scripted

Volume 5, Issue 2, August 2008

The "Efficacy" of Indian Patent Law: Ironing out the Creases in Section 3(d)

Shamnad Basheer & T. Prashant Reddy[*]

Abstract

Indian patent law recently landed itself in the eye of a TRIPS storm on account of the rejection of a patent application covering Novartis' famed anticancer drug, Glivec. The rejection stemmed, inter alia, from a unique section in the Indian patent regime (section 3(d)) that seeks to prevent "ever-greening" by prohibiting the patenting of new forms of existing pharmaceutical substances that do not demonstrate significantly enhanced "efficacy."

Not only did Novartis appeal the patent office decision, but in a rather controversial move, it challenged the TRIPS compatibility and constitutionality of section 3(d). The Madras High Court ruled that section 3(d) was constitutional. It also held that it did not have jurisdiction to rule on the TRIPS issue. This paper analyses this decision within the broader framework of section 3(d) and what it seeks to achieve. It argues

---

[*] Shamnad Basheer (Research Associate, Oxford IP Research Centre) and T. Prashant Reddy (Vth Year B.A.LLB (Hons.) Student, National Law School of India University). *A previous and somewhat distinct version of this article, authored by Shamnad Basheer, won the first place in a competition held by ATRIP, an international association of IP law teachers and researchers. The authors wish to sincerely thank Feroz Ali (Advocate), Tahir Amin (IMAK), Pravin Anand (Anand and Anand), Nihas Basheer (Wadia Gandhy), Caleb Gabriel (K&S), Mrinalini Kochupillai (Consultant), Janice Mueller (Univ of Pittsburgh), Dr Gopakumar Nair (Patent Gurukul), Promod Nair (Herbert Smith, UK), Chris Ohly (Schiff Hardin), Vivek Reddy (Advocate, Hyderabad), Bhaven Sampat (Columbia Univ), Swathi Sukumar (Anand and Anand), Steven Smith (NuPharm, UK), H Subramaniam (S&N Associates) Arun Kumar Thiruvengadam (NUS, Singapore), CH Unnikrishnan (Mint) and Vijayaraghavan (Ranbaxy) for their inputs and/or comments on earlier drafts. We also thank Shawn Harmon, Wiebke Abel and other editors of SCRIPTed for giving us ample time to build on our initial draft and for helping better the paper through their fine editing. Our gratitude comes with the usual caveat that they are in no way responsible for our mistakes. A separate paper focussing only on the constitutionality and TRIPS compatibility aspects of section 3(d) is being published in the National Law School of India Review. See Shamnad Basheer and T. Prashant Reddy* "Ducking TRIPS in India: A Saga involving Novartis and the legality of Section 3(d)" (2008) 20(2) *National Law School of India Review*.

that although the Madras High Court was correct in concluding that section 3(d) is constitutional, the court's reasoning leaves much to be desired. In particular, the court does not fully appreciate Novartis' alleged invention and the contours of section 3(d).

Though this lack of appreciation is not fatal to the constitutionality analysis by the court, it is reflective of some of the creases inherent in the wordings of section 3(d). The need of the hour is to iron out these creases in section 3(d) and to help brighten the line between pharmaceutical inventions that are patentable and those that are not. This paper not only offers suggestions on how these creases may be ironed out, but also goes on to suggest an amendment to section 3(d).

While some of the suggestions in the paper are immediately implementable, other issues will necessarily involve a more detailed empirical/policy investigation. This paper highlights some of the factors that one might consider whilst undertaking such empirical investigation, a task which is likely to go to the very heart of the age-old debate about what constitutes optimal intellectual property norms for developing countries.

DOI: 10.2966/scrip.050208.332


© Shamnad Basheer & T. Prashant Reddy 2008. This work is licensed under a Creative Commons Licence. Please click on the link to read the terms and conditions.

1. Introduction

Indian patent law recently landed itself in the eye of a TRIPS storm on account of the rejection of a patent application covering Novartis' famed anticancer drug, Glivec.[1] The rejection stemmed, *inter alia*, from a unique section in the Indian patent regime (section 3(d)) that aims to prevent "ever-greening" by prohibiting the patenting of new forms of existing pharmaceutical substances that do not demonstrate significantly enhanced "efficacy."[2]

Not only did Novartis appeal the patent office decision, but in a rather controversial move, it challenged the TRIPS[3] compatibility and constitutionality of section 3(d). The Madras High Court ruled that section 3(d) was constitutional.[4] It also held that it did not have jurisdiction to rule on the TRIPS issue. It is therefore an opportune moment to examine the various issues thrown up by section 3(d), a section with no parallel anywhere else in the world.

The paper begins by introducing the reader to the facts of the Glivec patent dispute and to section 3(d). It then discusses the decision of the Madras High Court and argues that although it was correct in concluding that section 3(d) is constitutional, the court's reasoning leaves much to be desired. In particular, the court does not fully appreciate Novartis' alleged invention and the contours of section 3(d).

Though this lack of appreciation is not fatal to the constitutionality analysis by the court, it is reflective of some of the creases inherent in the wordings of section 3(d). This paper not only offers suggestions on how these creases may be ironed out,[5] but also goes on to propose an amendment to section 3(d).

While some of the suggestions in this paper are immediately implementable, other issues will necessarily involve a more detailed empirical/policy investigation. One such issue is the definition of efficacy: ought "efficacy" to be restricted to only therapeutic efficacy, or should it be widely defined to encompass non therapeutic advantages as well, such as heat stability, manufacturing efficiencies etc? This issue will, in many ways, determine the scope of protection of incremental pharmaceutical inventions in India. Illustratively, if efficacy is restricted to only "therapeutic" efficacy, new drug delivery mechanisms, a category of inventions in which Indian companies are particularly proficient, will fall out of the scope of protection.

---

[1] *Novartis AG v Natco Pharma and Others,* Indian Patent Office, Application No.1602/MAS/1998 (25 January 2005): http://lists.essential.org/pipermail/ip-health/2006-March/009200.html (last visited on Mar. 8 2008).

[2] *Patents Act*, 1970, § 3(d), amended by Patents (Amendment) Act, 2005.

[3] The Agreement on Trade Related Aspects of Intellectual Property Rights (15 April 1994) LT/UR/A-1C/IP/1: http://www.wto.org/english/docs_e/legal_e/27-trips.doc (last visited on Jul. 16 2008).

[4] *Novartis AG & Anr. v Union of India & Othrs*., (2007) 4 MLJ 1153.

[5] We owe the phrase "ironing out the creases" to one of the most distinguished jurists of all times, Lord Justice Denning, who eloquently articulates it in the context of a principle of statutory construction in *Seaford Court Estates, Ltd.v. Asher* [1949] 2 KB 481, 499 (CA): *"A judge must not alter the material of which it [an act] is woven, but he can and should iron out the creases."*

Given time and space constraints, this paper does not engage with extensive policy analysis to determine the optimal breadth for the term "efficacy." However, it highlights some of the factors that one might consider whilst undertaking this task. In many ways, an empirical investigation of these factors (which we hope to undertake in another paper) is likely to go to the very heart of the age-old debate about what constitutes optimal intellectual property norms for developing countries.

Finally, in our conclusion, we reiterate a key point that we make throughout the paper – although section 3(d) is constitutional, it is crude. The need of the hour is to refine the crudities in section 3(d) and to help brighten the line between pharmaceutical inventions that are patentable and those that are not.

2. The Glivec Patent Saga

Like all drug sagas, the story of Glivec begins with two outstanding scientists, who rarely figure in the "patent" narratives that are doing the rounds today.

In 1960, Peter C Nowell, then a junior faculty member at the University of Pennsylvania School of Medicine, together with a graduate student, David Hungerford, discovered a genetic mutation in patients with chronic myelogenous leukemia (CML), a debilitating form of cancer. The discovery of this abnormality, designated the Philadelphia chromosome after the city in which it was discovered, broke fresh ground and spurred the search for a potential cure for CML.[6] In the 1980's, researchers determined that the chromosomal abnormality produced a cancer-causing kinase enzyme. With this enzyme as a target, Novartis researchers (led by Drs. Zimmermann and Buchdunger) in close collaboration with a prominent scientist, Brian Drucker[7] created and tested 400 molecules to find one that would target this enzyme, without disrupting any of the hundreds of other similar enzymes in a healthy cell.[8] Pioneering the concept of rational drug discovery, they closed in on a promising candidate, "Imatinib," a free base.[9] In 1993, Novartis filed a patent covering this free base and all pharmaceutically acceptable salts.[10]

Imatinib was then further researched upon and improved – first, by converting it to a particular salt form, namely imatinib mesylate. From this salt, Novartis found that the most stable version was a particular polymorphic form, namely the beta crystalline form. Novartis then formulated the beta crystalline form of imatinib mesylate into a

---

[6] G A Koretzky, "The Legacy of the Philadelphia Chromosome" (2007) 117 *The Journal of Clinical Investigation*, 2030.

[7] Recently, in an opinion piece published in an Indian newspaper, Dr Brucker lambasted Novartis for what he alleged were extremely high prices for a drug that he helped invent. See Brian Drucker, "Don't Abuse Patents" Mint, August 15, 2007: http://www.livemint.com/2007/08/15003521/Don8217t-abuse-patents-sci.html.

[8] See R Capdeville et al "Glivec (STI571, Imatinib), A Rationally Developed, Targeted Anticancer Drug" *Nature Reviews Drug Discovery* 1, 493-502 (July 2002). See also E Buchdunger and J Zimmerman, "*The Story of Gleevec"*: http://www.innovation.org/index.cfm/StoriesofInnovation/InnovatorStories/The_Story_of_Gleevec.

[9] See B Vastag, "Leukemia Drug Heralds Molecularly Targeted Era" (2000) 92(1) *Journal of the National Cancer Institute*, 6-8. See also "Gleevec: Highlighting the Power of Rational Drug Design" (2008) 18(4) *The Journal of Young Investigators*.

[10] US Patent Number 5521184 titled "Pyrimidine derivatives and processes for the preparation thereof" (filed in April 1993 and issued on May 28, 1996) (hereafter referred to as the '184 patent).

pharmaceutically useful drug, Glivec.[11] After its approval by the FDA in 2001, Glivec has proven effective for innumerable patients and has been hailed as nothing short of a wonder drug.[12]

The patent dispute that sets the tone for this paper centres around the beta crystalline form of imatinib mesylate referred to above. Novartis claims that around 40 patents covering this polymorph have been granted to it in various countries.[13] However, owing to the unavailability of drug patents in India until 1 January 2005, Novartis claimed this polymorph[14] in a "mailbox" application.[15]

Novartis also applied for an exclusive marketing right (hereinafter EMR) pending grant of a product patent, and was granted the same in November 2003.[16] Consequently, Novartis sued generic drug makers such as Ranbaxy and CIPLA before the High Courts of Madras and Bombay on the strength of its EMR. The Madras High Court upheld the EMR and restrained the said drug producers on various grounds, including, *inter alia*, the fact that Novartis ran a free patient access programme titled "GIPAP" (Glivec International Patients Assistance Program) and undertook to make this programme even more user friendly to patients that could not afford the drug.[17] This, the court held, was

---

[11] *Novartis AG v Natco Pharma and Others, see* note 1. Glivec is sold as "Gleevec" in the US.

[12] See Buchdunger and Zimmerman, *see* note 8. Later, it was found that Glivec is also useful in treating Gastro-Intestinal Stromal Tumours (GIST), a very rare cancer affecting the digestive tract or nearby structures within the abdomen. *See* http://www.gistsupport.org/treatments/current-treatments/gleevec.php (last visited on Oct, 20 2007).

[13] *See* Novartis, G*livec Patent Case in India: FAQs:* http://www.novartis.com/downloads/about-novartis/india-glivec-patent-case-faq.pdf (last visited on Oct, 22 2007). 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 and that it had procured patents in 35 of them. See *Novartis AG and Anr v Union of India and Ors*, WP No. 24759 of 2006, High Court of Judicature at Madras, paragraph 9.

[14] "*Crystal Modification of A N-Phenyl-2-Pyrimidineamine derivative, processes for its manufacture and use*," Application No.1602/MAS/98 (July 17, 1998).

[15] Under Art 65 of TRIPS, India had 10 years from the date of coming into force of TRIPS to implement product patent protection in pharmaceuticals. However, in the interim, as per Article 70.9 of TRIPS, all applications claiming pharmaceutical inventions were be accepted and put away in a mailbox, to be examined in 2005 – these applications are commonly referred to as 'mailbox applications.' Pursuant to a WTO dispute filed by the United States against India for a failure to comply with this TRIPS provision, India amended her patent regime to provide for such a "mailbox" facility. *See The Patents (Amendment) Act 1999 (Act 17 of 1999)*. This Act was given retrospective effect from 1 January 1995. *See* WTO Appellate Body, *India: Patent Protection For Pharmaceutical And Agricultural Chemical Products*, WT/DS50/AB/R (Dec. 19, 1997): http://docsonline.wto.org/imrd/directdoc.asp?DDFDocuments/t/WT/DS/50ABR.WPF (last visited on Oct, 20 2007).

[16] Under TRIPS, countries such as India that utilised the 10 year window for introducing product patents for pharmaceuticals had to provide for an interim "pipeline" protection in the form of exclusive marketing rights, provided the drug in question had a patent abroad, a patent application pending in India and drug marketing approval both in India and abroad. Here again, pursuant to a WTO ruling, India amended her regime in 1999 to provide for exclusive marketing rights. See Chapter IVA of *The Patents (Amendment) Act 1999 (India)*.

[17] The High Court of Madras first granted an order of ex-parte injunction in favour of Novartis in Suit Nos. 5-9 of 2004. Subsequently by a detailed order dated April 28, 2004, the High Court confirmed (but slightly modified) the order of the ex-parte injunction. See *Novartis AG v Adarsh Pharma & Anr*., 2004 (29) PTC 108 (Mad). The injunction was then further confirmed by a division bench of the Madras High Court, in an appeal filed by the Indian generic companies. See *Intas Laboratories Pvt. Ltd. v Novartis A.G.* 2005 (1) CTC 27.

sufficient to take care of any "public interest" ground that might have militated against the grant of an injunction. The Bombay High Court however disagreed with the ruling of the Madras High Court, noting that the validity of the recently issued EMR had been seriously challenged by the defendants. Besides, the fact that the drug was more expensive and was being imported by the plaintiff (triggering fears of sustained supplies of such a critical life-saving drug in India) influenced the court to deny the grant of an injunction.[18]

Pursuant to the 2005 amendment to India's patent regime,[19] which introduced product patents for pharmaceuticals, the mailbox application by Novartis, as above mentioned, was opened and examined. The grant of a patent was opposed by several generic drug companies (and an NGO, the Cancer Patients Aid Association (CPAA)) on several grounds including:

i) lack of novelty/anticipation;
ii) lack of significantly enhanced "efficacy" under section 3(d);
iii) obviousness, and;
iv) wrongful priority.

Agreeing with the above arguments, the Assistant Controller of Patents rejected the patent application.[20] It is pertinent to note that upon rejection of the patent application, the EMR by Novartis died a natural death.[21]

Aggrieved by this rejection, Novartis AG, along with its Indian subsidiary, Novartis India, filed two writ petitions in the Madras High Court. These petitions not only sought a reversal of the Assistant Controller's order, but also a declaration that Section 3(d) was unconstitutional and in violation of India's obligations under TRIPS.[22]

Pursuant to a government notification,[23] the High Court transferred the first petition to the Intellectual Property Appellate Board (IPAB) – a specialist tribunal set up to deal with appeals from the various intellectual property offices across the country. As of the date of writing this paper, the matter was still pending before the IPAB.[24]

---

[18] *Novartis AG v Mehar Pharma & Anr.*, 2005 (30) PTC 160 (Bom). For an excellent review of the EMR cases, see Feroz Ali Khader, *The Law Of Patents: With A Special Focus On Pharmaceuticals In India* (2007) pp 242.

[19] The Patents (Amendment) Act, 2005 was published as law in the Gazette of India on April 5, 2005 (herafter "2005 amendments").

[20] *Novartis AG v Natco Pharma and Others, see* note 1.

[21] See section 24B (1) of the Patents Act 1970 (as amended by the 1999 amendments) which states that the duration of the EMR shall be 5 years from the date of EMR grant or till the date of grant of a patent or the date of rejection of the patent, whichever is earlier. The chapter on EMR's (including section 24B) was repealed by the 2005 amendments, which introduced pharmaceutical product patents into India.

[22] *Novartis AG and Anr v Union of India and Ors*, WP No. 24759 of 2006, High Court of Judicature at Madras.

[23] The notification under the Patents (Amendment) Act (section 117G), provided that all pending appeals in the High Court shall be transferred to the newly constituted Appellate Board. See Notification No.12/15/2006-IPR-III, dated 2/4/2007 issued by the Ministry of Commerce & Industry: http://ipindia.nic.in/ipr/patent/gazetteofindia_apr2007.pdf (last visited on Oct, 19 2007).

[24] *See* http://www.ipab.tn.nic.in/ for more details on the IPAB (last visited on Oct. 19 2007). The IPAB is currently embroiled in a controversy around the appointment of one of its members, Mr.

In order to contextualize the constitutional challenge to section 3(d) and to appreciate the various drafting problems inherent in section 3(d), one needs to delve briefly into the merits of the patent dispute before the IPAB, i.e. whether Novartis' beta crystalline form is patentable or not under section 3(d).

3. Section 3(d): The Structure and Context

Section 3 is the key section on "patent eligibility" and lists out what are not "inventions" under the Indian Patents Act. Section 3 (d) lists out one such non eligible patentable subject matter:

> *d)* ***the mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy*** *of that substance or the mere discovery of any new property or new use for a known substance or of the mere use of a known process, machine or apparatus unless such 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.***

In essence, section 3(d) aims to prevent a phenomenon commonly referred to as "ever-greening"[25] by providing that only those pharmaceutical derivatives that demonstrate significantly enhanced "efficacy" are patentable.[26]

According to a report of the US National Institute of Healthcare and Medicines (NIHCM):[27]

Chandrasekharan, who was the Controller of Patents when the patent office rejected Novartis' application. When Novartis objected to the appointment of Mr. Chandrasekharan on the grounds of bias, the IPAB decided to hear the matter without Mr. Chandrasekharan i.e. without a technical expert. The High Court confirmed the IPAB Decision to hear the appeal without a patent expert. However, Natco Pharma, one of the parties opposing Novartis in this case, objected to this ruling by the High Court. Section 84(2) of the Trade Marks Act, 1999 states that every IPAB Bench sitting in a patent matter must consist of at least one technical member i.e. a patent expert. See CH Unnikrishnan "*Natco to challenge HC Ruling on Glivec Patent Case"*: http://www.livemint.com/2007/11/18180746/Natco-to-challenge-HC-ruling-o.html (last visited on Mar. 8 2008).

[25] Under one definition, "ever-greening" occurs when a manufacturer 'stockpiles' patent protection by obtaining separate 20-year patents on multiple attributes to a single product. See *Patentee Attorneys Challenge Assertions re FTA Patent Practices* (Press Release dated 4 August 2004): http://www.ipta.com.au/forms&notices/FTA_Release.doc (5 July 2005) (last visited Aug. 30 2007).

[26] During the Parliamentary debates, Sri Kamal Nath, Minister of Commerce and Industry, in response to concerns by other Parliamentarians over "me too" drugs and the likely impact on prices, stressed that section 3(d) was introduced to prevent "ever-greening." Suresh Kurup, a Parliamentarian, specifically cited the ongoing case of Glivec to demonstrate the ill effects of ever-greening. See *Lok Sabha Debates* (22 March 2005): http://164.100.24.230/Webdata/datalshom001/dailydeb/22032005.htm (last visited on Oct, 20 2007).

[27] National Institute For Health Care Management, *Changing Patterns of Pharmaceutical Innovation*, May 2002: http://www.nihcm.org/~nihcmor/pdf/innovations.pdf (last visited on Oct, 20 2007).

> *Drug manufacturers patent a wide range of inventions connected with incremental modifications of their products, including minor features such as inert ingredients and the form, colour and scoring of tablets.*

The underlying assumption behind section 3(d) is that derivatives, such as salt forms, polymorphs, isomers etc that are structurally similar to known pharmaceutical substances are likely to be functionally equivalent as well, and if this is not the case and the new form of an existing substance works better than the old form, it is up to the patent applicant to demonstrate this and justify the claim to a patent.

To this extent, section 3(d) draws a distinction between "ever-greening" and incremental innovation.[28] By making derivates with enhanced efficacy patentable, section 3(d) encourages the sequential development of existing products or technologies to help bring in improved products that address unmet public health needs.

In order to determine whether the Novartis' invention is more "efficacious" than an earlier known form or a mere "ever-greened" variety, let us examine what the "invention" entails. Broadly speaking, it involves a transition from the discovery of a free base in the laboratory to the useful drug, Glivec. The various steps in this transition can be encapsulated as under:

i) Synthesizing imatinib as its free base, a compound that was patented in the US, EU and several other countries.[29] However, this could not be patented in India, owing to the fact that in 1993, India did not provide product patents for pharmaceutical substances.
ii) Converting the free base to a particular salt form, imatinib mesylate, by adding methanesulfonic acid.
iii) Crystallising the imatinib mesylate to obtain the beta crystalline form, which is allegedly the most stable polymorphic form of the salt. A patent application was filed for this and it is this application that is the subject matter of dispute.[30]
iv) Formulating the beta crystalline form of imatinib mesylate into a pharmaceutically useful drug, Glivec.

Novartis claims that the active ingredient in Glivec (beta crystalline form of imatinib mesylate) is more effective than the imatinib free base, since it displays better bio-availability properties, i.e. it is absorbed more easily into the blood.[31] To this effect, it

---

[28] Classifying all "incremental innovations" as tantamount to "ever-greening" is misguided. See Shamnad Basheer *Limiting the Scope of Pharmaceutical Patents and Micro-organisms: A TRIPS compatibility Review*, (Intellectual Property Institute, London, 2005).

[29] '184 Patent, *see* note 10. See also corresponding European Patent No. 0564409.

[30] *Novartis AG v Natco Pharma and Others, see* note 1. Novartis also filed a patent application covering the alpha crystalline form of imatinib mesylate, which is currently being opposed by Okasa, an Indian pharmaceutical company. However, Novartis claims that that the beta form *"stores better, is less hygroscopic, is easier to process and guarantees a constant quality of the final drug product." Novartis AG v Union of India*, WP *see* note 22, para 4. Interestingly, CIPLA claims that it owns a process patent covering the alpha crystalline form and that it has been selling a drug containing this particular form. See CH Unnikrishnan, *Novartis Faces Fresh Patent Fight in India*, Mint, 10 Jan 2008: http://www.livemint.com/2008/01/10000215/Novartis-faces-fresh-patent-fi.html.

[31] In its writ petition filed before the Madras High Court, Novartis claimed that "*The Beta Crystalline form of Imatinib Mesylate also results in a higher bio- availability over the 1993 compound and, hence, differs significantly in properties with regard to efficacy.*" *Novartis AG v Union of India*, WP, *see* note

submitted evidence before the Assistant Controller demonstrating an increase in bio-availability of up to 30%. However, the Assistant Controller held that this was not sufficient to constitute "increased efficacy:"[32]

> *As per the affidavit the technical expert has conducted studies to compare the relative bioavailability of the free base with that of beta crystalline form of imatinib mesylate and has said that the difference in bioavailability is only 30% and also the difference in bioavailability may be due to the difference in their solubility in water. The present patent specification does not bring out any improvement in the efficacy of the beta crystal form over the known substances – rather it states the base can be used equally in the treatment of diseases of in the preparation of pharmacological agents wherever the beta crystal is used. Even the affidavit submitted on behalf of the Applicant does not prove any significant enhancement of known efficacy.*

As can be seen from the above, the decision of the patent office is not very illuminating and the patent controller did not give any detailed reasons as to why he thought the beta crystalline form lacked enhanced "efficacy." The following questions remain unanswered.

i) What did the term "efficacy" mean? Did it connote only "therapeutic efficacy"? Assuming this is the case, would "bioavailability" qualify?[33] Would advantages such as heat stability and increase in manufacturing efficiency qualify?[34]

ii) What would constitute a "significant enhancement in efficacy" under the Explanation to section 3(d)? Would a 30% increase in bio-availability suffice?

iii) What would qualify as the "known substance" against which the comparison under section 3(d) ought to be made? In the case at hand, would the "known" substance be the imatinib free base (in relation to which it is far easier to show increased efficacy) or the later salt, imatinib mesylate?[35] Or the alpha crystalline form of imatinib mesylate?

It is hoped that a final resolution of this dispute at the IPAB will provide guidance in this regard.

---

22. See also Gauri Kamath, *Interview with Paul Herrling, Head of Corporate Research, Novartis AG*, BUS. WORLD, Feb. 19, 2007: http://www.businessworldindia.com/feb1907/indepth04.asp (last visited on Oct 21 2007).

[32] *Novartis AG v Natco Pharma*, *see* note 1.

[33] For a definition of this term, *see* note 48.

[34] *See Torrent Pharmaceuticals Limited v Astra Aktiebolag*, Indian Patent Office, Decision on application no: 1354/DEL/98 dated May 21st. 1998, where the claimed enhancement appears to relate to "manufacturing efficiencies".

[35] A recent update of the Patent Office Manual suggests that the comparison would have to be with respect to imatinib mesylate (irrespective of whether or not imatinib mesylate was factually known or anticipated from the earlier '184 patent covering the free base) and not the imatinib free base. *See* Controller General of Patents, Designs & Trade Marks, India, *Draft Manual of the Indian Patent Office*, 3rd ed, 2008 at para 4.5.3.

4. Section 3(d): Constitutionality Analysis

Under Indian constitutional law, a statute can be challenged as violating the constitution on two main grounds:

1. that it impinges on the fundamental rights of the petitioner, and;
2. that the parliament lacks legislative competence to enact the statutory provision in question.

Novartis urged only the first of these two grounds whilst challenging the constitutionality of section 3(d). First, it alleged that section 3(d) violated the fundamental right to equality as enshrined in Article 14 of the Constitution of India. More specifically, it argued that the usage of terms such as "enhancement of known efficacy" and "differ significantly in properties with regard to efficacy" without accompanying guidelines elucidating their scope rendered section 3(d) vague and arbitrary.[36] And such arbitrariness, facilitated in large part by the conferment of uncanalised power on a statutory authority[37] hits at the very root of the concept of equality enshrined in Article 14 of the Constitution of India.

Novartis' second argument, related in many ways with the first one discussed above, stated that the structure of section 3(d) vested the patent office with unfettered discretion to devise its own policy and determine as to what constituted a significant enhancement of efficacy.[38] Novartis urged that this violated the Constitution, as it amounted to a delegation of an essential legislative function.

The court however disagreed with each of the contentions above. First, the threshold for any statutory provision to qualify as "arbitrary" and therefore violative of Article 14 is considerably high and Indian courts have shown great reluctance in striking down legislations on this count.[39]

The Madras High Court also followed this trend of judicial circumspection and highlighted that merely because legislation is skeletal and does not contain definitions or guidelines, it does not necessarily mean that it is arbitrary. Rather, one has to look into factors such as the wordings of the statute, the amount of discretion conferred, the possibility of appeal to correct any wrong decision and the object of a statute to gauge the contours of a section. Further, a determination of when a new form demonstrates a "significant" enhancement of efficacy, when compared with the old substance is not amenable to a uniform formula, but is to be based on the facts of each specific case.

Therefore, it is extremely difficult to qualify section 3(d), a section brought in to prohibit a phenomenon widely known as "ever-greening" as "arbitrary" or vague.[40]

---

[36] *Novartis AG & Anr. v Union of India & Othrs*., *see* note 4, at para 14.

[37] *Ibid.*

[38] During the course of oral arguments before the Madras High Court, Novartis also challenged section 3(d) as violating the fundamental right to practice one's business, as enshrined in Article 19(1)(g) of the Constitution. However, at a later stage, they dropped this specific challenge. See *Novartis Update*, 29th Jan 2007: http://www.lawyerscollective.org/content/novartis-update-%3A-29th-jan-2007.

[39] *See* T Khaitan, "*Anuj Garg v Hotel Association of India* – Equality Jurisprudence Coming of Age?" (Draft on file with authors).

[40] Novartis also argued that all derivatives (polymorphs, metabolites, salts and combinations) need not necessarily be the same "substance" and therefore the deeming fiction created by the Explanation is bereft of any guidelines and is bad in law. The court however appeared to agree with a Supreme Court judgment

The Madras High Court correctly notes that:

> *The argument that the amended section must be held to be bad in Law since for want of guidelines it gives scope to the Statutory Authority to exercise its power arbitrarily, has to be necessarily rejected since, we find that there are in-built materials in the amended section and the Explanation itself, which would control / guide the discretion to be exercised by the Statutory Authority. In other words, the Statutory Authority would be definitely guided by the materials to be placed before it for arriving at a decision.*[41]

Second, the Supreme Court has ruled in several cases that while Parliament may delegate some functions to administrative bodies, it ought not to delegate an "essential legislative function."[42] In other words, it is permissible for the legislature to lay down broad policy and delegate powers of rule making to the statutory authority to implement the policy. Delegated legislation is particularly common in areas of specialised knowledge, where the legislature lacks the knowledge and expertise to frame detailed rules.[43]

Drawing on the above proposition, the Madras High Court correctly hinted that section 3(d) is an example of delegation of a non-essential legislative function. And that merely because it is "skeletal" or that it does not define terms such as enhancement of known efficacy" does not mean that "uncanalised discretion" has been vested on the patent office.[44]

Though it cannot be faulted for its conclusions, some of the court's propositions reveal a lack of appreciation for the technology in question, the nature of pharmaceutical innovation and the contours of section 3(d). These flaws are likely to have stemmed from the slipshod manner in which section 3(d) has been drafted. We discuss some of them below.

(*M/s.J.K.Cotton Spinning and Weaving Mills Ltd. v Union of India*, AIR 1988 SC 191) which held that "*the Legislature is quite competent to enact a deeming provision for the purpose of assuming the existence of a fact which does not really exist." Novartis AG & Anr. v Union of India & Othrs*., *see* note 4, at para 13.

[41] *Ibid* at para 16.

[42] See *In Re Delhi Laws* case AIR 1951 SC 332 at para 252, where the court stresses that "*that in the absence of express powers of delegation allowed by the Constitution, the Parliament has no power to delegate its essential legislative functions to others, whether State legislatures or executive authorities, except, of course, functions which really in their true nature are ministerial.*"

[43] AIR 1961 SC 1602.

[44] The court relied on the Supreme Court Decision in *Jyoti Pershad v Union Territory of Delhi*. It bears noting in this regard that Indian Courts have demonstrated a great reluctance to strike down legislations solely on the ground of 'excessive delegation'. A commentary on constitutional law has pegged the ratio of success at 4:41. See A P Datar, *Datar on Constitution of India* 883 (2001).

5.1 What is "Efficacy"?: A Madras High Court Perspective

The court's pronouncement, that the term "enhancement of known efficacy" is not vague, rested to some extent on the premise that the term "efficacy" meant therapeutic efficacy. The court relied on a medical dictionary and held that:[45]

> *Dorland's Medical Dictionary defines the expression "efficacy" in the field of Pharmacology as "the ability of a drug to produce the desired therapeutic effect"… [The] dictionary meaning of "Therapeutic" is healing of disease – having a good effect on the body.*

The court stressed that "*efficacy is independent of potency of the drug*," and went on to hold that:

> *the position therefore is, if the discovery of a new form of a known substance must be treated as an invention, then the Patent applicant should show that the substance so discovered has a better* ***therapeutic*** *effect.*[46]

And later:

> *Going by the meaning for the word "efficacy" and "therapeutic" extracted above, what the patent applicant is expected to show is, how effective the new discovery made would be in healing a disease / having a good effect on the body?*[47]

Under such a definition, the kinds of derivatives that qualify for patent protection are likely to be limited. For instance, it is not clear if increased "bio-availability" (which is what Novartis claims in its application for Glivec) may count as "therapeutic" efficacy.[48]

Consider a hypothetical, where an earlier known substance (X) is not bio-available at all and therefore cannot be administered to a patient. It is reasonable to assume that a later invention (Y, a new form of X) which is more bio-available than X and therefore "druggable" should qualify as "therapeutically" more efficacious than X. However, if we now amend the hypothetical slightly, the answer appears less clear. Assume that X is druggable in its own right: however it is less bio-available than Y. In other words, Y is more advantageous than X, since a patient could consume lower quantities of Y to achieve the same impact as X. Is Y "therapeutically" more effective than X? Unless one can effectively demonstrate that both X and Y have side effects (toxicity) and that lesser portions of Y would mean less toxicity, it might be difficult to qualify Y (the new form

---

[45] *Novartis AG v Union of India & Othrs, Mad HC*, *see* note 4, at para 13.

[46] *Ibid (emphases added).*

[47] *Ibid.*

[48] Bioavailability has been defined as: "*the proportion of a drug which reaches its site of pharmacological activity when introduced into the body; more loosely, that proportion of any substance so introduced which enters the circulation.*" See *Oxford English Dictionary Online*, Oxford University Press, 2nd edn, 1989: http://dictionary.oed.com. (last visited on Jul. 16 2008).

under section 3(d)) as "therapeutically" more effective. Of course, this begs the question of whether or not lower levels of toxicity translate to increased "therapeutic" efficacy.

Further, derivatives of existing substances that provide for increased heat stability may not qualify as patentable, since they supposedly lack "therapeutic efficacy." Most importantly perhaps, new drug delivery mechanisms, a category of incremental inventions that Indian companies profess particular proficiency in, will not qualify under section 3(d). We discuss this point in greater detail in the last section of this paper.

Novartis could challenge the court's assumption that section 3(d) is limited to drugs and therefore "efficacy" ought to be construed as "therapeutic efficacy." A plain reading of section 3(d) would make clear that the section also applies to other "chemicals" such as agro-chemicals. A pesticide or fertilizer cannot be tested for patentability on the basis of whether it enhances a "therapeutic" effect on the human body! The court overlooks this aspect of section 3(d) and assumes that the Explanation is limited to the field of pharmacology.[49]

In the absence of a specific meaning for the term "efficacy" to be found in either section 3(d) or the accompanying rules/guidelines, Novartis could argue that "efficacy" ought to be interpreted in accordance with its plain English meaning. The Oxford English Dictionary (OED) defines efficacy as the "*power or capacity to produce effects.*"[50] Under such a definition, any advantageous properties of the new form such as an increase in bio-availability would qualify as an increase in efficacy, without the patent applicant having to demonstrate that this increase in bio-availability necessarily results in an increase in "therapeutic" efficacy. However, as to whether Novartis' claim of a 30% increase in bio-availability is "significant" enough under section 3(d) is another issue altogether.

Notwithstanding the plain/literal meaning of efficacy, from a policy perspective, how ought "efficacy" to be defined? Should one restrict its definition to therapeutic efficacy, in the way that the Madras High Court did? Or should it be more widely defined to include heat stable drugs and various other incremental inventions such as new drug delivery systems, a field of technology in which Indian companies are proficient? We discuss this issue in some detail in the last section, titled "Defining Efficacy." Till such time as such policy analysis is undertaken and amendments effectuated to reflect this policy preference, a pragmatic option would be to define "efficacy" in accordance with it plain literal meaning.

It is interesting to note that a large part of section 3(d) is copied from a drug regulatory directive. Article 10(2)(b) of Directive 2004/27/EC[51] defines a "generic medicinal product" as:

---

[49] The court notes that "*…we have no doubt at all that the Explanation would operate only when discovery is made in the pharmacology field.*" *Novartis AG v Union of India & Othrs, Mad HC, see* note 4, at para 13.

[50] Oxford English Dictionary, *see* note 48. The Dictionary also defines it as "*A process or mode of effecting a result.*"

[51] '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.

> *a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.* ***The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy****. In such cases, additional information providing proof of the safety and/or efficacy of the various salts, esters or derivatives of an authorised active substance must be supplied by the applicant. (Emphasis by author).*

Given that section 3(d) was imported from a drug regulatory directive, should one define it in accordance with drug regulatory law? Or ought one to be wary of importing a regulatory concept into patent law?

Unfortunately, neither the US FDA nor the EU regulatory authorities have defined "efficacy" in any concrete or meaningful way. Illustratively, the FDA defines it as "*the findings in an adequate and well-controlled clinical trial or the intent of conducting such a trial and the term effectiveness refers to the regulatory determination that is made on the basis of clinical efficacy and other data.*"[52]

Needless to state, this definition, which speaks of an "intent of conducting a trial," is not particularly helpful in the context of section 3(d). The same is the case with EC drug regulatory directives, which appear to treat efficacy as a variable concept, depending on the disease under consideration.[53]

With both the FDA and the EC avoiding the arduous task of defining "efficacy," it is intriguing to note that an Indian court which is faced with a unique term for the first time assumes that this has to necessarily be defined in accordance with a medical dictionary to mean "therapeutic efficacy."

Of course, this definition by the court begs the question: was the definition necessary for the court's conclusion that section 3(d) was constitutional?

One might argue that the court's pronouncement on efficacy was not really critical to its determination that section 3(d), and in particular, the terms "enhancement in known efficacy" and "differ significantly in properties with regard to efficacy," were not "vague" and "arbitrary." In other words, the constitutionality issue did not revolve around the word "efficacy" per se, i.e. irrespective of how "efficacy" was defined (narrowly or widely), the court's conclusion that section 3(d) is constitutionally valid, and the reasons underlying it, as listed below, hold good.

---

[52] *See Guidance for Industry: Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products*: http://www.fda.gov/cder/guidance/1397fnl.pdf. Most FDA guidelines use the term "effectiveness" rather than "efficacy."

[53] The EMEA has published various guidance notes on how to demonstrate clinical safety and efficacy for various types of medicinal products. *See* http://www.emea.europa.eu/htms/human/humanguidelines/efficacy.htm. A draft EU guidance note attempts to spell out what a "significant clinical benefit" is, but here again there is no definition of "efficacy." *See* http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2005/12-05/guideline_on_14_11__for_public_consultation.pdf.

i) That the mere absence of guidelines does not render the terms "*enhancement of efficacy*" and "*differ significantly in properties with regard to efficacy*" vague and arbitrary.
ii) That any determination of the above terms is likely to be based upon material submitted by the patent applicant to the patent office.
i) That a wrong determination in regard to the above is appealable.
ii) That what amounts to a "significant" enhancement of efficacy is not amenable to a uniform formula, but is to be based on the facts of each specific case.

Based on the above, one could argue that the court's determination of the meaning of "efficacy" does not constitute the *ratio decidendi*[54] of the case, but qualifies only as *obiter dicta*.[55] Therefore the findings do not bind the IPAB, which is currently deciding the merits of the dispute, i.e. whether the beta crystalline form is significantly more "efficacious" and therefore patentable.

On the other hand, one may argue that the court's definition of "efficacy" is necessary for its conclusion that the term "enhancement of efficacy" did not suffer from arbitrariness and vagueness, so as to render section 3(d) unconstitutional. This argument gains credence from the fact that Novartis alleged that the term "efficacy" itself was vague and arbitrary in its pleadings.[56] However, one is not certain if during the course of oral arguments, Novartis dropped its challenge to the term "efficacy" and advanced the Article 14 challenge solely in terms of "enhancement of known efficacy" and "significant differences in property with regard to efficacy." From a portion of the courts judgment citing the argument of Novartis' counsel, it appears that this is the case. The court stated that the counsel argued as below:

> *Though the **expression "efficacy" has a definite meaning**, yet, no definite meaning could be attributed to the expression "enhancement of the known efficacy" and "differ significantly in properties with regard to efficacy"*[57] *(emphasis by authors).*

Given the uncertainty in the pleadings and the court's judgment above, how does one go about determining whether or not the court's findings on "efficacy" amounted to the *ratio decidendi* and therefore binds the IPAB? A prominent jurist notes in this connection that, "*wherever judgments are considered to be binding on courts, it is not*

---

[54] *Ratio decidendi* is defined as "*The rule of law on which a later court thinks that a previous court founded its decision; a general rule without which a case must have been decided otherwise*." *See Black's Law Dictionary* (8th ed. 2004).

[55] Obiter dictum is defined as "*a judicial comment made during the course of delivering a judicial opinion, but one that is unnecessary to the decision in the case and therefore not precedential*. *Ibid*.

[56] Interestingly, in written pleadings filed before the court, Novartis does not mention Article 14 of the Constitution even once. Rather most of its attack was on the TRIPS compatibility of section 3(d). It was only during the course of oral arguments that Novartis fleshed out its Article 14 challenge. However, in one paragraph of its pleadings, it appears to argue that section 3(d) violates Article 14. It states that "*…the term "efficacy" has not been defined in the Act which makes the provision vague and arbitrary. Moreover, the requirement of "efficacy" is unique to India; it is not to be found in any other patent statute in the world.*" See *Novartis AG v Union of India*, WP *see* note 22, at para D (VI) of "grounds." *See* also *Novartis Update*, 29th Jan 2007: http://www.lawyerscollective.org/content/novartis-update-%3A-29th-jan-2007.

[57] *Novartis AG & Anr. v Union of India & Othrs*., *see* note 4 at para 11.

merely the ratio decidendi of the judgment, but the judgment itself which is binding."[58] He cites Lord Dunedon with approval, who held:

> *…when any tribunal is bound by the judgment of another court, either superior or coordinate, it is of course, bound by the judgment itself. And if from those opinions delivered it is clear – as is the case in most instances –what the ratio decidendi was which led to the judgment, that that ratio decidendi is also binding. But if it not clear, then I do not think it is part of the tribunals duty to spell out with great difficulty a ratio decidendi in order to be bound by it.*[59]

Relying on the above proposition, this paper argues that owing to the apparent uncertainty in determining whether or not the definition for "efficacy" amounts to the *ratio decidendi*, the IPAB should consider itself bound by it, without having to split hairs over this issue. Which begs the next question: is the IPAB bound by a ruling of the High Court?[60]

A reading of Article 227 of the Constitution of India suggests that this is the case. Article 227(1) states that "*Every High Court shall have superintendence over all courts and tribunals throughout the territories in relation to which it exercises jurisdiction.*" The logical inference from this article is that all the lower courts and tribunals are obligated to follow the law set down by the High Court. This proposition has been endorsed by a Supreme Court judgment, *East India Commercial Co* v *Collector of Customs*, which states:[61]

> *An administrative tribunal cannot ignore the law declared by the highest court in the State. Taking into consideration the provisions of Arts. 215, 226 and 227 of the Constitution of India, it would be anomalous to suggest that a Tribunal over which the High Court has superintendence can ignore the law declared by that Court and start proceedings in direct violation of it. If a Tribunal can do so, all the subordinate Courts can equally do so, for there is no specific provision, like in the case of Supreme Court (Art. 141), making the law declared by the High Court binding on subordinate Courts.*
>
> *It is implicit in the power of superintendence conferred on a superior Tribunal that all the Tribunals subject to its supervision should conform to the law laid down by it.*

The next question is whether or not the patent office is bound by the definition of efficacy, as laid down by the Madras High Court? Here again, the answer is in the affirmative.

---

[58] H M Seervai, *Constitutional Law of India: Critical Commentary*, Vol. 1 (4th Ed. 1999), at 2242.

[59] *Great Western Rly co v Owners of ss Mostyn* (1928) AC 57, 73; Cf Seervai, *Id.*.

[60] S Basheer, "Why Novartis should challenge the Madras High Court Patent Decision", *BusinessLawyer.in*, October 22, 2007: http://businesslawyer.in/3_3.php (last visited Jan. 3, 2008).

[61] AIR 1962 SC 1895 (paras 29, 14).

First, it is important to appreciate that while certain acts of the patent office qualify as "purely administrative," others could be said to be of a "quasi judicial" nature.[62] Whilst determining whether an application meets the criteria of patentability, the patent office could be said to be performing a quasi-judicial role.[63] This conclusion is buttressed by the fact that the Patents Act grants certain "court like" powers to the Controller while she performs these specific functions. Thus for example, the Controller may receive evidence on affidavits, summon witnesses, require discovery of documents, review her decision etc.[64] It was such an analysis that formed the basis for the ruling in *Re Martin & Bottling Developments Limited*, where it was held that "*[t]he Controller is, therefore, a tribunal, performing quasi-judicial functions…*"[65]

Since the patent controller is a "tribunal" (at least when deciding on whether or not something is patentable), it will be bound by the supervisory jurisdiction of the High Court under Article 227. And in much the same way as the IPAB, it is bound by decisions of the High Court. This however begs another tricky question: what if two different High Courts render different interpretations of the term "efficacy"? Barring a final resolution of the issue by the Supreme Court, a patent office may be free to follow either of the two High Court decisions.

Interestingly, a recent rejection of a patent application by the Delhi patent office was based upon the fact that the new anti HIV composition claimed did not demonstrate significantly enhanced "therapeutic efficacy" over and above a previously known substance.[66] Further, an update of the patent office manual quotes the Madras High Court definition of "efficacy," indicating thereby that the patent office will continue to rely on this definition.[67]

5.2 Self-Certifying "Efficacy"?

In the course of determining the import of section 3(d), the court lays down other questionable propositions. It denies any scope for vagueness and uncertainty in the term "enhancement of known efficacy" by claiming that Novartis, being a pharmaceutical

---

[62] *See* S Basheer, "Policy Style Reasoning at the Indian Patent Office" (2005) (Issue No 3) *Intellectual Property Quarterly*, 319.

[63] The Madras High court notes that: "*The Statutory Authority in this case is the Patent controller. There is no doubt that he is exercising a quasi-judicial function namely, considers the patent claim application in the context of the objections received; hears parties on both sides and then passes an order, either granting the patent or rejecting the patent application, by giving reasons.*" *Novartis AG & Anr. v Union of India & Othrs*, *see* note 4 at para 10.

[64] Section 77 of the Patents Act titled "Controller to have certain powers of a civil court."

[65] Decisions on Patents and Designs (The Patent Office Technical Society Calcutta 1982) (1) 356, 364.

[66] *Boehringer Ingelheim Pharmaceuticals v Indian Network for People Living with HIV/AIDS & Positive Women's Network*, Indian Patent Office, Application no: 2845/DEL/1998 (19th June, 2008): http://www.lawyerscollective.org/content/patent-nevirapine-rejected (last visited Jul 16, 2008). For more detailed analysis of this decision, see S Basheer, *AIDS Patent Rejection: Differential Patentability Standard for Essential Drugs?*, http://spicyipindia.blogspot.com/2008/06/aids-patent-rejection-differential.html (last visited Jul 16, 2008).

[67] *Draft Manual*, *see* note 35 at para 4.5.

giant, knows what this means.[68] This proposition strikes us as puzzling – is the court suggesting that Novartis self certify the increase in efficacy demonstrated by its drug? In which case, neither the patent office nor the courts need waste their time over this issue. Important flashback – Novartis assumed that its demonstration of a 30% in bio-availability would be sufficient to qualify its beta crystalline form as more "efficacious"; unfortunately the patent office did not agree.

Second, the court's proposition above rests on the assumption that the term "efficacy" means "therapeutic efficacy," an assumption that is questionable in the light of a plain, literal reading of the section, as we have demonstrated above.

Third, the court's assumption that a patent applicant such as Novartis is well aware of the precise meaning and ambit of section 3(d) ignores the obvious fact that section 3(d) is unique to India. No other patent regime in the world uses the specific term "efficacy" to draw the line between pharmaceutical inventions that are patentable and those that are not. Given the uniqueness of section 3(d) and the fact that it essentially incorporates a drug regulatory norm into patent law, the assumption that section 3(d) and its various parameters are crystal clear to Novartis is misplaced.

In its judgment, the court goes on to specifically note that:

> *…the patent applicant is definitely aware as to what is the "therapeutic effect" of the drug for which he had already got a patent and what is the difference between the therapeutic effect of the patented drug and the drug in respect of which patent is asked for. Therefore it is a simple exercise of, though preceded by research, – we state – for any Patent applicant to place on record what is the therapeutic effect / efficacy of a known substance and what is the enhancement in that known efficacy.*[69]

Here again, the judge makes incorrect assumptions, i.e. that a patent applicant being judged under section 3(d) will always have an earlier patent and a drug corresponding to such earlier patent. This is clearly not true in all cases – in fact, it flies in the face of the facts in the Novartis case itself, facts that were before the judge. Novartis had an earlier patent covering the imatinib free base;[70] however, as per the contention of Novartis, "imatinib," by itself, was not druggable.[71] Therefore, there was no earlier "drug" against which to compare the efficacy of Glivec. It is unfortunate that the judge overlooked this vital piece of information.

---

[68] "*….the writ petitioner is not a novice to the pharmacology field but it, being pharmaceutical giant in the whole of the world, cannot plead that they do not know what is meant by enhancement of a known efficacy…*" *Novartis AG v Union of India & Others*, *see* note 4 at para 4.

[69] *Novartis AG & Anr. v Union of India & Others*, *see* note 4 at para 13.

[70] U.S. Patent No. 5,521,184 (issued May 28, 1996), *see* note 10. See also corresponding European Patent No. 0564409. However, owing to the absence of pharmaceutical product patents in India in 1993, Novartis did not apply for a patent covering the free base in India.

[71] A Novartis press release states that the molecule in the '184 patent could not be administered directly to patients. Novartis, "Glivec case: FACT V FICTION": http://www.novartis.com/downloads/about-novartis/facts-vs-fiction-india-glivec-patent-case.pdf (last visited Oct. 29 2007).

5.3 An Expansive "Explanation"

While reflecting on the explanation to section 3(d) and the phrase "significant differences in properties with regard to efficacy," the Madras High Court makes inconsistent observations. First, it relies on a Supreme Court decision to hold that an Explanation can only "explain" the main provision and cannot add to or subtract from it.[72]

And yet, a few paragraphs later**,** the court notes:

> *In Hiralal Ratanlan v State of U.P it was ruled that if on a true reading of an Explanation it appears that it has widened the scope of the main section, effect be given to legislative intent notwithstanding the fact that the legislature named that provision as an Explanation. In all these matters courts have to find out the true intention of the legislature.*

It is not clear how to reconcile the above contradictory propositions of the court. Can an explanation expand the scope of main provision or not? If it cannot, then what are the implications of a section that in fact expands the scope?

Most importantly, the court does not dwell on whether or not the Explanation to section 3(d) does, in fact, expand the scope of the main section. From a plain reading, it appears to do so.

While the main section speaks of an "enhancement of known efficacy," the Explanation uses a broader term "significant difference in properties with regard to efficacy." This difference has implications when assessing the patentability of the new use of a new form of a known substance.

We explain with the help of the following hypothetical.

Assume that X is a "known" substance that is used to treat cervical cancer. Y is a new form of X, and equally effective in the treatment of cervical cancer. However, it is found that Y is also very effective in treating pancreatic cancer. In other words, Y demonstrates a "new use" when compared with X. However, under the main part of section 3(d), Y does not qualify for a patent, i.e. Y works only as well as X in treating cervical cancer and therefore does not demonstrate an enhancement in "known" efficacy.

If the intention behind section 3(d) is to heighten the obviousness standard and weed out frivolous and fairly obvious patents, this seems a rather illogical result – as a "new use for a new form" (Y's use in treating pancreatic cancer) is certainly more inventive than a mere increase in the already "known" efficacy.

Under the Explanation to section 3(d) however, Y appears to qualify for a patent. The Explanation does not use the term "known efficacy." Rather it states that if the new form "*differs significantly in properties with regard to efficacy*," then it will be considered as a new substance altogether. Y (a new form with a new use) will clearly qualify as "differing significantly in properties with regard to efficacy," since the

---

[72] The court noted that "*An Explanation, as was found in Bihta Marketing Union V Bank of Bihar, may only explain and may not expand or add to the scope of the original section*." See *Aphali Pharma. Ltd. v State of Maharashtra* 1989 (4) SCC 378.

alleged efficacy itself (treating pancreatic cancer) is completely different from the known one (treating cervical cancer).

In other words, the Explanation expands the scope of the term "enhancement of known efficacy" as used in the main section. This inconsistency can be resolved through a simple amendment, as proposed later on in this paper.

6. Ironing Out the Creases in Section 3(d)

The Madras High Court's inability to appreciate the import of section 3(d) and how pharmaceutical applications are to be judged under it may have stemmed, in part, from the fact that the drafting of section 3(d) leaves much to be desired. This is not very surprising, given that section 3(d) was introduced in haste. We reproduce below extracts of a speech by Uday Singh, one of the Members of the Lok Sabha, the lower house of the Indian Parliament, constituted by directly elected representatives of the people:

> *….I do not know why this rush. I am not doubting the intention of the Government. I am not saying that the Government is trying to do something which it should not be doing. The entire House is in agreement that India has to live globally and must honour its global commitment. But why this hurry? Why can it not wait for a couple of weeks and be done?*[73]

Illustratively, we list below some of the key problems with the structure and wording of section 3(d). Our intention is to make out a case for amending/clarifying section 3(d) to cure these infirmities. These amendments/clarifications could be executed through statutory amendments, government rules or patent office guidelines. The merits/demerits of each of these approaches will be discussed at the end of this section.

6.1 Patent Eligibility Standard v Patentability Standard

Section 3(d) may be construed as a refinement of patentability criteria to cater for "ever-greening" – a specific problem inherent in pharmaceutical innovations. More specifically, the "enhanced efficacy" criterion can be seen as refinement of "non-obviousness" principles, i.e. most forms of existing pharmaceutical substances are deemed obvious, unless they demonstrate increased "efficacy."[74] At some level, section 3(d) could also be said to embody a utility test, i.e. unless the new form has significantly enhanced utility over and above what existed before in the art, it is not patentable.

Under the present scheme of the Indian Patents Act, section 3(d) is part of a section that begins with the phrase "*the following are not inventions within the meaning of this Act…*" In other words, any pharmaceutical invention that does not comply with section 3(d) represents excluded patentable subject matter, i.e. section 3(d) is structured as a patent eligibility test and not as a patentability test. At a conceptual level and drawing from the patenting practices of most member states, one can draw a distinction between "patent eligibility" and "patentability."

---

[73] Lok Sabha Debate, Mar. 22, 2005: http://164.100.24.230/Webdata/datalshom001/synopsis/220305.html (last visited Nov 30, 2007). *See* also, S Basheer, "India's Tryst with TRIPS: The Patents (Amendment) Act, 2005" (2005) 1 *Indian Journal of Law and Technology*, 30, at 43.

[74] *See* S Basheer, IPI, *see* note 28.

"Patent eligibility" broadly refers to the requirement that a subject matter for which a patent is sought be inherently suitable for patent protection, in the sense of falling within the scope of subject matter that patent law *prima facie* exists to protect. In most jurisdictions, patent eligibility manifests itself in the term "invention," i.e. a poem, though new, non-obvious and useful is still not patentable, as it is not an "invention."[75] The term "patentability," on the other hand, refers to those set of principles that inform the requirements that must be satisfied for a patent eligible subject matter (i.e. an invention) to be granted a valid patent. Principally they are the requirements of novelty, inventive step (non-obviousness), utility (industrial applicability) and sufficient description.[76]

The term "patent eligibility" or "inherent patentability" denotes limitations in terms of the kind of "subject matter" that would qualify for patent protection – this question is different from and often precedes the question of whether the said subject matter meets the "patentability" criteria.

By mandating that a new form without increased efficacy would not amount to an "invention," section 3(d), in effect, constitutes a patent eligibility standard. Although this is more a matter of form than substance and is not likely to make an impact on the outcome of the case, it will influence the stage at which the examination is conducted. Being a patent eligibility standard, an examination is conducted right at the start. Compare this with a non-obviousness or inventive step examination which is done at a later stage.[77] Since an examination under section 3(d) is likely to call into question some of the very same issues used in a non-obviousness determination, it may help to explicitly state section 3(d) as a "patentability" criterion rather than a patent eligibility criterion.

6.2 What is a "Derivative"?

Section 3(d) states that new forms of known substances such as polymorphs, salts, ethers, esters and all "*other derivatives*" amount to the same "substance," unless they differ significantly in properties with regard to efficacy. The meaning of the term "derivative" as used in the section is not clear and is currently the subject of a big-ticket litigation between Roche, which owns a patent covering Tarceva (Erlotinib), an anticancer compound and Cipla, which manufactures and sells a generic version, Erlocip.

In interim proceedings which concluded some months back, the court declined to grant a temporary injunction to Roche on the grounds of "public interest". On account of the substantial price differential between the drugs sold by the parties, the court found that "public interest" was likely to be impacted, if consumers were prevented from having access to the cheaper version of the drug sold by Cipla.

---

[75] *See* s. 3(l) of Indian Patents Act which excludes "a literary, dramatic, musical or artistic work…" *See* also Article 52 (2) (b) of the European Patent Convention (EPC) which excludes all "aesthetic creations."

[76] See J Pila, "Bound Futures: Patent Law and Modern Biotechnology" (2003) 9 *Boston University Journal of Science & Technology Law* 326.

[77] Section 2(1)(ja) of the Indian Patents Act defines "inventive step" as "*a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to the person skilled in the art.*" For a discussion of this provision, see S Basheer, "India's Tryst with TRIPS: The Patents (Amendment) Act 2005" (2005) 1 *Indian Journal of Law & Technology* 22.

The court also appears to have been swayed by the forceful arguments of Cipla that the patent was invalid on several grounds, including section 3(d). In particular, Cipla claimed that that Erlotinib was not significantly more efficacious than Gefinitib, an earlier known structurally similar substance.[78] Owing to the "temporary" nature of the proceedings, the judge did not investigate this issue in detail and determine whether or not Erlotinib, which was merely structurally similar to Gefatinib, could also qualify as a "derivative" under section 3(d). If it is a "derivative," then under the explanation to section 3(d), unless it demonstrates "a significant difference in property with regard to efficacy," it will be construed as the "same substance" as Gefatinib. It is hoped that a final decision after trial will resolve this issue and determine the parameters of the term "derivative."

Structurally, both Erlotinib and Gefatinib have a common 4-quinazolinamine nucleus, but the substitution patterns are quite different. In other words, although they are derivates of 4-quinazolinamine, qualifying them as derivatives of each other may be incorrect.

However, it may be conceptually easier to qualify Erlotinib and Gefatinib as "structurally similar", subject of course to a determination of how "similar" the structures were. A far-fetched similarity ought not to suffice, as then almost every pharmaceutical substance might be said to be "structurally similar," on the basis that it is in some way related to "carbon."

From a reading of section 3(d) and an appreciation of its intention to eliminate ever-greening, one could argue that the drafters were getting at "structurally similar" forms and not derivatives, strictly defined. The underlying assumption appears to be that similar structures (new forms) were likely to function in substantially similar ways – and if this were not the case, then it was up to the patent applicant to demonstrate this. This interpretation also sits well with intellectual property standards in the more mature IP jurisdictions such as the US and the EU, where there is an assumption of *prima facie* obviousness if the patent applicant claims a compound that is structurally similar to a previously known substance.[79]

At this stage however, one cannot read the term "derivative" as amounting to "structurally similar," unless the section is explicitly amended by Parliament.

6.3 What is a "Known Substance"?

Under section 3(d), it is not clear what would qualify as the "known substance" against which the "efficacy" comparison ought to be made.[80] In the Novartis case, would the "known" substance be the imatinib free base (in relation to which it is far easier to show increased efficacy) or the later salt, imatinib mesylate? Or the alpha crystalline form of such later salt? Of course, we are not clear at this point as to whether "imatinib mesylate" was anticipated from the '184 patent covering the free base or not.[81]

---

[78] *F. Hoffman-La Roche Ltd. & Anr. v Cipla Ltd*., CS(OS) 89/2008, Delhi High Court. For an extensive discussion of this case, see S Basheer and P Reddy, "Roche vs Cipla: The "Price" of a Patent Injunction in India" (draft on file with the authors).

[79] *See* note 105.

[80] *Draft Manual*, *see* note 35 at para 4.5.

[81] US Patent Number 5521184, *see* 10. The patent office decision did not delve into this issue explicitly and the matter is still pending at the IPAB. It is interesting to note that the international search report for a

Assuming that it was not anticipated from the '184 patent, but only obvious from it, would it be fair to qualify it as a "known substance"? A reasonable reading of section 3(d) would suggest not. And this ought to be made clear in the section itself, i.e. that "known" substance under section 3(d) would have the same meaning as something which is not "new" or "novel."[82]

A recent update of the Patent Office Manual suggests that the comparison would have to be with respect to imatinib mesylate (irrespective of whether or not imatinib mesylate was factually known or anticipated from the '184 patent) and not the imatinib free base.[83] This inclusion seems to be an attempt to prejudge the Novartis case, currently being argued at the IPAB. More importantly, this is a point that ought to be decided on the facts of each case and not included as a deeming provision in a Patent Office Manual. Having said this, it bears noting that the Manual does not carry the force of law;[84] therefore this proposition by the Patent Office is not binding on applicants.

6.4 "New Use" Issues

As was already discussed in an earlier section, there is some inconsistency between the main section and the explanation when it comes to patentability of a new form with a new use. Under the main section, a new use of a new form would not be patentable, since it speaks about "enhancement of known use." However, it appears to qualify for a patent under the explanation, which speaks about a "significant difference in efficacy with regard to property." If the intention behind this provision is to heighten the obviousness standard and weed out frivolous and fairly obvious patents, this seems a rather illogical result – as a new use for a new form is certainly more inventive than a mere showing of an increase in known efficacy. Therefore, section 3(d) needs to be amended to provide expressly for the patentability of new uses of new forms of existing pharmaceutical substances.

PCT application claiming the beta crystalline form (filed on 16th July, 1998 and claiming a priority date of 18th July 1997) suggested that imatinib mesylate is anticipated from the '184 patent (filed in 1993 in the US):

"Methanesulfonic acid addition salts of the present compound....are disclosed in D1(D1: US Patent Application)....However, no mention is made of a particular crystalline form of the monomethanesulfonic acid addition salt of said compound. The novelty of the present claim can therefore be acknowledged."

See International Preliminary Examination Report, 8, PCT/EP98/04427. See also PCT/EP98/04427 at <http://www.wipo.int/ipdl/IPDL-IMAGES/PATENTSCOPE/45/ad/71/00ad71.pdf>.

[82] The Indian patent regime appears to endorse a "relative novelty" ground i.e. section 25 (1) (d) of the Patents Act stipulates that a patent application can be opposed on the ground that the invention was "publicly known or publicly used in India before the priority date of that claim". However, in so far as the opposing party relies on "documentary" prior art (a previously published patent application or any other document), the test is one of "absolute novelty" i.e. any document published anywhere in the world can be deployed to anticipate the patent. See section 25 (1) (b) of the Patents Act. For a detailed discussion in this regard, see S Basheer, *see* note 77.

[83] "*The examiner makes comparison with regard to properties or enhancement of efficacy between the known substance and the new form of known substance. In case the new form is further converted into another new form, the comparison is made between the already existing form and another new form but not between the base compound and another new form.*" *See Draft Manual*, note 35 at para 4.5.3.

[84] The patent controller has expressly stated in the preface of the new draft manual of the patent office that the manual shall not have the force of law. *See Draft Manual*. *Ibid*, at page 3.

6.5 Discovery v Invention

Section 3(d) only prohibits the "mere discovery of new forms." One could argue, as Novartis does in its writ petition before the Madras High Court, that "discovering" a new form that already exists is very different from creating a new form.[85] Therefore, new forms such as the beta crystalline version of imatinib mesylate (the form claimed by Novartis in the patent dispute), does not fall within the purview of section 3(d): such new forms are "invented" or "created" and not "discovered."[86] Since this appears to be a very technical reading of the section that does not comport fully with Parliamentary intent to prevent "ever-greening", a judge may not be likely to endorse such a proposition. However, in view of the fact that a judge could interpret the section literally, section 3(d) ought to be amended to remove references to "discovery."

6.6 Standard of Proof

The Madras High Court judge assumes that it is easy to procure "efficacy" related information. As one may appreciate, this depends on the kind of "proof" that a patent applicant is required to offer in this regard. Thus, if efficacy were interpreted in a drug regulatory sense, then the patent applicant would need to conduct trials and generate information of the kind that is normally submitted to procure regulatory approval. Needless to state, this would make it a very onerous requirement. Also, if this were the standard, then mandating a comparison with an earlier known substance (that may not be druggable or known to work well) would be unethical and irresponsible.

On the other hand, if pre-clinical trial/lab tests were to suffice as "proof," such a standard would be easier to fulfill. The court did not make any pronouncements of what it thought should be the standard of proof – and one is therefore unsure of the current standard in this regard. Having said this, it bears noting that in a recent case, the patent office appeared to rely, *inter alia*, on an article in a leading academic journal to hold that Roche had established that its drug was more efficacious than earlier known substances.[87]

Given the fact that the section was derived from a drug regulatory directive, there is a slight risk that the patent office or the courts might be inclined to interpret "efficacy" and the standard of proof required in a drug regulatory sense. If it is interpreted this

---

[85] "*It is submitted that while discovery of a new property is understandable, 'discovery' of a new form is not. In fact, discovery of new form is a contradiction in terms. For something to be 'discovered' it must already exist. This is against the very concept of patents which rewards human intervention and creation.*" *See Novartis AG v Union of India*, WP (*see* note 22) at para D (I) of the "grounds" cited before the court.

[86] One might draw a distinction between new forms of existing substances that were merely discovered i.e. merely observed in that form, in its natural state, for the first time in the course of a search and new forms that were "invented" in the lab. And argue that only the former would be subject to the section 3(d) hurdle and would therefore have to demonstrate significantly enhanced efficacy over the previously known substance in order to merit a patent.

[87] *F. Hoffman-La Roche Ltd. & Anr. v Cipla Ltd.* (*see* note 78 at para 71). In connection with the kind of "efficacy" proof mandated by section 3(d), Janice Mueller notes: "Section 3(d) thus raises both qualitative and quantitative questions i.e. what kind of data will be required to establish "efficacy" and how great an improvement over the efficacy of the prior art invention will be required to obtain a patent." See J Mueller, "The Tiger Awakens: The Tumultuous Transformation of India's Patent System and the Rise of Indian Pharmaceutical Innovation" (2007) 68 *University of Pittsburgh Law Review* 491, 553.

way, it will be a very onerous requirement for the patentee to fulfill. Pharmaceutical companies generally file patent applications at the initial stages of discovery and development of a drug; it is only much later in the development process that clinical studies are conducted to gather information pertaining to the therapeutic efficacy of the drug.[88] Requiring "clinical trial" information at the stage of filing a patent application is therefore an onerous requirement.[89]

Further, requiring full-fledged clinical trials to be undertaken to establish efficacy prior to the filing of a patent application may compromise the "novelty" of the invention in question. If the invention in question has been disclosed to the public via clinical trials, one may oppose the application on grounds that it is not novel. One may argue that the experimental use exception (or "secret use" exception) encapsulated in Section 32[90] of the Patent Act takes care of this. However, for this exception to apply, the priority date of the patent application should fall within one year of the "public" disclosure of the clinical trial. Given that clinical trials take longer than one year in many cases, this provision may not help.

For all of the above reasons, it ought to be made clear in section 3(d) that the standard of proof is one that is easier to fulfill, requiring only that amount of data that is relatively more ethical to generate. One could perhaps take a leaf out of the USPTO guidelines on patentability of pharmaceutical substances.[91]

These guidelines, in keeping with case law from the US Court of Appeals for the Federal Circuit (CAFC), state that when a patent application asserts a "therapeutic use" for an invention, he/she does not have to prove that a correlation exists between a particular pharmacological/biological activity and the asserted therapeutic use as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, all that is required is a reasonable correlation between the activity and the asserted use.[92]

Such reasonable evidence of the correlation can be established by relying on statistically relevant data documenting the activity of a compound or composition, arguments or reasoning, documentary evidence (e.g. articles in scientific journals), or any combination thereof. The guidelines note in particular that:

---

[88] For a discussion of the various steps involved in drug discovery, see Richard B Silverman "The Organic Chemistry of Drug Design and Drug Action, 2nd ed, Elsevier Academic Press, 2004. *See* also T P Ross, "Intellectual Property: Patents and Transfer Agreements Preceding Clinical Trials and Commercialization" (2005) 25(8) *Retina, The Journal of Retinal and Vitreous Diseases*, 92.

[89] It would appear that this is likely to delay the date of disclosure of important scientific information to society; however, many scholars are sceptical of this "information disclosure" function of patents. Illustratively, see B Roin, "The Disclosure Function of the Patent System (or Lack Thereof)" (2005) 118 *Harvard Law Review* 2007.

[90] It states that an "*invention claimed in a complete specification shall not be deemed to have been anticipated by reason only that at any time within one year before the priority date of the relevant claim of the specification…the invention was publicly worked in India – for purpose of reasonable trial only and if it was reasonably necessary, having regard to the nature of the invention, that the working for that purpose should be effected in public.*"

[91] *See Special Considerations for Asserted Therapeutic or Pharmacological Utilities*: http://www.uspto.gov/web/offices/pac/mpep/documents/2100_2107_03.htm.

[92] *Nelson v Bowler*, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980).

> *if reasonably correlated to the particular therapeutic or pharmacological utility, data generated using in vitro assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process.*[93]

The guidelines go on to note that the office should not impose on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders, even with respect to situations, where no art-recognised animal models existed for the human disease encompassed by the claims.[94]

6.7 Determining "Significance"

Unlike defining "efficacy" (which could either be restrictively defined as "therapeutic efficacy" or broadened to include any kind of "advantageous property"), it is not possible to lay down a definitive guideline or a bright line rule for determining when such increase in efficacy is sufficient enough to constitute a "significant" enhancement. Pegging "significance" at arbitrary percentages to apply in all circumstances does not make for optimal policy. And this is something that even the Madras High Court points to in its judgment:

> *Therefore it would be unwise to fix any specific formula to be applied, as a matter of static measure, to find out whether the new form of a known substance resulted in the enhancement of the known efficacy or the derivatives differ significantly in properties with regard to efficacy. Having regard to the inventions that are made and are likely to be made in the time to come,* ***it is humanly impossible to prescribe a fixed formula*** *to decide the issue as indicated above and if it is so done without even knowing what would be the new discoveries, then, the hands of the Statutory Authority would be completely tied to a fixed and definite situation, from which it cannot even wriggle out. Discoveries that are likely to be made in the future may not be alike and they may vary from each other in their therapeutic effect and properties.*[95] *(Emphasis by authors).*

Therefore, it is best to determine "significance" on a case by case basis. A recent draft of the Patent manual hints at such an approach, by noting that "*efficacy need not be quantified in terms of numerical value to determine whether the product is efficacious because it is not possible to have a standard numerical value for efficacy for all products including pharmaceutical products*."[96]

---

[93] *See Special Considerations for Asserted Therapeutic or Pharmacological Utilities.*

[94] *See Ex parte Balzarini*, 21 USPQ2d 1892 (Bd. Pat. App. & Inter. 1991).

[95] *Novartis AG v Union of India & Othrs, Mad HC* (*see* note 4 at para 11).

[96] *Draft Manual* (*see* note 35) at para 4.5.5.

We propose the application of a "person having ordinary skill in the art" (PHOSITA)[97] test in this context, i.e. as to whether a new form demonstrates "significantly enhanced efficacy" is a factual determination to be assessed with reference to the views of a person skilled in the art. This proposition ought to be expressly introduced into the text of section 3(d) or provided through government rules/patent office guidelines.

6.8 Towards Bright Line Rules

Section 3(d) strives to represent a sector specific bright line rule that can help filter out non–meritorious pharmaceutical inventions. In a country with a relatively understaffed patent office that is currently confronted with a huge number of pharmaceutical patent applications, the advantage of such a bright line rule cannot be stressed enough. More importantly, clear-cut and objective legal rules will provide more certainty for patent applicants. And such certainty is tremendously important from the point of view of incentivising more innovation and investment in the pharmaceutical sector.

Though noble in intent, the drafting of section 3(d) leaves much to be desired. Riddled with uncertainty, the current version of section 3(d) is a litigators' El Dorado. Based on our discussion above, this is the amendment that we propose to section 3(d).

> *"**3. What are not inventions: The following are not inventions within the meaning of this Act….***
>
> *d) a new form of a known substance, unless it differs significantly in properties with regard to efficacy, when compared with the known 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 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 structurally similar forms of a known substance shall be deemed to constitute "new forms of a known substance."*
>
> *For the purposes of this clause, a "known substance," against which the efficacy of a "new form" ought to be compared, shall be taken to be a substance which is not "new," in that it does not satisfy the "novelty" criterion for patentability.*
>
> *For the purposes of establishing that a "new form" differs significantly in properties with regard to efficacy, an applicant must provide data comparing the efficacy of the new form with that of a "known" substance. Such data need not prove this "difference" in property as a matter of statistical certainty, nor does the applicant have to provide actual evidence of trials in humans. Instead, the applicant has to demonstrate a reasonable correlation between the*

---

[97] R S Eisenberg, "Obvious to whom? Evaluating inventions from the perspective of PHOSITA" (2004) 19 *Berkeley Technology Law Journal* 885.

> *efficacy claimed and the data provided in support of this. Such reasonable evidence of the correlation can be established by relying on, inter alia, statistically relevant data documenting the activity of the new form and/or known substance, documentary evidence (e.g. articles in scientific journals), data generated using in vitro assays, or from testing in an animal model, other preclinical test data or any combination thereof.*
>
> *For the purposes of this clause, a determination as to whether a difference in property with regard to "efficacy" is "significant," shall be assessed with reference to the views of a person skilled in the relevant art."*

The optimal way to effectuate the above change in section 3(d) is through a statutory amendment by the Parliament. However this may take time and given the politics of pharmaceutical patents, any such move is likely to come with its fair share of politicking.

Another option is to effectuate the change through government rules. Section 159 of the Patents Act states that "*the Central Government may, by notification in the Official Gazette, make rules for carrying out the purposes of the Act.*" However, this option comes with certain limitations. First, under principles of delegated legislation, a rule cannot go beyond the ambit of what the statutory provision expressly provides.[98] Therefore, substituting the term "derivative" with the term "structurally similar" may not be permissible via the rule making powers, even if one argues that it conforms to the intention underlying the section, i.e. to prevent ever-greening. It bears noting that to date, rule-making powers under the Indian Patents Act have been exercised in relation to procedural issues, and not to clarify the meanings of substantive terms used in the section.

Second, introducing changes via rules is not necessarily less cumbersome and problematic than express statutory amendments. Section 160 of the Patents Act provides that "*every rule made under this Act, shall be laid, as soon as may be after it is made, before each House of Parliament while it is in session….*"

If a rule has to be taken through Parliament, the concerns with politicization of pharmaceutical patents and resulting parliamentary deadlocks apply here as well.

A third option is to effectuate the above change via patent office guidelines in the patent manual. Here again, the key limitation is that such patent office guidelines do not have the force of law. In other words, these guidelines are explanatory and recommendatory at best. Therefore, only in so far as some of the above changes to section 3(d) are explanatory, patent office guidelines may be drafted and implemented.

Finally, one could also rely on the judiciary to interpret section 3(d) in accordance with the proposed changes. A large part of the proposed changes are clarificatory in nature

---

[98] In *General Officer Commanding-in-Chief and Anr. v Dr. Subhash Chandra Yadav and Anr.,* (1988 SC 876 at para 14), it was held that: "*Before a rule can have the effect of a statutory provision, two conditions must be fulfilled, namely, (1) it must conform to the provisions of the statute under which it is framed; and (2) it must also come within the scope and purview of the rule making power of the authority framing the rule. If either of these two conditions is not fulfilled, the rule so framed would be void.*" *See* also *Kunj Behari La Butail v Himachal Pradesh* (2000) 3 SCC 40.

and seek to remove ambiguities associated with uncertain terms/phrases in section 3(d). To the extent that courts have the power to interpret uncertain terms in a statute, most of the proposed changes could be executed by judicial interpretation. However, the difficulty here is that one is not entirely certain of the direction that courts are likely to take whilst interpreting statutory provisions such as this. Further, different high courts may interpret the section differently, till such time as the Supreme Court steps in.

Notwithstanding difficulties in the mode of implementation, most of the changes recommended above are clarificatory in nature and immediately implementable. However, other definitional issues call for an in-depth empirical investigation and policy analysis. We discuss one such issue below.

7. Defining "Efficacy"

The Madras High Court judgment relied on a medical dictionary definition to hold that the term "efficacy" in section 3(d) meant "therapeutic" efficacy. Under such a definition, the kind of derivatives that qualify for protection are likely to be severely limited. For instance, salt forms that provide more stability and enable the drug to remain on the shelf for longer or be transported to various parts of rural India without refrigeration will not be patentable.[99] As shown above, this narrow definition may not sit well with a plain/literal reading of section 3(d), since the section is not limited to pharmacology.

As with other concepts in patent law, the term "efficacy" is a useful policy lever[100] and India could define it either narrowly or broadly. We discuss the implications of both options below.

7.1 Narrow interpretation

In line with what the Madras High Court suggests, section 3(d) could be restrictively interpreted to mean only "therapeutic efficacy." Therefore, all other kinds of advantages such as increased heat stability and new drug delivery forms do not qualify. Such a "bright line" rule has the advantage of being administratively easy to enforce by a patent office that is understaffed and a relative novice when it comes to examining pharmaceutical product patent applications. However, such a rule will also foreclose the possibility of patents for a large number of incremental inventions that come out of the Indian pharmaceutical majors, as detailed in the section below.

7.2 Wide definition

The term "efficacy" should not be restricted to just therapeutic efficacy, narrowly defined. Rather it should include all kinds of advantageous properties exhibited by the

---

[99] In particular, see the recent pre-grant opposition filed by I-MAK against Abbot's application claiming "Aluvia," a "heat stable" form of an anti-retroviral drug, consisting of Lopinavir and Ritonavir. The advantages of this new combination include increased solubility in water and better bioavailability and stability – translating to a lower pill burden and the ability to store without refrigeration. *See* http://www.i-mak.org/lopinavirritonavir/.

[100] Two prominent intellectual property scholars propose that courts ought to apply patent "policy levers" to tailor patent protection to suit specific industries. See D L Burk & M A Lemley, "Policy Levers in Patent Law" (2003) 89 *Virginia Law Review* 1575, at 1630.

new form including heat stability, enhanced bioavailability, humidity resistance, new drug delivery mechanisms etc. Illustratively, a patented drug delivery system for a vaccine has the capability to withstand heat up to 55 degree centigrade for months; conditions that would destroy the vaccine in any other drug delivery system. According to a paper that details this technology: "*By eliminating the need for refrigeration, the technology could save up to $300 million a year in global vaccine costs, which means another ten million children could be protected. Currently 50 percent of all vaccines may be wasted in part due to temperature damage.*"[101]

Apart from the above, an important reason for expanding the scope of efficacy may be the fact that some of the most well known inventions from Indian pharmaceutical majors have been efficacious in non-therapeutic ways. One of the oft-cited examples is that of Ranbaxy's CIPRO pill, a novel drug delivery mechanism.[102] The invention, sold as Cipro-OD, enables a patient to take the medicine just once a day (OD).[103] A recent paper notes that developing NDDS products is now a thrust area for most of the larger Indian companies.[104]

An expansive definition of efficacy is mirrored, to some extent, in the patent regimes of the US and the EU, where structural similarities between a pharmaceutical substance that is sought to be patented and an earlier known substance trigger off a presumption of *prima facie* obviousness. However, this presumption can be dislodged if the patent applicant demonstrates that the applied for substance exhibits "unexpected or surprising results."[105] Unexpected results are not limited to "therapeutic" advantages alone.[106]

---

[101] U.S. Patent Number 6,623,762 granted in 2004. *See* World Intellectual Property Organization Secretariat, *Follow-on Innovation and Intellectual Property*, 13-14 (20 May 2005) (Submission to WHO's CIPIH): http://www.who.int/entity/intellectualproperty/submissions/Innovation%20&%20Intellectual%20Property%20WIPO.pdf (last visited Jan. 4, 2008).

[102] P Gehl Sampath, *Economic Aspects of Access to Medicines after 2005: Product Patent Protection and Emerging Firm Strategies in the Indian Pharmaceutical Industry* 30, at 43.

[103] Under the Explanation to section 3(d) of India's Patent Act, Ranbaxy's drug will qualify as a "combination." Therefore, unless it demonstrates significantly enhanced "efficacy" over and above Bayer's CIPRO, it is not patentable.

[104] *See* S Chaudhuri, "Is Product Patent Protection Necessary in Developing Countries for Innovation: R&D by Indian Pharmaceutical Companies After TRIPS" (Indian Inst. of Management, Kolkotta, Working Paper No. 614, 2007), at 15.

[105] For a recent application of the US standard, see *Takeda v Alphapharm,* 480 F.3d 1348 (Fed. Cir. 2007), where the court relied on two of its earlier decisions: *In re Dillon*, 919 F.2d 688, 692 (Fed. Cir. 1990), which held that "structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a *prima facie* case of obviousness." And *In re Deuel* (51 F.3d 1552, 1558 (Fed. Cir. 1995), where the court held that "A known compound may suggest its homolog, analog, or isomer because such compounds "often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." Id page 9.

[106] See *Eli Lilly and Company v Premo Pharmaceutical Laboratories*, Inc., 630 F.2d 120 (1980), where the court upheld the patentability of an oral antibiotic that was superior in terms of its mode of administration (it could be taken in tablet form, when compared with its predecessor that had to be taken intravenously). To this extent, the drug did not strictly exhibit increased "therapeutic efficacy", but was a more advantageous dosage form/drug delivery mechanism. However, in *Pfizer v Apotex*, 480 F.3d 1348 (2007), the CAFC (Court of Appeals for the Federal Circuit) strikes a distinction between therapeutic properties and other properties (physical properties such as process-ability) of a pharmaceutical substance and appears to give the latter relatively much less weight while assessing non-obviousness. A scholar

However, it is important to appreciate that there are critical differences between section 3(d) and the corresponding US law on the patentability of chemical/pharmaceutical substances.[107]

As per the current US approach, even if a claimed substance is shown to be structurally similar to a previously known substance, that by itself is not sufficient to make out a "prima facie" case of obviousness. Rather, one has also to show that additionally, there was some motivation "*that would have led one of ordinary skill in the art to select and then modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound*." [108]

Compare this with a section 3 (d) approach, which does not require the demonstration of any kind of motivation or reason that would have led one to identify the lead compound or modify it in the manner suggested. Rather it merely stresses on two fairly "objective" questions:

i) Is the claimed substance a derivate of an existing substance?

ii) If so, does it demonstrate increased efficacy over and above the existing substance?

If the answer to ii) is "yes", then the section 3(d) hurdle is cleared and the patent may be granted, subject to fulfilling other patentability criteria.

However, if the answer is "no", then the patent application is rejected outright.

Although the above considerations that are part of US case law (identification of lead compound and motivation to modify it) do not impact a section 3(d) analysis, it is bound to creep in during an obviousness analysis. In this regard, it is important to bear in mind that even after the section 3(d) hurdle has been crossed, an invention is tested for compliance with other patentability criteria such as novelty, non obviousness or

---

however takes issue with this decision noting that "….the Federal Circuit improperly discounted the *physical*, as opposed to *biological* (i.e., therapeutic), properties of the claimed composition. The *Pfizer* opinion repeatedly emphasized that the besylate part of the claimed compound was merely a drug delivery vehicle that did not improve amlodipine's therapeutic effect. Because the Federal Circuit discounted the physical properties of improved stability and tablet processing, Pfizer was unable to rebut the *prima facie* case of obviousness based on the prior art." See JM Mueller, "Chemicals, Combinations, and 'Common Sense': How the Supreme Court's KSR Decision is Changing Federal Circuit Obviousness Determinations in Pharmaceutical and Biotechnology Cases*"* (2008) 35(4) *Northern Kentucky Law Review*, forthcoming.

[107] Some commentators are of the view that in the aftermath of *KSR International Co. v Teleflex, Inc.* (127 S.Ct. 1727), where the Supreme Court rejected the Federal Circuit's ''rigid'' application of the teaching, suggestion, or motivation to combine (TSM) test, it was likely going to be more difficult to obtain secondary pharmaceutical patents and to defend them against validity challenges. *See* A McTague "Secondary Pharmaceutical Patents Post-KSR: Do They Have A Future?" (2008) 6 *Pharmaceutical Law & Industry Report*, No. 3, 01/18/2008. *See* also JM Mueller, note 106.

[108] Judge Rader of the CAFC (Court of Appeals for the Federal Circuit) in *Eisai Co. v Dr. Reddy's Laboratories, Ltd*., (Fed. Cir. 2008) (page 4) citing *Takeda Chem. Indus. v Alphapharm Pty., Ltd*., 492 F.3d 1350, 1356 (Fed. Cir. 2007). Illustratively, in both *Eisai v Dr Reddy's* and *Takeda v Alphapharm,* the CAFC found against a motivation to either start with the lead compound in question or to modify it in the manner suggested by the patentee. In fact, the prior art "taught" away from using the respective lead compounds in both these cases.

inventive step[109] and utility.

The second difference between the two regimes comes out of a recent decision, *Pfizer v Apotex,* where the court held that:

> *"Even if Pfizer showed that amlodipine besylate exhibits unexpectedly superior results, this secondary consideration does not overcome the strong showing of obviousness in this case… Although secondary considerations must be taken into account, they do not necessarily control the obviousness conclusion."*[110]

In other words, under US law, even if the claimed derivative shows a better and unexpected "efficacy" over its predecessor substance, it could still be held as "obvious", as the prior art may offer a person skilled in the art ample motivation to get to such derivative.

Here again, although such a derivative may cross the section 3(d) hurdle in India, it will still have to answer to a charge that it does not involve an inventive step. And at the stage of assessing "inventive step", it is possible that the Indian patent office or a court may reach the same conclusion as the US Court of Appeals did in *Pfizer v Apotex*, i.e. that since a skilled person in the art had only a limited range of substances to work with, finding the particular salt would have been nothing more than "routine optimization."

7.3 Policy Considerations

As to whether "efficacy" ought to be defined broadly or narrowly depends, *inter alia*, on the following policy considerations.

i) Does the Indian patent regime matter for the R&D incentives of Indian pharmaceutical companies?
ii) Does the Indian patent regime matter for R&D incentives of multinational companies (MNCs)?

More specifically:

---

[109] Section 2(1)(ja) of the Indian Patents Act defines "inventive step" as "*a feature of an invention that involves technical advance as compared to the existing knowledge or having economic significance or both and that makes the invention not obvious to the person skilled in the art.*" See note 77.

[110] *Pfizer v Apotex*, 480 F.3d 1348 (2007). Rebecca Eisenberg argues that the erroneous qualification of "unexpected properties" as "secondary evidence" in US patent jurisprudence may have led the Federal Circuit to such a decision. She notes: *"Although the Federal Circuit has been fairly consistent in holding that evidence of surprising properties should be considered in evaluating an invention for (non)obviousness, it often categorizes such evidence as "secondary evidence" of nonobviousness, putting it in the same category as evidence of commercial success, failure of others, and long-felt but unsolved need. Evidence of surprising or unexpected properties is unlike these other sources of "market" evidence that indicate obviousness only through a chain of inferences. It is primary, technological evidence going directly to the statutory inquiry as to "the differences between the subject matter sought to be patented and the prior art."* See RS Eisenberg, "Pharma's Non Obvious Problem", (2008) 2 *Lewis & Clark Law Review* 375, 418.

i) To what extent will a narrow interpretation of efficacy affect R&D incentives in relation to diseases of specific concern to India, such as malaria, tuberculosis and other neglected diseases?
ii) To what extent will a narrow interpretation of efficacy affect R&D incentives in relation to traditional/herbal medicines?
iii) To what extent will a narrow interpretation of efficacy impact foreign direct investment (FDI) by multinational corporations?
iv) To what extent will a narrow interpretation of efficacy impact the introduction of new drugs into the Indian market by MNCs?
v) To what extent will a wide interpretation of efficacy impact the smaller Indian pharmaceutical companies and their markets, both domestic and international?
vi) To what extent will a wide interpretation of efficacy affect public health imperatives, such as access to affordable medicines?

A recent paper attempts to answer the first issue raised above, i.e. does the Indian patent regime matter for the R&D incentives of Indian pharmaceutical companies?[111] This paper argues that since the focus of the top Indian pharmaceutical companies such as Ranbaxy and Dr Reddy's is more on the high earning developed country markets such as the US and Europe, the Indian market and the Indian patent regime does not matter to them. In other words, as long as these Indian drug majors enjoy patent protection in the developed country markets, they are likely to continue with their normal rate of innovation. The grant or non-grant of a patent in India is not going to significantly shift their R&D choices one way or the other.

However, the assumption of this paper (that the Indian market will never matter for the R&D incentives of the large Indian pharmaceutical companies) needs to be empirically tested. The paper cites the example of Ranbaxy, whose biggest market is the US, followed by India. The paper notes that while 28% of global sales come from the US market, only 20% come from India.[112] The paper assumes that 20% of revenues (from India) is not important enough and that a 30% share from the US will induce Ranbaxy to continue innovating with the same gusto. This assumption is questionable. By this same logic, one could equally contend that a market that only constitutes 30% of Ranbaxy's total revenues is immaterial for Ranbaxy. Therefore, a US patent is as unlikely as an Indian patent to make a difference to the innovation incentives of Ranbaxy.

Secondly, assuming that the Indian markets will continue to remain relatively unimportant for the R&D incentives of Indian companies may not hold true for all time to come. Consider the following factors that may or may not play out in the coming years.

i) The Indian pharmaceutical market is one of the most rapidly growing markets in the world.[113] Given that there is a great untapped rural market for medicines in India, it is possible that the Indian market will grow exponentially in the coming years.

---

[111] *See* Chaudhuri, note 104.

[112] Ranbaxy, *Annual Report, 2005*, p. 7. Chaudhuri, *ibid*, at 10.

[113] G Kumara et al, McKinsey & Co., Indian Pharma 2015: Unlocking the potential of the Indian Pharmaceuticals Market (2007).

ii) With the dollar rapidly losing value, the returns from the US are diminishing and may dip even further in the coming years.[114]

iii) With para IV litigations getting riskier and more expensive, expected revenues from the 6 month exclusivity may experience a downward spiral.

iv) The growing competition from China may lead to a decrease in market shares of Indian companies in the US and EU.[115]

Lastly, the paper ignores the collective action problem.[116] What if the regimes in other countries change to approximate a section 3(d) like position, where section 3(d) is interpreted in a restrictive manner? Are Indian pharmaceutical companies willing to risk this "collective action" problem? The most liberal patent regimes such as those of the US may never adopt such a conservative approach to patentability, but there is a possibility that developing countries such as Brazil might do so. Given that a large part of the international revenues of Indian majors such as Ranbaxy come from outside the US and EU, this factor assumes tremendous importance.[117]

In short, we need to empirically investigate and procure more data on the above issues before determining an optimal patentability threshold.

8. Conclusion: Constitutional, Yet Crude

As we repeatedly note, the Madras High Court was right in defending the constitutionality of section 3(d). This is consistent with earlier Supreme Court precedents that the mere absence of guidelines or definitions in a section ought not to mean that the section is arbitrary or vague or that it confers uncanalised discretion on a statutory authority.

Notwithstanding the constitutionality of section 3(d) and its laudable intent of preventing "evergreening", it is a crudely worded provision. Illustratively, the main section and the explanation are inconsistent, particularly when it comes to the patentability of a "new form" that has a "new use".

The creases in section 3(d) needs to be ironed out to make it work more "efficaciously" and to help lend more certainty to the law. This becomes even more pertinent, given that there are more cases at the patent office that hinge on section 3(d)[118] and several countries that are seeking to emulate this unique statutory provision.[119]

---

[114] V Aseem Grover, *Re-hit pharma cos await Central balm*, Fin. Exp., Dec. 8, 2007: http://www.financialexpress.com/news/Rehit-pharma-cos-await-Central-balm/248113/ (last visited Dec. 11 2007).

[115] *Cheaper Import of Formulations Threaten Indian Formulation Producers,* Pharmabiz.com Feb. 29th 2008.

[116] For an understanding of this concept in the context of pharmaceutical innovation, *see* B Pazderka and K Stegemann "Pharmaceutical Innovation as a Collective Action Problem: An Application of the Economic Theory of Alliances" (2005) 8(2) *Journal of World Intellectual Property* 157.

[117] Illustratively, in an annual report tracking Ranbaxy's performance till December 31, 2005, it is stated that total sales were at US $1,178 million, with overseas markets accounting for 75% of this figure. Of the overseas markets, the sales from the emerging economies, Brazil, Russia and China (29%) were the highest, followed by the US (28%) and the EU (17%). *See* Ranbaxy, *Annual Report, 2005*.

[118] To date, there have been very few cases where Section 3(d) of the Patent Act, 2005 has been used as the basis for the rejection of a patent application. The first was the patent application for Glivec, filed by Novartis and which was rejected for reasons already discussed in this paper. More recently, the patent

This paper not only offers suggestions on how these creases could be ironed out, but also goes on to build on such suggestions and propose an amendment to section 3(d).

While some of the suggestions in the paper are of a clarificatory nature and immediately implementable, other issues such as the definition of "efficacy" will necessarily involve a more detailed empirical/policy investigation. This paper highlights some of the factors that one might consider whilst undertaking such empirical investigation, a task which is likely to go to the very heart of the age-old debate about what constitutes optimal intellectual property norms for developing countries.

---

office rejected the claim for an anti HIV Nevirapine composition, as falling short of satisfying the increased efficacy hurdle under section 3(d). *See* note 66. It is also pertinent to note a recent court case, where the Delhi High Court declined to grant a temporary injunction to Roche, who sued CIPLA for infringement of its patent covering its anticancer drug, Tarceva. CIPLA counterclaimed invalidity, citing section 3(d) as one of the grounds. See *F. Hoffman-La Roche Ltd. & Anr. v Cipla Ltd*., CS(OS) 89/2008, Delhi High Court, discussed at text to note 78.

[119] GC Prasad, *Copycats Popping Patent Law Pill*, *Economic Times*, August 13, 2007: *http://economictimes.indiatimes.com/News/News_By_Industry/Healthcare__Biotech/Pharmaceuticals/Copycats_popping_patent_law_pill/articleshow/2276358.cms* (last visited on Oct, 20 2007). A recent law passed by Philippines bears strong resemblance to Section 3(d). *See* P Ollier, *Philippines plans to follow India in limiting patentability*, May 6, 2008: http://www.managingip.com/Article/1927492/Philippines-plans-to-follow-India-in-limiting-patentability.html (last visited on Jul, 16 2008).