patents might have on medicine supply. A clause - Section 3(d) - has been redesigned in the Indian patent legislation to restrain the ever-greening of drug patents. Section 3(d) of the Indian Patents Act allows patents on variants of only those chemical compounds that show significant enhancement in therapeutic efficacy. The revised Section 3(d) is deterrent against ever-greening of patent and subsequent monopoly of the multinational drug corporations. Since its introduction, it has been widely discussed for not supporting innovation. The multi-national pharma companies (MNCs) and the US-India Business Council (USIBC) have suggested in their report for elimination of Section 3(d) so that drug patents can be granted in India for incremental improvement and modification. As per US 301 report, India is listed among countries with inadequate IP regime. Keeping all these aspects into consideration, this paper discusses various issues and key concerns pertaining to impact of Section 3(d) with special emphasis to its interpretation.

Keywords: TRIPS, Indian Patent Law, ever-greening, pharmaceutical sector, Section 3(d), public health, access to medicine

The crucial phase in development of India's patent system is the accession to World Trade Organization (WTO) in 1995.¹ Universal Intellectual Property Rights (IPR) protection among member countries is worked and monitored by WTO that influences the economic relations between those countries.² Trade related aspects of intellectual property rights (TRIPS) agreement signed on 1st January 1995, is one of the important provision of WTO agreement and is crucial outcome of the Uruguay round negotiation. The key focus of TRIPS agreement is to cover the trade of IPRs internationally. It deals with wide range of IPRs and includes the subject matters like patent, trademark, designs, copyright, geographical indication and trade-secret.³ In the Indian context, the IPRs in India; particularly the patent system is governed by the Indian Patents Act, 1970 and it has been amended several times and latest amendment was carried out in 2005. Patent is granted for novel invention having inventive step/steps and commercial utility. Grant of a patent provides exclusive rights to the patent holder to make, practice, sell, license, trade the patented invention for a period of 20 years. A balance needs to be maintained between the rights of patentee and public goods by restricting monopoly over invention

of national interest.⁴ While designing its Patents Act, India included a number of key concerns regarding the public health safeguards, which fully affirm to international trade rules outlined in the WTO's Agreement on TRIPS.⁵ It not only promotes member countries towards protecting their invention but also to use enough safety measures by member states as per their own judicial system. So a fair and equitable balance is created between the interest of patent owner and the ultimate buyer of Intellectual Property.

Developing countries were given time period to make their patent law TRIPS compliant. Prior to this, The Patents Act, 1970, abolished product patents and only process patents could be granted. The Patents Act, 2005 amendment provides scope for filing product patent applications. The amended Indian Patents Act, 2005 introduced product patents under food, drugs, pharmaceuticals and chemicals categories. Therefore, several amendments have been made from time to time in the existing-laws and the patent judicial system to have new legislations in conformity with TRIPS.⁶

Amendments 1999 (effective from January 2005) in Indian Patents Act-

- Exclusive Marketing Rights (EMR) and mail box application provision introduced.

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Amendments 2002 in Indian Patents Act-

- Term of patent extended for 20 years from filing date (substitution of Section 53)
- India became member of two international treaties
 - Paris convention, 1998.
 - Patent Cooperation Treaty, 1998.
- Redefining of 'Invention' and 'Inventive step' (Section 2(1) (j)).
- Microorganism covered under patentable subject matter (Section 3 (j)).
- Deletion of license of right provision from compulsory license.
- Incorporation of 'research exemption' (Section 107-A).

Amendments 2005 in Indian Patents Act-

- Product patent introduced for invention in food, medicine and other drug substances.
- Pre-grant opposition initiated only after publication of the patent application.
- Section 3(k) included which excluded patenting of computer program *per se*.
- Section 3(d) modified to introduce significant enhancement in therapeutic efficacy of the variant of existing compounds.

(Indian Patents Act, 1970 (Amended in 1999, 2002 and 2005))

India is the key supplier of low cost generic version of drugs to other developing countries. Antivirals required for treating HIV/AIDS have also been supplied by India to economically poor countries.⁷ Monopolizing the pharmaceutical sector raises the price of the drugs as competition between the generic manufacturers is restricted by patenting. Before accession to TRIPS, the developing countries used restrictive clauses in designing their patent law to prevent product patent in pharmaceutical sector. Accession to TRIPS in 1995 however has changed the whole scenario. To mitigate the potential negative effect of drug patents such as increase in drugs price, certain flexibilities have been provided in TRIPS which have been utilized by the member countries. India has used flexibilities such as compulsory license grant provision during health crisis; scope to redefine standards for patentability and Section 3(d) antievergreening provision that restricts patenting on incremental innovation. The agreement also leaves space to deal with the national level issues and process of executing TRIPS obligations.⁸

Section 3(d)

In order to safeguard the interest of the public and to maintain a balance for the accessibility of life saving drugs to patients (public goods), The Indian Patents Act, 1970 (amended) has stipulated various provisions (exceptions) making patentable subject matter non-patentable. For example, Section 3 of The Patents Act has included the subject matter as 'what are not inventions'. In order to promote the quality patent grant and to avoid ever-greening in pharmaceuticals field, Section 3(d) was redesigned to prohibit patents on the variants of existing compounds without appreciably raised efficacy besides second use of known substance.

Prior to 2005, Section 3(d)⁹ was: "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."

2005 amendments promote and encourage patenting of new form of a known substance which resulted in the enhancement of a known efficacy. The revised Section 3(d) of 2005 amendment further explains: *"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."*

Prior to Patents Act 1970, India fulfilled most of its drugs requirement from the drugs sold by foreign multinationals. Due to the dependency for availability of drugs from foreign manufacturers the drug prices rose. Hence, after the passage of The Patents Act, 1970, companies in India started their own drug-manufacturing units. This rapid increase in local manufacturing raised the number and status of pharmaceutical industry and India became a major exporter for the cost-effective drugs to other countries. Thus, The Patents Act, 1970 supported the generic industry influenced innovation in pharmaceutical sector. In the year 2005, revised Section 3(d) was introduced for the first time for drug patents in India. The Indian generic industries which had a hold in the drugs market due to expertise in reverse engineering were influenced by this decision.¹⁰ Section 3(d) can be envisaged to protect the interest of patients who are dependent on

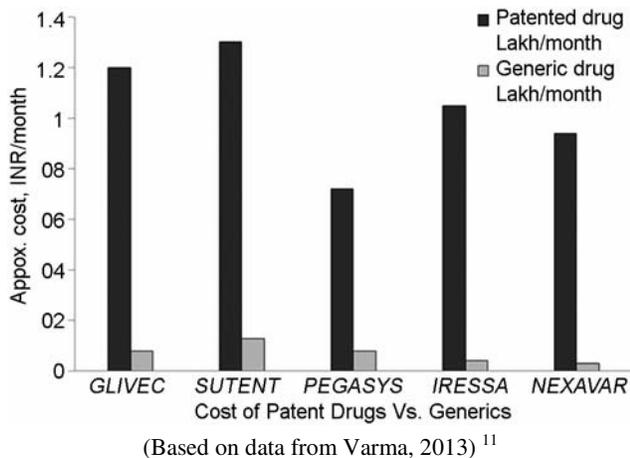


Fig. 1– Price Comparison of Patented Drugs versus Generics

inexpensive generic drugs. The patented drugs are many fold expensive in comparison to generics as is evident from Fig.1. Section 3(d) restricts patentability of patent expired drugs and pharmaceutical inventions with minor changes and prevents the abuse of pharmaceutical product patents and show balanced public goods with improved access of medicine to the citizens.

The amendment in Section 3(d) favors the generic pharmaceutical industry as well as innovators. Depending upon which category it falls, its interpretation and explanation varies accordingly. Globally it is influenced by under-developed/developing verses developed status. Nationally different political ideologies have a great influence over it and any decision or amendments may be made by the ruling government. Corporate entities are not humanitarian in their approach and their sole target is to make money by increasing number of patents in their patent portfolios while availability of cheap drugs which can be accessed easily and timely is the target of masses. So a proper balance is required to be maintained between different sections of the society before any law comes into existence.¹²

Section 3(d), Patentability and Patent Eligibility

To apply for patent, the subjective element of the patent application must be patent competent. It means that it should not fall under the categories of invention exempted for patentability i.e. Section 3 of the Indian Patents Act. The patentable invention must be novel, involving innovative step and have commercial utility. The invention which falls under Section 3(d) has to undergo patent eligibility test first in the form of efficacy along with the other patentability test.¹³

Section 3(d) further denies patent eligibility to new use or new form of known molecules, unless they contribute to higher therapeutic efficacy over the previous form. The other patent eligibility condition under Section 3(d) is that the derivative of existing substance is considered to be identical to the existing substance except for significant difference in properties in consonance with efficacy. Efficacious derivative of known substance capable of satisfying patentability criteria can only become patent eligible under section 3(d).¹⁴

Section 3(d) and Efficacy

Efficacy is of vital importance under Section 3(d) but as per the Indian Patents Act it has not been much elaborated. Quantitatively also it is not mentioned that how much efficacy can be counted to be significant. There is a difference in the standard of efficacy requirement in the main section ‘enhancement in the known efficacy’ and its corresponding explanation which is ‘differ significantly in properties’ with regards to efficacy in Section 3(d).¹⁵

The oxford English dictionary¹⁶ define ‘efficacy’ as the potential of a drug to produce the desired therapeutic effects. The Madras High Court¹⁷ observed in context to ‘efficacy’ of pharmaceutical product as the effectiveness of a newly discovered drug in relieving from disease and production of a desired effect on the patient body. The applicant for seeking patent for a novel drug has to bring out the difference between his patent application and already granted patent on the grounds of therapeutic effect.

Article 10 (2) (b) of European Drug Regulatory Directive, 2004¹⁸ defined ‘generic medicinal product’. A drug is considered to be generic if the active chemical constituent of the drug is identical in construction, constitution, conformation and arrangement, qualitative as well as quantitative to that of the reference drug. Bioequivalence check of the newly formulated drug is to be done by various bioavailability studies in context to the reference drug. Further, significant difference must be found between the variants (salts, esters, isomers, mixtures of isomers, complexes or derivatives) of an active substance in relation to efficacy and/or safety otherwise it shall be considered as of the same active substance. In addition to this, information providing proof of safety and/or efficacy of various salts, esters or derivatives of an authorized active substance must be supplied by the applicant.

From this interpretation of EU directive, it can be concluded that the term 'efficacy' would be understood in context of drug regulation. It might be challenging for patent applicant to pacify the patent examiners as most of the applications are filed by pharmaceutical industry at initial stage of drug discovery. Only at later development stage after having sufficient clinical trials the applicant will be able to gather required information regarding the therapeutic efficacy of the drug.¹⁹

Section 3(d) Promotes Innovation

Innovation is the key driver in the modern economy. Sometime minor changes, improvements and innovation over the existing product lead to breakthrough inventions which in general understanding need to be incentivized and protected. It often expedites appreciable benefit over existing product or processes. Innovation in today's world is not only invention considered to be absolutely novel or breakthrough inventions driven by technology advancement but by invention emanate from regular exploitation of the prevailing technologies.²⁰

In pharmaceutical sector the scenario is different. Patenting of minor modifications may lead to 'ever-greening' of patents. Ever-greening occurs when manufacturer obtains independent patent protection for 20-year on various characteristics of one product.²¹ US National Institute of Healthcare and Medicines (NIHCM)²² has commented on ever-greening that immense number of drugs with cumulative modifications like change in color, form, having better tablet scoring etc. have been patented by the drug producers. Its outcome is the loss of market for already existing drugs which is effectively similar with respect to new drug and inventor claims that the invented drug shows better potency while the claim has not yet proved. Pharma giants are not in favor of Section 3(d) and argue that Section 3(d) stands in the way of innovation. It in turn affects the public health of the countries.²³ From India's perspective; Section 3(d) keeps a check over ever-greening by patenting the chemical entity which is new and the variants of existing substance with significantly enhanced therapeutic efficacy. The explanation for Section 3(d) says that various salt forms, esters, isomers, metabolites, ethers, polymorphs, isomers etc. are similar in configuration, hence, it can be interpreted that they are likely to be equivalent functionally. If the newly developed drug gives better performance to that of existing one then it is patentable. This must be

proven experimentally and then only the applicant can claim for monopoly right by having claimed patent.⁹

To some degree, Section 3(d) provides marked dissimilarity between incremental improvement and "ever-greening".²⁴ Ever-greening is a 'patent life enhancement technique' and it is the strategy used by pharmaceutical companies to expand impervious patent regime around rewarding drug molecule.²⁵ US-India Business Council (USIBC) are of view that incremental pharmaceutical innovation leads to newly discovered form and new usage of existing compounds that ultimately show enhanced safety which are in compliance with needs of specific patient profiles and resulted in overall development of patient.²⁶ Section 3(d) promotes subsequent expansion of existing chemical substance, compounds, technologies, processes and products which are helpful in fulfilling the health requirement of the public and balance public goods with exclusivity provided by the patent rights.¹²

Section 3(d): Concern for Public Health

The quality drugs with reasonable cost have majorly been provided by India to many countries. Huge numbers of pharmaceutical companies manufacturing drugs are in existence, but only small number of pharmaceutical multinationals rule the market. MNCs monopolize inventions by doing immense patenting activity and thus restrict developing countries to execute its possibility of attaining commercial gains.²⁷ In certain countries mere tweaking of drug molecules to make it different from existing one without any improvement in the efficacy, is patentable and results into incremental pharmaceuticals with no real novelty. This strategy is used by certain multinational corporations to capture the drug market. Sometime, smaller players treat the drug molecules to make it appear different and capture the market they enter into underhand with other market players who work in their own territories. It adversely affects the public health by raising the drug prices. The amendment in 2005 for product patent in the field of pharmaceutical patent, has further stressed the public interest groups.²⁸

India's patent legislation is strict about patentability criteria due to Section 3(d) and to obtain patent over new drug compounds simultaneously repressing modifications of existing compounds not having significant therapeutic improvement. The incremental improvement would be patentable only if efficacy increases unless it is process improvement.

For example, cost reduction by reducing the number of steps or using cheaper alternate starting materials. Thus, it keeps an efficacy check over ever-greening of pharmaceutical derivatives. It further ensures that protection is given only to creditable and deserving inventions and not to some frivolous innovations.

Section 3(d) and US Concern

US has classified India under priority watch list country since 1998 due of inadequate protection and unfair market access to the US personnel engaged in IPR protection. These countries need high awareness and attention. The US trade representatives categorize them as having 'serious intellectual property rights deficiencies'. Section 3(d) of Patents Act is one of the key issue of concerned to the US pharmaceutical companies which prohibits grant of patent to the incremental innovation unless there is therapeutic efficacy enhancement. This provision keeps a check over complete monopoly to big pharmaceutical industries.²⁹ The Utility Model (UM) legislation suitable for protection of incremental innovations is not yet operative in India.

The US government tried to impose unilateral step to put pressure on priority watch list countries to enhance IPR protection beyond TRIPS.³⁰ USIBC (US India business council) prepared a report in 2009 promoting incremental innovation. The outcome of the report says that Section 3(d) of Indian Patents Act discourages research and development. This ultimately discourages the foreign direct investment (FDI) into India which is very much needed to raise the economic status of the Indian society.²⁶ Another issue is that Section 3(d) does not specify and quantify 'therapeutic efficacy'. Fyan (2014)³¹ is of the view that Section 3(d) is ambiguous and does not clearly guide the pharma patent applicants as to which incremental improvements to the art are patentable and which are not since 'efficacy' is not defined.

Patentability standards of India and US are quite different as India restricts patenting of already known drugs without significantly enhanced efficacy. Patent application related to several antiretroviral and cancer medications have been rejected to prevent ever-greening and to have many similar products in the market. This would also avoid monopoly by US corporations charging exorbitant prices. While US patent law supports the patent grant over new form or new uses or combination of known compositions as they have lower level of patentability standards as compared to Indian patent law. Because of lower

patentability criteria, US multiply the patent quantity and keep a check on generics entering in to the market. The focus of pharmaceutical companies in US is to maintain monopoly and to create huge profits as the cost of R&D incurred for the development of drugs is very high. At the same time it also has impacted the access of medicine as business creation is the motto of MNCs. To deal with such issues, India is a welcome destination to collaborate with MNCs to produce cost effective quality drugs and provide various development solutions.

Provision Similar to Section 3(d) In Other Countries

In some countries, the features of patent legislation are similar to India's Section 3(d). Countries in the Asia-pacific regions are also planning to adapt similar provision of Section 3(d) to patent those drugs only which are breakthrough inventions. To toughen the criteria of patentability, Philippines has already proposed to amend its law on identical lines. Brazil Patent Office drafted guidelines to restrict the patentability of new forms of compounds (polymorphs) or new property or new use of a known process unless this known process resulted in new product.³² The guidelines for patentability in Argentina for pharmaceutical and chemical inventions also exclude subject matter of polymorphs, hydrates and solvates as it is considered to be the intrinsic property of the substance so not an invention but a mere discovery. Further, in Argentina new form, new use, and new formulations are not patentable. The description of the product in accordance with the pre-existing formulation is not eligible for patent protection. The patent office of Argentina also provides definition for new form, new use, and new formulation in The Patents Act. Japan's patent legislation mentions the subject matter as the new use of a drug can be patented if the usage is absolutely novel over the original and its use must be clearly differentiated.³³ Mexico IP law in Article 19 (Mexican Industrial Property Law, 1991) mentions that "*Juxtaposition of known inventions or mixtures of known products, or alteration of the use, form, dimensions or materials thereof, except where in reality they are so combined or merged that they cannot function separately or where their particular qualities or functions have been so modified as to produce an industrial result or use not obvious to a person skilled in the art*".³⁴ EPO had also given guidelines regarding patentability of polymorphs. For polymorphs to be considered as inventive it must

produce extraordinary technical effect compared to already known.³⁵

The benefits of provisions in other countries similar to Section 3(d) can be summarized as:

- Restriction of ever-greening due to therapeutic efficacy clause.
- Accessibility of patients to drugs at reasonable prices.
- Raised the grant standards of quality drug patents by encouraging innovative drug development and posing bar on incremental or secondary patenting of known drugs.
- This type of provision in patent legislation along with the other provisions like patent opposition can act as a safeguard and can be used by the public activist groups to successfully challenge patents for minor improvements in life saving drugs used for treatment of dreaded disease such as HIV, Cancer and CAD etc.

Major Recent Section 3(d) Rejections (Table 1):

Novartis AG Drug *Glivec*

Amended Indian Patents Act 2005 has opened scope and opportunity for product patenting and the first important challenge towards it was the patent application rejection for anti-cancer drug sold under the brand name *Glivec* used to treat chronic myeloid leukemia.³⁶ The *Glivec* patent application was opposed and rejected on the grounds of Section 3(d) that aims to restrict ever-greening and patenting of new use or new form of existing pharmaceutical substance without any noticeable increase in efficacy.⁹

In 1993, Novartis filed a patent for *Imatinib* free base and all of its pharmaceutical acceptable salts.³⁷ The patent (US Patent No. 5,521,184) was issued on 28 May, 1996. Further, experimentation of *Imatinib* led to its conversion into the salt form Imatinibmesylate. Incremental improvement of this salt suggested that the Imatinibmesylate is most stable in β -crystalline form. This particular polymorphic form was then formulated into a pharmaceutically useful drug; *Glivec*.³⁸ Forty patents were granted to Novartis in different countries with this polymorphic form.³⁹ In India, Novartis claimed the β polymorph *via* mailbox⁴⁰ application as product patent facility in India was unavailable up to 1 January 2005. The amendment in the Indian patent regime in 2005 introduced product patent in food, pharmaceutical and agrochemicals areas.⁹ Meanwhile, Novartis also

applied for Exclusive Marketing Right (EMR) of this drug and obtained an EMR in 2003 for 5 year duration.³⁸ Novartis sold *Glivec* for US \$ 2,666 (1, 20,000 INR) per patient per month and the generic version of this drug was sold at US \$ 177 to 266 (8000 to 10, 000 INR) per patient per month by the generic companies Ranbaxy and Cipla in India.⁴¹ Novartis obtained injunction against Ranbaxy and Cipla for producing the generic version of *Glivec* in the Madras and Bombay High Courts. Further on various grounds the Madras High Court upheld the EMR and said that Novartis ran a free *Glivec* International Patient Assistance Program (GIPAP) for those patients which are having poor affordability of this drug.⁴² This decision on EMR was refused by Bombay judiciary on the grounds that the drug was more expensive and is not accessible to patient who cannot afford it.⁴³

Patent amendment in 2005 introduced product patent in India. Novartis mailbox application filed for obtaining patent on β -crystalline form of *Imatinib* was then open for examination. The application was opposed by several generic companies on the ground of not being novel, obvious, not showing increase in therapeutic efficacy under Section 3(d) and obtaining unfair priority. Patent application was rejected by the Controller of Patents on above mentioned grounds. In Madras high court two appeals were filled by Novartis challenging the patent Controller's order with a statement on unconstitutionality of Section 3(d) and violating India's TRIPS obligations. Pursuing Government orders, the high court transferred first petition about the reversal of the Controller's rejection order to the IPAB. The second petition on Section 3(d) was finally held to be constitutional and non-violative of India's obligations under TRIPS.

As it has been discussed earlier, 3(d) is a key Section for maintaining patent eligibility criteria which promotes innovation and does not allow ever-greening of patented drugs. The Novartis application is about the conversion of free base of *Imatinib* to cancer drug useful for patients having blood cancer. The claimed invention was the active ingredient in *Glivec* in its β -crystalline form that have shown better bioavailability (30% increases) as it is absorbed more easily in blood than the *Imatinib* free base. The Assistant Controller of Patents revealed that it does not signify "increased efficacy". As bioavailability increased for salt form of Imatinibmesylate over *Imatinib* free base could be due to solubility

Table 1– Representative landmark cases of Section 3(d) rejections/oppositions⁵¹

Applicant	Application no./ Patent no.	Name of the drug/ trade name/Date of revocation/ rejections	Opponents	Utility	Grounds of objection under Section 3(d)
Novartis AG	1602/MAS/1998 (Pre-grant opposition)	Imatinibmesylate (<i>Glivec</i>) (Revoked April 2013)	Cancer Patients Aid– Association Natco Pharma Ltd. Cipla Ltd. Ranbaxy Laboratories Ltd.	Anti-leukemia drug	No significant difference with regard to therapeutic efficacy in spite of increased bioavailability of the salt form over Imatinib.
Hoffmann-La Roche	IN'507	(Rejected)	–	Lung cancer drug	The application IN'774 was rejected as there was no significant enhancement in the therapeutic efficacy.
<i>Abraxis</i> Bioscience	4572/CHENP/2006 (Pre-grant opposition)	<i>Abraxane</i> (Revoked June 2015)	Natco Pharma Ltd.	Anti-cancer drug	Combination of known substances, namely paclitaxel and anti-SPARC antibody, no demonstration of enhanced efficacy.
Boehringer Ingeleim	558/DELNP/2003/IN254813 (Post-grant opposition)	Crystallinetiotropium bromide monohydrate salt (<i>Spiriva</i>) (Revoked March 2015)	Cipla Ltd.	Asthma drug	No considerable enhancement related to therapeutic efficacy over existing tiotropium bromide.
Hoffmann-La Roche	959/MAS/1995/IN207232 (Post-grant opposition)	<i>Valganciclovir</i> (Revoked Jan 2014)	Ranbaxy laboratories Ltd. Cipla Ltd., Bakul Pharma Pvt. Ltd., Matrix Laboratories Ltd. INDIA network for people living with HIV/AIDS and TAMILNADU networking people living with HIV/AIDS	HIV drug	Mere use of a known process and known compound with no improvement in efficacy.
Novartis AG	1440/MAS/1998 (Pre-grant Opposition)	Crystalline Ascomycin derivatives (Revoked July 2007)	Ranbaxy Laboratories Ltd.	Anti-inflammatory (used in the treatment of auto-immune diseases)	Therapeutic efficacy of the crystalline form was not disclosed by the applicant
Novartis AG	237/MAS/1998 (Pre-grant Opposition)	<i>Oxcarbazepine</i> (Revoked January 2007)	Ranbaxy laboratories Ltd., Torrent Pharma Ltd	Treatment of psychosomatic disturbances, of epilepsy and of trigeminal neuralgia	Applicant failed to prove efficacy
Gilead Pharmasset LLC	6087/DELNP/2005 (pre-grant opposition)	<i>Sofosbuvir</i> (Sovaldi) (Revoked January 2015)	Delhi Network of Positive People (DNP+), Initiative for Medicines, Access & Knowledge (I-MAK),	Treatment of Hepatitis C	Cytotoxicity data produce by the applicant to prove the difference in properties over known compounds which is not sufficient to prove significant increase in the therapeutic efficacy.
Glaxo SmithKline (GSK)	WO2000018383 (pre-grant opposition)	<i>Combivir</i>	The Indian Network for People Living with HIV / AIDS and the Manipur Network of Positive People	Anti-retroviral drug	Combination of two known essential AIDS drugs, <i>Zidovudine</i> and <i>Lamivudine</i>
Glaxo SmithKline (GSK)	IN221171 (Post-grant opposition)	<i>Tykerb</i> (Revoked JULY 2013)	Fresenius Kabi Oncology Ltd.	Breast cancer drug	Physicochemical improvement data was shown which has no connection with therapeutic efficacy

difference in water. The patent specification of current invention threw no light on efficacy improvement over its polymorphic form while comparing to the base compound. Further the two forms, the base compound as well as its salt, could be equally used for disease treatment. An affidavit submitted on behalf of Novartis did not prove any noticeable therapeutic efficacy enhancement.

In the second petition Novartis challenged the legal sanctity of Section 3(d) of Indian Patents Act and compatibility with TRIPS. Madras High Court commented that it has no jurisdiction to administer issues related to TRIPS and the right place to channelize this issue is framed in the WTO Agreement which directs its disputes between member countries in the Dispute Settlement Body (DSB). The DSB has power to resolve any issues between the WTO member countries.

Madras High Court further declared that the amended Section 3(d) is lawful and is compatible with TRIPS. The challenges could not be legally sustained before the court as India constitutionally follows the policies of welfare state. Its first obligation is to impart quality health care and medication to its citizens. Compulsory licensing grant provision is available to cope up with national need during emergency as stated in Doha Declaration (Article 4 & 5). Further the patentability requirement is mentioned in Article 27 of TRIPS with which the member countries can protect their inventions in various technological domains.⁴⁴

It can be concluded from above that Section 3(d) can be viewed as important criteria under the patent eligibility for pharmaceutical innovations. The improvement in efficacy over the new forms that shows substantially raised potency is eligible for patenting compared to already existing one. Hence, Section 3(d) is in full compliance with TRIPS.

Hoff-Man La- Roche Drug Erlotinib

Roche v Cipla

Another major decision which outlines Section 3(d) is the Roche case.⁴⁵ The dispute commenced over anti-cancer drug between Roche and Cipla. Roche sold *Erlotinib* (IN'774) drug with brand name '*Tarceva*' which was introduced by Roche in the Indian market in 2006. Cipla planned to launch the generic version of this drug in 2007-2008. The drugs of both pharmaceutical companies were based on a compound 'Erlotinib Hydrochloride'. Soon after its

launch of lung cancer drug of the brand name *Erlocip* (brand name) by Cipla, the patent infringement proceeding was commenced against Cipla by Roche. Justice Manmohan Singh gave the judgment in favor of Cipla stating that Cipla did not infringe Roche's Indian Patent IN 196774 as the Cipla's generic drug (*Erlocip*) is the polymorphic form B which is different from Roche's patented drug (*Tarceva*) which is a mixture of polymorph A & B.⁴⁶

3(d) Rejection

Roche's later filed IN'507 application in India for the polymorphic form B which was rejected under Section 3(d) since it did not show increased efficacy in comparison to the drug of IN'774 patent which was for a mixture of polymorph A & B.

Abraxis Biosciences Drug Abraxane

Another patent that has been refused by the patent office is for the anti-cancer drug *Abraxane*⁴⁷ sold by the US firm Abraxis BioSciences which was claimed to be a combination of new form of a known substance Paclitaxel and anti-SPARC antibody. The patent application on the *Abraxane* formulation was refused by the Controller of Patents on the basis of lack of inventive step and Section 3(d) violation as the new form of a known substance is patentable only when it exhibits enhanced efficacy. It paved way for generic companies to launch affordable versions in the domestic market.⁴⁸

Hoff-Man La- Roche Drug Valganciclovir

Drug patent related to *Valganciclovir*⁴⁹ drug used against active cytomegalovirus retinis (CMV) infection affecting the eye of the patients living with HIV, has been rejected. The drug showed improved bioavailability when administered orally but the Controller of Patents ruled that improved bioavailability cannot be correlated with the efficacy and hence was rejected on Section 3(d) grounds.

Boehringer Ingelheim Drug Spiriva

Very recently patent for a respiratory drug *Spiriva* (crystalline tiotropium bromide monohydrate salt)⁵⁰ sold by German MNC, Boehringer Ingelheim, has been revoked. The applicant maintained that the crystalline tiotropium bromide monohydrate salt is a new form of known substance and could not satisfy the requirement of enhanced therapeutic efficacy under Section 3(d). Patent was rejected on the ground of obviousness and Section 3(d) violation for not demonstrating enhancement in therapeutic efficacy.

Conclusion

India has a robust and strong legislative, administrative and judicial framework which is in accordance with TRIPS Agreement. Section 3(d) can be viewed as a parameter of patent eligibility for pharmaceutical inventions. The efficacy enhancement can be evaluated on non-obviousness grounds by person skilled in art where new forms that show substantially high potency are eligible for patent compared to what existed. In order to meet the developmental aspects and concerns, India also uses flexibilities provided in the international regime.

Undoubtedly, Section 3(d) has created a significant impact in determining the patentability of pharmaceutical derivatives in India. Section 3(d) debars minor incremental inventions and prevents ever-greening which was prevalent before 2005. If incremental inventions are allowed there are surely, fair and equitable chances of ever-greening of patents. The outcome can be that the drug prices may remain high because of monopolistic scenario in the future Indian market and which may result in pushing the prices outside the affordability of the majority of Indian population. Hence a strong patent protection regime is required to promote innovation as ever-greening does not promote innovation in pharmaceutical sector.

Minor modifications in the drug molecules are not the need of the day for uplifting their effectiveness. In order to raise the standard and quality of pharmaceutical drugs the domestic pharmaceutical companies should be provided with more incentives and soft loans for example and the government should make it lucrative and easy for them to go for R&D to develop new drugs and subsequent clinical trials. The government may also negotiate price of the life-saving drugs sold by MNCs and regulate them.

The healthcare sector fully relies upon the patent system. As per US perspective, India does not promote incremental innovation. Pharmaceutical giants always strategize to keep a hold on the market thereby patenting minor modifications, as a result only a few blockbuster drugs are discovered. Section 3(d) of the Indian Patents Act keeps a check over ever-greening; thereby maintaining balance between medical aspect of public and innovation. Hence, a good approach would be to use resources efficiently to research the new blockbuster drugs in the area of concern to the developing countries. New efficacious

drugs will surely promote and expand the market and thereby creating a cost-effective transaction with easy access to public.

References

- 1 Patent procurement in India <http://www.ipo.org/wp-content/uploads/2013/03/Whitepaper-PatentprocurementinIndia.pdf> (accessed on 3 April 2015).
- 2 Nair M D, TRIPS, WTO and IPR: Counterfeit drugs, *Journal of Intellectual Property Rights*, 15 (10) (2010) 380-382.
- 3 Sandhya H V, A critical study of harmonization of patent law and its impact on Indian legal system, (2014) Karnataka University, <http://shodhganga.inflibnet.ac.in/bitstream/10603/21666/9/chapter-vi.pdf> (accessed on 7 January 2015).
- 4 Martin K Y, Intellectual Property, Competition and Development, http://www.wipo.int/edocs/mdocs/mdocs/en/isipd_05/isipd_05_www_103984.pdf (accessed on 10 April 2015).
- 5 Medicines Sans Frontiers, A timeline of U.S. attacks on India's patent law & generic competition, http://www.msfaaccess.org/sites/default/files/MSF_assets/IP_Docs/IP_factsheet_TimelineUSPressureIndia_ENG_2014.pdf (accessed on 4 February 2015)
- 6 Raju K D, WTO-TRIPS obligations and patent amendments in India: A critical stocktaking, *Journal of Intellectual Property Rights*, 9 (5) (2004) 226-241.
- 7 Waning B, Diedrichsen E and Moon S, A lifeline to treatment: The role of Indian generic manufacturers in supplying antiretroviral medicines to developing countries, *J Int AIDS Soc*, 13 (35) (2010).
- 8 Nair G G, Impact of TRIPS on the Indian pharmaceutical industry, *Journal of Intellectual Property Rights*, 13 (8) (2008) 432-431.
- 9 The Indian Patents Act, 1970, Section 3(d), as amended by Patents (Amendment) Act, 2005.
- 10 Greene W, The Emergence of India's Pharmaceutical Industry and Implications for the U.S. Generic Drug Market, *U.S. International Trade Commission* No. 2007-05-A (2007). <http://www.usitc.gov/publications/332/EC200705A.pdf> (accessed on 4 April 2015).
- 11 Verma S, Supreme Court rules for cheap cancer drug (2013), <http://timesofindia.indiatimes.com/business/india-business/Supreme-Court-rules-for-cheap-cancer-drug/articleshow/19331267.cms> (accessed on 20 December 2015).
- 12 Kant A, Section 3(d): 'New' Indian Perspective, *Journal of Intellectual Property Rights*, 14 (9) (2009) 385-396.
- 13 Bhaven N, Sampat B N, Shadlen K C & Amin T M, Challenges to India's Pharmaceutical Patent Laws, *Science*, 337 (2012) 414-415, <http://personal.lse.ac.uk/shadlen/Science,%20July2012.pdf> (accessed on 5 June 2015).
- 14 Basheer S & Reddy P, The 'Efficacy' of Indian Patent Law: Ironing out the Creases in Section 3(d), *SCRIPT-ed* 5(2) (2008) 232-266, http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1086254 (accessed on 15 May 2015)
- 15 Kant A, An attempt at quantification of 'efficacy' factors under Section 3d of the Indian Patents Act, *Journal of Intellectual Property Rights*, 18 (7) (2013) 303-315.
- 16 Efficacy, In Oxford English Dictionary online, <http://dictionary.oed.com> (accessed on 6 May 2015).
- 17 Gopalakrishnan N S & Agitha T G, The Indian patent system: The road ahead, *The Future of the Patent System*, 2012, 229-275.

- 18 'Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use,' (2004) OJ (L 136) 34, http://ec.europa.eu/health/files/eudralex/vol-1/dir_2004_27/dir_2004_27_en.pdf.
- 19 Basheer S, The "GLIVEC" Patent Saga: A 3-D Perspective on Indian Patent Policy And Trips Compliance, <http://www.scribd.com/doc/93770719/Shamnad-Basheer-Glivec-Patent-Saga#scribd> (accessed on 12 January 2015).
- 20 Foray D, Production and distribution of knowledge in the new systems of innovation: The role of intellectual property rights, *Science, Technology Industry Review*, 16 (1992) 119-52.
- 21 Shukla K U, Ever-greening patents, *Science Reporter*, 9 (2011) 31-34, [http://nopr.niscair.res.in/bitstream/123456789/12535/1/SR%2048\(8\)%2031-34.pdf](http://nopr.niscair.res.in/bitstream/123456789/12535/1/SR%2048(8)%2031-34.pdf) (accessed on 20 May 2015)
- 22 National Institute for Health Care Management Research and education foundation, Changing Patterns of Pharmaceutical Innovation, (WASHINGTON D.C.: NIH, 2002), <http://www.nihcm.org/pdf/innovations.pdf> (accessed on 23 March 2015).
- 23 James T C, Patent Protection and Innovation, Section 3(d) of The Patents Act and Indian Pharmaceutical Industry, <http://www.nipoonline.org/Section-report.doc> (accessed on 10 March 2015).
- 24 Shamnad B, Limiting the Patentability of Pharmaceutical Inventions and Micro-organisms: A TRIPS Compatibility Review n.151 (November 2005) (on file with the Intellectual Property Institute, Oxford, UK), SSRN: <http://ssrn.com/abstract=1391562> or <http://dx.doi.org/10.2139/ssrn.1391562> (accessed on 17 January 2015).
- 25 Bansal S I, Sahu D, Bakshi G & Singh S, Ever-greening - a controversial issue in pharma milieu, *Journal of Intellectual Property Rights*, 14 (7) (2009) 299-306.
- 26 U.S-India Business Council. 2009. The Value of Incremental Pharmaceutical Innovation. http://www.indiaenvironmentportal.org.in/files/USIBCIncrementalInnovationReport_Final.pdf (accessed on 20 February 2015).
- 27 Chaudhuri S, Multinationals and Monopolies Pharmaceutical Industry in India after TRIPS. Indian Institute of Management Calcutta WPS No. 685/ November 2011 https://facultylive.iimcal.ac.in/sites/facultylive.iimcal.ac.in/files/WPS%20685_0.pdf (accessed on 22 March 2015).
- 28 Chopra S, FICCI's Position on Section 3(d) of The Patents Act, 1970. http://www.ficci.com/SEDocument/20142/Report_on_section_3d.pdf (accessed on 10 June 2015).
- 29 Special 301 Report: Section 3(d) of the Indian Patents Act opposed by the US, <http://currentaffairs.gktoday.in/special-301-report-section-3d-indian-patent-act-opposed-07201414201.html> (accessed on 10 December 2015).
- 30 Persistent US attacks on India's Patent Law & Generic Competition https://www.msfacecess.org/sites/default/files/IP_US-India_Briefing%20Doc_final_2%20pager.pdf (accessed on 5 April 2015).
- 31 Fyan S, Pharmaceutical patent protection and Section 3(d): A comparative look at India and the U.S, *Virginia Journal of law & Technology*, 15 (2010) 198-226.
- 32 Amin T, Re-visiting the patents and access to medicines dichotomy: An evaluation of TRIPS implementation and public health safeguards in developing countries. The Global Governance of HIV/AIDS: *The Global Governance of HIV/AIDS, Intellectual Property and Access to Essential Medicines*, 2013 109-130, https://books.google.co.in/books?id=Ttjs4WU2t_8C&pg=PA114&dq=philippine+and+section+3d+of+indian+patent+act&hl=en&sa=X&ved=0CB0Q6AEwAGoVChMI5IWI-sW0xwIVw56mCh2bFQBD#v=onepage&q=philippine%20and%20section%203d%20of%20indian%20patent%20act&f=false (accessed on 15 May 2015).
- 33 Brazil's Patent Reform Innovation towards National Competitiveness. Center for Strategic Studies and Debates, 2013, http://infojustice.org/wp-content/uploads/2013/09/Brazilian_Patent_Reform.pdf (accessed on 15 April 2015).
- 34 Mexican Patent Law (1991), Amended 2011, http://www.jpo.go.jp/shiryu_e/s_sonota_e/fips_e/pdf/mexico_e_e_sangyou.pdf.
- 35 Kilburn & Strode, Patentability of Polymorphs at the EPO, October 2014, <http://www.kilburnstrode.com/assets/Patentability%20of%20polymorphs%20at%20the%20EPO%20-%20Final.pdf> (accessed on 25 January 2015).
- 36 *Novartis AG v Union of India*, (2007) 4 MADRAS L.J. 1153, <http://www.scribd.com/doc/456550/High-Court-order-Novartis-Union-of-India> (accessed on 15 January 2015).
- 37 US Patent Number 5521184 titled "Pyrimidine derivatives and processes for the preparation thereof" (filed in April 1993 and issued on 28 May 1996) (referred to as the '184 Patent) (accessed on 25 January 2015).
- 38 *Novartis AG v NatcoPharma and Others*, Glivec is sold as "Gleevec" in the US, <http://www.scribd.com/doc/456550/High-Court-order-Novartis-Union-of-India> (accessed on 25 January 2015).
- 39 Novartis, Glivec Patent Case in India: FAQs: <http://www.novartis.com/downloads/aboutnovartis/india-glivec-patent-case-faq.pdf>. However, in pleadings filed before the Madras High Court, Novartis claims that it filed patent applications covering the beta crystalline form in over 50 countries. *Novartis AG and Anr v Union of India and Ors*, WP No. 24759 of 2006, High Court of Judicature at Madras, Paragraph 9 (accessed on 22 December 2015).
- 40 Raju K D, Interpretation of Section 3(d) in the Indian Patents Act 2005: A Case Study of Novartis (footnote 5 and 6) <http://www.nalsar.ac.in/IJPL/Files/Archives/Volume%201/2.pdf> (accessed on 14 March 2015).
- 41 Supreme Court Rules for Cheap Cancer Drug <http://timesofindia.indiatimes.com/business/india-business/Supreme-Court-rules-for-cheap-cancer-drug/articleshow/19331267.cms> (accessed on 2 April 2015). The Novartis drug costs Rs.1, 20,000 per month in India. At the same time, the generic versions are available in the country which cost only Rs.8000 to Rs.10, 000/month (accessed on 22 March 2015).
- 42 Hanns U, Technology and Competition, 2009, 359, https://books.google.co.in/books?id=32LiSHEmNYIC&pg=PA359&lpg=PA359&dq=The+High+Court+of+Madras+first+granted+an+order+of+ex-parte+injunction+in+favour+of&source=bl&ots=Q1CNt38D9s&sig=6iR_XPxBmRpQcFQzue-TKXRAM&hl=en&sa=X&ei=S1ajVZrgIjK0gT2ypM4&ved=0CCwQ6AEwAw#v=onepage&q=The%20High%20Court%20of%20Madras%20first%20granted%20an%20order%20of%20ex-parte%20injunction%20in%20favour%20of&f=false (accessed on 10 February 2015).
- 43 Deshmukh D, *Novartis AG and Anr. v Mehar Pharma and Anr.*, 23 December 2004, <http://indiankanoon.org/doc/50284/> For an excellent review of the EMR cases, Feroz Ali Khader, *The Law of Patents: With a Special Focus on Pharmaceuticals in India*, 2007, 242 (accessed on 5 November 2014).

- 44 Iyer D, Analysis of Section 3(d) of Indian Patents Act, *IP Frontline*, 2012, <http://ipfrontline.com/2012/04/analysis-of-section-3d-of-indian-patent-act> (accessed on 5 March 2014).
- 45 Thomas Z, IP case law developments, *Journal of Intellectual Property Rights*, 14 (9) (2009) 437-445.
- 46 Nair G G, Landmark pharma patent jurisprudence in India, *Journal of Intellectual Property Rights*, 19 (3) (2014) 79-88.
- 47 4572/CHENP/2006 "TREATMENT METHODS UTILIZING ALBUMINBINDING PROTEINS AS TARGETS", <http://ipindiaservices.gov.in/decision/4572-CHENP-2006-10560/4572-chenp-2006%20order-Final.pdf> (accessed on 15 July 2015).
- 48 Mukherjee R, US Co. Abraxis denied patent on cancer drug, <http://timesofindia.indiatimes.com/business/india-business/US-co-Abraxis-denied-patent-on-cancer-drug/articleshow/47521553.cms> (accessed on 4 June 2015).
- 49 959/MAS/1995 '2-(2-Amino-1, 6- Dihydro-6-Oxo-Purin-9-Yl) Methoxy-1,3-Propanediol Derivative', <http://static1.1.sqspcdn.com/static/f/129694/3032540/1241580850867/F+Hoffmann+La+Roche+App+No+959-MAS-1995+v+INP+2009.pdf?token=5rWDSHcTpLNEs%2FD1hxIzMe9Mskg%3D> (accessed on 10 June 2015).
- 50 558/DELNP/2003 "Crystalline Tiotropium Bromide Monohydrate and Process Thereof" [http://ipindiaservices.gov.in/decision/00558-DELNP-2003-9637/558-delnp-2003%2025\(2\)%20decision.pdf](http://ipindiaservices.gov.in/decision/00558-DELNP-2003-9637/558-delnp-2003%2025(2)%20decision.pdf) (accessed on 25 June 2015).
- 51 Controller's decisions - Indian Patent Office, <http://ipindiaservices.gov.in/patentdecisionsearch/patentsearch.aspx> (accessed on 25 July 2015).