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170

INTELLECTUAL PROPERTY RIGHTS AND INNOVATION: MNCs in Pharmaceutical Industry in India after TRIPS

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CONTENTS

List of Table(s)

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Sudip Chaudhuri*

*[**Abstract**: The principal economic rationale for granting patents is that it will stimulate investment for research for innovation. This is the expected positive effect. But, patent rights which exclude others from producing and marketing the product, lead to inhibition of competition and hence high prices and hence less access. This is the negative effect. After India re-introduced product patents in pharmaceuticals in line with TRIPS, MNCs have started marketing new patented drugs at exorbitant prices particularly for life-threatening diseases such as cancer. In this paper we focus on innovation where the impact is supposed to be positive. The paper analyses whether the MNCs are contributing to technological progress in the country to justify product patent protection. Among the ways the MNCs can contribute are by enhancing their R&D efforts; by properly using the patent system for genuine inventions and not for preventing generic entry and by locally working the patents obtained. The study shows that MNCs have not enhanced their R&D activities in India after TRIPS. In fact, one observes deterioration in recent years. The paper discusses several patent cases to argue that MNCs are aggressively asserting their patent rights not for getting genuine patents which they are entitled to but for preventing generic competition. The paper also finds that the MNCs are more keen to import patented drugs and market these in the country rather than to manufacture these and contribute to technological progress.]*

The history of India's pharmaceutical industry and the role played by multinational corporations (MNCs) and Indian companies are well known. Despite the fact that India recognized product patents in pharmaceuticals before the 1970s and despite enjoying quite a liberal investment environment, MNCs did not take much initiative to develop the industry. They took advantage of the patent system to import these rather than to manufacturing the drugs in the country and charge exorbitant prices preventing

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competition. The industry actually developed since the 1970s after India abolished product patents in pharmaceuticals essentially through the efforts of indigenous companies. The MNCs were relegated to the background (see, for example Chaudhuri. 2005).

But the environment and situation has changed since then. From 1st January 2005, drug product patent protection has been re-introduced in India to comply with the requirements under the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) of the World Trade Organization. As a part of the process of liberalization since the 1990s, restrictions on manufacturing and investment applicable to the MNCs have also been withdrawn.

Intellectual property rights cover a broad range of subjects including, patents, copyrights, trademarks and trade secrets. In this paper we focus on patents. The principal economic rationale for granting patents is that it will stimulate investment for research for innovation. This is the expected positive effect. But, patent rights which exclude others from producing and marketing the product, lead to inhibition of competition and hence high prices and hence less access. This is the negative effect. In another study (Chaudhuri 2012), we found that reminiscent of the period before the 1970s, the MNCs have started marketing new imported patented drugs at exorbitant prices particularly for life-threatening diseases such as cancer. In this paper we focus on innovation where the impact is supposed to be positive.

That product patent protection may provide incentives for R&D for innovation is acknowledged in the literature (Mazzoleni and Nelson, 1998) (though what is increasingly being discussed is the desirability of having non-patent incentives). But if the benefits of technological progress which are supposed to follow from patent protection take place in developed countries, not in developing countries, then how does the latter gain? Penrose (1951) as well as some later studies, such as those by Vaitsos (1972) and Greer (1973), have questioned the desirability of granting patent protection by developing countries precisely on this ground. The argument is that developing countries lose by granting patent protection since they suffer from higher prices but do not benefit technologically. India now has a much more developed pharmaceutical industry. Has the behaviour of MNCs changed? Are they contributing to technological progress in the country to justify product patent protection? Among the ways the MNCs can contribute are by enhancing their R&D efforts; by properly using the patent system for genuine inventions and not for preventing generic entry and by locally working the patents obtained. In the following three sections we take up these issues.

1. R&D

In 2012-13, 49 MNCs sold medicines worth ₹1,67,733 million in the Indian retail market of formulations. It constituted 23.8 per cent of the entire market. Out of these 49 companies, the larger 22 companies each with sales more than ₹1,000 million accounted for 95 per cent

of the MNC market (*Table 1*). Systematic data on R&D, sale and other variables are available from the CMIE Prowess database for only 8 MNCs - Glaxosmithkline Pharmaceuticals, Pfizer, Sanofi-Aventis, Abbott India, Novartis India, Wyeth, Merck, AstraZeneca Pharma India. These 8 MNCs accounted for 61 per cent of the MNC market in 2012-13 in India. We focus here on the R&D of these 8 major MNCs.[1]

Table 1. Retail Formulations Sales by MNCs in India, 2012-13

Name of company	*Sales, 2012-13* ₹ *million*
1.Glaxosmithkline Pharmaceuticals	32385
2.Abbott Healthcare	27060
3. Pfizer	17145
4. Sanofi-Aventis	14217
5. Abbott India	14041
6. Novartis India	11306
7. Novo Nordisk India	6222
8. Wyeth	5207
9. Merck	4718
10.MSD Pharmaceuticals	4505
11. Johnson & Johnson	3430
12.AstraZeneca Pharma India	3294
13.Win-Medicare Pvt.	3158
14.Allergan India	2409
15.Eli Lilly And Company	1961
16.Fulford (India)	1562
17.UCB India	1402
18.Organon (India)	1395
19.Roche	1312
20.Universal Medicare	1159
21.Serdia Pharmaceuticals (India)	1099
22.Danone	1057
23. Total (1 to 22 above)	160044
24. Other MNCs in India	7689
25. Total MNCs in India (23 + 24)	167733
26. Total Pharmaceutical market in India	705291

Source and Notes: From *Sales audit data* of AIOCD Pharmasofttech AWACS Pvt. (hence forth referred to as AIOCD-AWACS). Other MNCs include BMS India, Bayer Pharmaceuticals, Lundbeck India, Fresenius Kabi India, Boehringer Ingelheim, Ferring Pharmaceuticals, Stiefel India, Eisai Pharmaceuticals India

[1] The MNCs mainly focus on retail formulation sales. There is however one major foreign company, Mylan Laboratories which is not active in retail domestic formulations but in APIs (active pharmaceutical ingredients) and exports. Before taken over by the US generic company, it was an Indian owned company - Matrix Laboratories.

In the early 1990s before TRIPS came into effect, these MNCs spent on R&D only about 1 per cent of sales. Since then rather than going up, R&D expenditure as a percentage of sales has actually declined to about 0.3 per cent in 2012-13. In absolute terms too R&D expenditure has started falling recently. Compared to ₹570.2 million in 2009-10, these MNCs spent ₹246.7 million in 2011-12 and ₹337.1 million in 2012-13 (*Table 2*).

Table 2. R&D Expenditure by MNCs in India

	Sales ₹ million	*R&D expenditure ₹ million*	*R&D expenditure (Col (3) as per cent of col (2)*
1992-93	14386.9	192.3	1.3
1993-94	22694.9	205.8	0.9
1994-95	24982.5	214.3	0.9
1995-96	26312.1	264	1.0
1996-97	27324.1	308	1.1
1997-98	29955.5	311.7	1.0
19998-99	32623.6	296.2	0.9
1999-2000	36011.9	303	0.8
2000-01	33081.5	302.2	0.9
2001-02	37040.6	291.5	0.8
2002-03	43221.7	349.7	0.8
2003-04	44295.1	343.9	0.8
2004-05	48525.8	374.7	0.8
2005-06	52021.7	375.1	0.7
2006-07	55450.9	408.6	0.7
2007-08	57847.8	439.6	0.8
2008-09	61869.6	563.5	0.9
2009-10	65687.7	570.2	0.9
2010-11	81170.2	325.5	0.4
2011-12	89134.7	246.7	0.3
2012-13	98362.9	337.1	0.3

Source: Calculated from CMIE Prowess database.
Note: Data refers to top 8 MNCs as explained in the text.

Currently R&D expenditure is more than 1 per cent of sales only for Pfizer. The R&D expenditure for Pfizer increased steadily from about ₹20 million in the early 1990s. But after reaching a peak of ₹292.7 million in 2009-10 (3.7% of sales), it has started declining. In 2012-13 it spent only ₹175.8 million (1.6%). For the largest MNC in India GSK, R&D expenditure remained steady around ₹40-50 million before declining in recent years. In 2012-13 it spent only ₹24.6 million (0.1%). In the mid-1990s, two MNCs spent more than 1 per cent of their sales in R&D, AstraZeneca (2.8%) and Sanofi-India (3.1%). For AstraZeneca, it improved to 4.2 per cent in 2000-01 but it has gone down both in absolute and relative terms since then. Sanofi-India was the largest R&D spender in the mid-1990s. It further increased its expenditure to more than ₹100 million in the late 1990s. But it now spends only ₹41.7 million (0.3%) (*Table 3*).

Table 3. Company wise R&D by MNCs in India

	1994-95		*2000-01*		*2005-06*		*2012-13*	
	₹ *million*	*per cent*	₹ *million*	*per cent*	₹ *million*	*per cent*	₹ *million*	*per cent*
Abbott India	9.9	0.4	22.8	0.6	15.1	0.3	17.8	0.1
AstraZeneca Pharma India	15.3	2.8	46.1	4.2	21.7	0.9	NA	NA
Glaxosmithkline Pharmaceuticals	48.6	0.5	41.4	0.4	43.9	0.3	24.6	0.1
Merck .	4	0.3	6.4	0.2	16.1	0.4	64.2	0.9
Novartis India	14.6	0.3	16.4	0.4	16.2	0.3	2.2	0.02
Pfizer	22	0.9	142.3	3.8	223.6	3.1	175.8	1.6
Sanofi India .	91.9	3.1	15.2	0.4	33.4	0.4	41.7	0.3
Wyeth .	8	0.6	11.6	0.4	5.1	0.2	10.8	0.2
Total for 8 MNCs	214.3	0.9	302.2	0.9	375.1	0.7	337.1	0.4

Source and Notes: same as in Table 1.

So far as India is concerned, the MNCs disprove the hypothesis that strong intellectual property rights are important for their investments in R&D. MNCs locate their R&D laboratories primarily in developed countries. But three MNCs - Ciba Geigy (now part of Novartis), Hoechst (now part of Sanofi India) and Boots set up facilities for new drug development in India. After synthesizing a few new drugs, including Sintamil, an anti-depressant, Ciba Geigy discontinued new drug research in India. Boots India developed an anti-diabetic compound. But when it was at the clinical trials at phase II, the ownership of the company changed and the new discovery programme was discontinued in India. The Hoechst outfit has been purchased by an Indian company, Nicholas Piramal (Chaudhuri, 2005b).

The abolition of product patents in pharmaceuticals in India did not prevent Ciba-Geigy from continuing with its new drug R&D in India and getting these patented in other countries including in the United States of America (US). Between 1969 and 1981, it obtained 38 patents in the US. Ten of these patents were during 1969 to 1971 and the remaining 28 between 1972 and 1981 (after India abolished product patents in pharmaceuticals). After 1994, i.e., after TRIPS came into effect, it did not get any patents and only 4 patents were obtained between 1982 and 1993. Similarly Hoechst started getting patents in the US from 1976 and till 2000 it got 46 patents and none since then.[2]

[2] US patent data obtained from "Extended Year Set - Patenting By Geographic Region (State and Country), Breakout By Organization, Count of 1969 - 2012 Utility By Calendar Year of Grant Patent Grants" ("Extended Year Set - Patenting By Geographic Region (State and Country), Breakout By Organization, Count of 1969 - 2012 Utility By Calendar Year of Grant Patent Grants") (www.uspto.gov).

After TRIPS, except AstraZeneca none of the MNCs is involved in any R&D for new drugs. AstraZeneca set up a research facility in June 2003 in Bangalore to develop novel compounds for TB. It in fact obtained 7 US patents in the 2000s. However in 2014 it decided to close down the R&D centre which employed 168 scientists.[3]

In its *Annual Report, 2006*, AstraZeneca India wrote that " the Industry has welcomed the introduction of a product patent regime from January 2005 . . . These measures will encourage innovation and research in the Country more specifically in pharma industry". But in its *Annual Report, 2012-13* it reported that "No R&D activities were carried out by the Company during the year". In fact it did not spend any amount during the year. In its *Annual Report, 2013*, Sanofi India admitted that "No basic research is carried out by the Company" and further pointed out that "the Company interacted with its collaborators who continued to give the latest technology".

The same is true for other MNCs in India. Rather than doing much R&D in India they are getting technology and R&D services from their parent organizations. In its *Annual Report, 2012*, GSK wrote that "parent organization of your Company is one of the biggest investors in R&D to bring new products and vaccines to the market. Your company has been a beneficiary of this significant investment in R&D and it is the effort of the parent organization which has enabled your Company to bring a number of new drugs to market since inception".

Thus TRIPS and re-introduction of product patent protection in pharmaceuticals has not induced the MNCs to enhance their R&D activities. In fact one observes a deterioration in recent years. This is in sharp contrast to the R&D activities of the Indian companies particularly the larger ones comparable in size to the MNCs. Like the MNCs in India, the Indian companies too traditionally did not invest much in R&D. But since the mid-1900s, particularly since the early 2000s, there has been a remarkable improvement in a segment of the industry. In 2012-13, Natco Pharma which is a mid-sized Indian pharmaceutical company alone spent ₹377.8 million which is more than what the 8 MNCs together spent in the same year (₹337.1 million). There are 22 other Indian companies each of which spent more than the 8 MNCs put together. The larger Indian companies spend much more. Lupin, for example spent ₹71,507.8 (11.2%), Dr Reddys ₹83,946 (8.2%), Cadila Healthcare ₹4,927 (15.9%) etc in 2012-13.[4]

The above figures relate to what they do in India. Globally the MNCs spent much more as *Table 4* shows. Novartis and Merck spent more than 19 per cent of their sales on R&D and MNCs such as Pfizer, Sanofi, GSK and Abbott around 15 per cent. But as pointed out

[3] See, "AstraZeneca opens Indian research facility devoted to TB" (http://www.tballiance.org/newscenter/view-brief.php?id=52); "AstraZeneca to shut R&D centre in Bangalore", *Business Standard*, January 30, 2014

[4] R&D and sales data obtained from the CMIE Prowess database.

above, so far as innovation in India is concerned what is important is what they do in India. If they are doing R&D outside India and as we will see below, importing in India the new patented drugs resulting from such R&D, India does not gain technologically but suffers from the high prices. Moreover their operations in India are extremely small compared to their global operations. The same table shows that their sales in India constitute around 1 per cent or even less of their global sales. Thus if product patents are abolished in India, the funds for their global R&D are unlikely to be adversely affected but prices of patented medicines in the country would be much cheaper. Thus the conventional wisdom that developing countries should not grant product patents is still valid.

Table 4. Global R&D and sales of MNCs

	Global sales (USD mn)	*Global R&D (USD mn)*	*Global R&D (% of sales)*	*India sales (USD mn)*	*India sales as per cent of global sales*
Pfizer	47404	7046	14.9	201.45	0.4
Novartis	45418	8831	19.4	167.71	0.4
Merck	41143	7911	19.2	129.46	0.3
Sanofi	38370	6118	15.9	294.17	0.8
Glaxosmithkline	33107	5226	15.8	501.98	1.5
Abbott	23119	2900	12.5	305.75	1.3

Source: Global data from: "The 2013 Pharm Exec Top 50" (http://www.pharmexec.com/pharmexec/article/articleDetail.jsp?id=815158) and Indian data from CMIE Prowess database. Figures in rupees have been converted to US dollars using the annual average of exchange rate.

2. Patents for Genuine Inventions or for Preventing Generic Competition?

Under Article 27(1) of TRIPS, patents will have to be provided for inventions, which are 'new, involve an inventive step and are capable of industrial application'. Under Article 70(3) of TRIPS, a WTO member country has no obligation to provide patent protection for any subject matter which has fallen into the 'public domain' before WTO came into being, i.e., before 1 January 1995. Thus any drug patented abroad or for which an application has been made before 1995 can continue to be manufactured and sold in India after 1995 even though these may be under patent protection in other countries.

Drugs patented after 1 January 1995 can be classified into the following categories:

1. Those involving new chemical entities (NCEs) or new biological entities (NBEs) patented after 1995; and

2. Those involving NCEs/NBEs developed before or after 1995 but with patents for:
   a. new uses
   b. new formulations and compositions

c. new combinations
d. new chemical derivatives (salts, esters, etc.)

The TRIPS agreement, however, does not define the terms "new" and "inventive step". This provides some flexibility. Developed countries, for example, the US, follow very liberal patent standards. Patents are granted not only for NCEs and NBEs involved in the new drugs. Secondary patents can also be taken for new formulations, new combinations and new uses of existing NCEs/NBEs. CIPR (2002, p. 49) pointed out that there is no compulsion under TRIPS for the developing countries to follow the liberal patent standards of developed countries. The aim should be to ensure that patents are granted for true technical contributions and not for blocking innovation and legitimate competition by generic producers. Developing countries can interpret these terms so as to restrict the number of patents (Correa 2000; Abbott 2001). During the process of amending India's patent law in line with TRIPS, the Indian generic industry, scientists and lawyers and others in fact argued and urged that patents may not be granted for 'a new molecular modification or a salt or ester or a derivative or a formulation or dosage form of a known new chemical entity having the same or similar pharmaceutical activity' or new uses or new combinations of existing NCEs (Peoples' Commission on Patent Laws in India 2003, pp. 62, 76).

The Patents Act, 1970, as amended in line with TRIPS, defines the terms "new" and "inventive step" as terms as follows:

- '"invention" means a new product or process involving an inventive step and capable of industrial application' (Section 2(1) (j) and
- '"inventive step" means 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 a person skilled in the art (Section 2(1)(ja).

Further under Section 3(d) the following are not treated as "inventions" and hence not patentable:

- "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 … "

The following is added as an "explanation" in the same section:

- "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".

Section 3(d) has attracted both national and international attention. India has used an important flexibility permitted by TRIPS. Section 3(d) has attempted to restrict the number of patents - not all new formulations/combinations/chemical derivatives of NCEs are patentable in India.

To what extent are the MNCs following the patentability standards as laid down in Sections 2 and 3 of India's Patents Act? MNCs have obtained product patents legally in a large number of cases. But a number of the patent applications have been either rejected or revoked after being granted. Some of the patents which have been denied recently include: imatinib mesylate (brand name Glivec of Novartis); gefitinib (Iressa of AstraZeneca); peginterferon alfa-2a (Pegasys of Roche); Formoterol and mometasone aerosol suspension (Merck); bimatoprost and timolol (Ganfort of Allergan) (see *Table 1* in Harrison, 2013). The main grounds for which the patents have been denied are that the patented inventions are "obvious" (Section 2 (1)(j and ja)) and/or that these do not show enhanced efficacy (Section 3(d)). Denial of patents under these grounds does demonstrate that the MNCs have not restricted their claims to genuine invention. They have tried to take advantage of the patent system and tried to obtain patents even when they are not eligible to get these patents under the Indian law. Motivation clearly has been to prevent generic competition rather than to promote innovation.

We discuss below some high profile cases and analyse the implications for innovation and generic competition.[5]

Novartis case

This involves a landmark judgment by the Supreme Court of India and has attracted widespread attention including internationally.[6] The Supreme Court rejected in April 2013 the plea of Novartis for patent protection for its anti-cancer drug sold in the name of Glivec or Gleevec. Novartis applied for a patent for imatinib (and other derivatives of a compound) in the US in April 1994 (The judgment refers to this as the Zimmermann patent after the name of the inventor). After getting marketing approval, what the company started selling as the drug for treating chronic myeloid leukemia was not imatinib but a derivative of it viz., imatinib mesylate. It did not apply for a separate patent for imatinib mesylate in the US because as the judgment shows the Zimmermann patent covered not only imatinib but also imatinib mesylate.

Novartis could not at that time apply for a patent for imatinib/mesylate in India because as we have mentioned above, India is not required to provide protection for a patent applied or granted elsewhere before TRIPS came into being, i.e., before 1 January, 1995. What it did in India after 1995 (in July 1998) was to apply for a patent for the beta crystalline form of imatinib mesylate. Under the transitional arrangements used by India as permitted by

[5] These cases are based on Nair, Fernandes and Nair, 2014 updated with recent press reports- "Merck seeks to settle patent row with Glenmark", *Times of India*, July 12, 2014; " Roche and Cipla enter talks to settle Erlotinib patent row", *Economic Times*, June 13, 2014. See also Chaudhuri 2013 for the Novartis case.

[6] The text of the judgment is available from: http://supremecourtofindia.nic.in/outtoday/patent.pdf.

TRIPS, product patent applications between 1995 and 2004 were to be kept in a "mailbox" and were to be processed only after 2004. Accordingly the Novartis beta crystalline patent application was processed for grant of patent only after 2004. The patent was rejected initially by the patent office in January 2006 and then by the Intellectual Property Appellate Board (IPAB) in June, 2009. The Supreme Court judgment is basically related to the appeal of Novartis against this rejection of the patent by the IPAB.

Novartis argued before the Supreme Court that starting from the Zimmermann patent, beta crystalline form for which the patent was applied in India was developed through two inventions – from imatinib to imatinib mesylate and then from the latter to the beta crystalline form. The Supreme Court however ruled that imatinib mesylate was a known substance directly following from the Zimmermann patent and hence does not qualify as an "invention" in terms of clauses (j) and (ja) of Section 2(1). It also ruled that the beta crystalline form does not satisfy the section 3(d) criterion. The Supreme Court interpreted the word 'efficacy' to mean therapeutic efficacy. Novartis could not demonstrate that the new form (beta crystalline) of the known substance (imatinib mesylate) enhanced the therapeutic efficacy of the drug.

When Novartis applied for a patent for the beta crystalline form in India in 1998, it did not claim any therapeutic benefit. It was not required to do so at that stage because the section 3(d) efficacy criterion was introduced much later. After the patent was taken up for examination after 2004 and after the grant of the patent was opposed (India's legislation provides for pre-grant opposition), Novartis filed affidavits to satisfy the requirement of section 3(d). But it was admitted that no study had been done earlier since nowhere in the world had such conditions been imposed. Acknowledging the spirit of the law, Novartis had the honourable option to withdraw the patent application. Rather what it did was to wage a seven year long legal battle opposing not only the rulings of the patent office and the appellate board but filing writ petitions for declaring section 3(d) as unconstitutional! (The latter was dismissed by the Madras High Court in 2007).

What the Novartis case shows is the desperate attempt by an MNC to somehow get product patent monopoly. Noting that what Novartis was selling in the US and in India was imatinib mesylate and not the beta crystalline form, the Supreme Court remarked that the case of Novartis "appears in rather poor light and the claim for patent for beta crystalline form of imatinib mesylate would only appear as an attempt to obtain patent for imatinib mesylate, which would otherwise not be permissible in this country" (p. 96).

Erlotinib

As we have mentioned above, patents filed between 1995-2004 were taken up for examination for grant of patents after 2004. The application by Roche for its product, erlotinib (its brand name: Tarceva) belonged to this category. Roche obtained the patent but meanwhile Cipla had started manufacturing and marketing a generic version, Erlocib. Roche filed an infringement suit against Cipla in Delhi High Court in January 2008 and

specifically sought interim injunction against Cipla. Keeping in mind the interests of the public to have access to medicines, the judgment of S Ravindra Bhatt refused to grant injunction but asked Cipla to pay damages if the verdict ultimately goes in favour of Roche and Cipla was asked to maintain accounts of its sales. Roche appealed against this judgment in the Division Bench of Delhi High Court. The Division Bench dismissed in April 2009 the appeal with costs (Roche was asked to pay ₹15 lakhs to Cipla). Cipla had made a counter claim of revocation of the Roche patent and the Bench observed that Cipla has a prima facie case. Roche filed a Special Leave Application in the Supreme Court. The later however refused in August 2009 to intervene and asked a speedy disposal of the case pending in the Delhi High Court. Pending the disposal of the case, Roche filed infringement suits against several other generic companies as well from time to time including against Dr Reddys, Natco and Glenmark. Ultimately when the Delhi High Court passed the judgment in September 2012, the judge, Manmohan Singh upheld the validity of the Roche patent. But the judge also ruled that Cipla did not infringe this patent because Cipla has been marketing polymorph B of the basic erlotinib molecule and the patent application for this was rejected by the patent office as it did not pass the efficacy test of section 3(d). What both Roche and Cipla sold are the polymorph B form for which Roche did not get a patent. Both Roche and Cipla have appealed against this judgment in the Division Bench of Delhi High Court. In April 2014 the Division Bench referred the matter to mediation after both Roche and Cipla agreed to do so. But mediation has failed and the court appointed mediator has filed the "failure" report.[7]

Sunitinib

A patent was obtained for sunitinib in October 2007 (Pfizer brand name: Sutent). Cipla opposed the grant of the patent in 2008 and the Controller revoked it in 2012 since it was the invention was "obvious" - it did not satisfy the Section 2(1)(ja) criterion of "inventive step". Pfizer appealed against this decision in the Delhi High Court and got a stay preventing Cipla from marketing it. Cipla appealed against this in the Supreme Court. The latter asked the Patent office to have a fresh hearing. After re-hearing, the patent office did not change its decision to revoke the patent. The injunction against Cipla was lifted. But Pfizer appealed against this in IPAB. The latter set aside the revocation and asked the Patent office to re-assess the case after considering an affidavit (which Pfizer claimed was not considered) and after conducting a fresh hearing by another controller. An infringement suit is pending against Cipla.

Sitagliptin

Merck Sharp and Dohme (MSD) applied and got a patent for sitagliptin (brand name: Januvia). MSD licensed the Indian generic company, Sun Pharmaceuticals to market it.

[7] But mediation has failed and the court appointed mediator has filed the "failure" report.

MSD also applied for a patent for the phosphate salt of sitagliptin. This was however rejected by the Patent Office and MSD abandoned the patent application. Glenmark started marketing the phosphate salt form (brand name: Zita). MSD has filed an infringement suit in Delhi High Court in April 2013. The latter however refused to grant injunction on the ground that the product refers to the salt form and MSD has abandoned this patent. MSD has appealed against this judgment in the Division Bench. Pending the judgment in the appeal case, Merck later voluntarily approached the court for mediation and Glenmark has agreed to do so.

Implications of Patent Cases

What these patent cases demonstrate is that the MNCs have been aggressively asserting their patent rights and filing infringement cases against generic companies and that they invariably challenge any adverse decision and appeal to higher bodies. They have the right to do so under the Indian law. But what is important for us in this context is to see what the implications are for generic companies and generic competition. The generic companies are required to bear not only the huge legal expenses for protracted cases; they also run the risk of damages to be paid to the MNCs if they lose the infringement cases. These act as a deterrent for the generic companies. Not surprisingly only few generic companies such as Cipla, Natco, Glenmark are involved in patent challenges in India. In the Novartis case, Cipla fought till the last but in the erlotinib case, Cipla has agreed to mediate rather than to continue to fight. In the sitagliptin case too, Glenmark has agreed to mediate. Interestingly MSD and Sun filed six other infringement suits against companies such as Aprica Pharmaceuticals and WinBioz Remedies and obtained injunctions in each of these. In fact in four of these cases the generic companies did not pursue the matter opting to settle it mutually including in one case after paying for token damages (Anand 2014). As several cases show MNCs have lost the patent cases (as for example in the Novartis case) or have opted for mediation (as in the cases of erlotinib and sitagliptin). Thus in view of such litigation if generic companies desist from opposing the MNC patents, then what the patent cases actually imply is that MNCs will be able to enjoy patent monopoly even when they are legally not supposed to have these patents.

3. Local Working of Patents

The reason why patents are granted is not only that it will stimulate R&D for innovation. The expectation is that disclosing of inventions in patent applications and working of patents will lead to diffusion of technology and facilitate further progress.

Under Section 146 of the Patents Act, 1970, patentees are required to furnish to the Controller "the extent to which the patented invention has been worked on a commercial scale in India". Patent Rules, 2003 further specifies the Form (no 27) that needs to be used for furnishing the information. Form 27 is quite elaborate and requires the patentees to

provide information on not only whether the invention is worked or not but if not worked the reasons for not working and if worked the quantity and value of the patented product manufactured in India and imported.

Out of the 1115 patented products for which information were available for 16 MNCs, only 140 were commercially worked, i.e., were marketed in India (12.6%).[8] Again out of the 140 patented products worked in India, information about whether these were manufactured in India or not were available for only 92 products. Only 4 of these were manufactured in India including one which involves packaging of bulk imports. The remaining 88 patented products were being imported and marketed in India.

Providing information under Form 27 is a legal requirement and if the patentees do not provide these then as specified under Section 122 (1)(b), they are punishable with fine. As the above figures show in most cases MNCs have not provided the required information. But still the Patent Office is not known to have initiated any action to book the offenders.

Patent applications are made at early stages of the product life cycle when it is being developed for regulatory approval and marketing. In some cases the MNCs do cite this as the reason that the product is being developed or awaiting regulatory approval and hence not yet worked in India. But it is clear from the responses that this is not the only reason. In a number of cases the MNCs simply avoided the question by not responding at all or by giving an evasive reply by saying "nothing in particular". In some cases the MNCs have mentioned that they do not find it commercially worthwhile to work the patent in India. They may not find it commercially worthwhile but can the information disclosed in the patent be used to work the invention? In that case others can learn from the patents and contribute to technological development in the country. From the incomplete and casual information provided in Form 27 it is very difficult to find out whether actually adequate information have been disclosed or not.

In 48 out of the 140 cases, the patentees claimed that the patented product is worked in India but either the Form 27 document is not available (23 cases) or where available, the relevant details whether the product is manufactured in India or not are not provided (25 cases). In each of the 17 cases related to Sanofi-Aventis/Aventis (out of the 140 cases), the company claimed that the patented product is worked but did not disclose any further information simply saying that "Information are not readily available; efforts will be made to collect and submit further information, if asked for". The fact that same responses were given for different patented products suggests that the company has no intention of

[8] We accessed the Patent office website, http://www.ipindia.nic.in/ in December 2013 and tried to get Form 27 information submitted by the following 16 MNCs - Pfizer, Novartis, GSK, AstraZeneca, Abbott, Sanofi-Aventis, Wyeth, Merck, Roche, Bristol-Myers Squibb, Novo Nordisk, Allergan, Eli Lilly, Amgen, Boehringer Ingelheim and Eisai. The discussion in the text is based on the Form 27 submitted by these MNCs.

providing the information. GSK in 6 cases and Novartis and Novo Nordisk with one each too did not provide relevant details despite claiming that the patent is worked in India.

Only Allergan, Pfizer and Wyeth are involved in manufacturing three products covered by patent numbers, 219504, 247177 and 201649 respectively. MSD reported in 2012 that for its patent no 209816, it is involved in packaging in the country - converting bulk packs to consumer packs (strips and cartons) for Januvia (sitagliptin) and Janumet (sitagliptin/metformi). It also announced plans to get Januvia manufactured in the country by an Indian company Shasun.

For 88 patents as mentioned above, the MNCs are importing the products rather than manufacturing these in the country. Product details are available for 24 molecules. As can be seen from the *Table 5* some of the high priced patented products marketed in the country are not manufactured in the country - ixabepilone (BMS' Ixempra 45, mg injection (₹71,175/- per unit); Goserelin (AstraZeneca's Zoladex, 10.8 Mg Injection (₹28,320/-); Ixabepilone (BMS' Ixempra, 15 Mg Injection (₹26,596/-); Zoledronate (Novartis' Aclasta, 5 Mg Infusion 100 Ml (₹19,516/-); Pegylated Interferon Alpha 2a (Roche's Pegasys (₹18,200/-) etc.

Table 5. Prices of selected patented drugs imported by MNCs in India

Molecule	*Brand/Unit*	*Therapeutic Group*	*MNC*	*Unit Price* ₹
Ixabepilone	Ixempra 45 Mg Injection	Anti-Neoplastics	BMS India	71175.00
Goserelin	Zoladex 10.8 Mg Injection	Hormones	AstraZeneca Pharma India	28320.00
Ixabepilone	Ixempra 15 Mg Injection	Anti-Neoplastics	BMS India	26569.35
Zoledronate	Aclasta 5 Mg Infusion 100 Ml	Pain / Analgesics	Novartis India	19516.00
Pegylated Interferon Alpha 2a	Pegasys 180 Mcg Injection 10 Ml	Anti-Neoplastics	Roche	18200.00
Ibandronate	Bondronat 6 Mg Injection	Pain / Analgesics	Roche	13950.00
Pegylated Interferon Alpha 2a	Pegasys 135 Mg Injection 0.5 Ml	Anti-Neoplastics	Roche	13884.00
Goserelin	Zoladex 3.6 Mg Injection	Hormones	AstraZeneca Pharma India	9754.00
Erythropoietin Products	Mircera 100 Mcg Injection 0.3 Ml	Blood Related	Roche	8821.00
Sunitinib	Sutent 50 Mg Capsule	Anti-Neoplastics	Pfizer	8714.78
Everolimus	Afinitor 10 Mg Tablet	Anti-Neoplastics	Novartis India	7217.60

Molecule	*Brand/Unit*	*Therapeutic Group*	*MNC*	*Unit Price* ₹
Erythropoietin Products	Mircera 75 Mcg Injection 0.3 Ml	Blood Related	Roche	7207.00
Everolimus	Afinitor 5 Mg Tablet	Anti-Neoplastics	Novartis India	5052.30
Sunitinib	Sutent 25 Mg Capsule 7	Anti-Neoplastics	Pfizer	4357.39
Liraglutide	Victoza 6 Mg Injection 3 Ml	Anti Diabetic	Novo Nordisk India	4315.00
Erlotinib	Tarceva 150 Mg Tablet	Anti-Neoplastics	Roche	4030.00
Dasatinib	Sprycel 50 Mg Tablet	Anti-Neoplastics	BMS India	3287.30
Dasatinib	Sprycel 70 Mg Tablet	Anti-Neoplastics	BMS India	2953.67
Long Acting, Crystalline Zinc Suspension (Ultra-Lente)	Novomix 30 Penfill	Anti Diabetic	Novo Nordisk India	2211.65
Long Acting, Crystalline Zinc Suspension (Ultra-Lente)	Novorapid Penfill	Anti Diabetic	Novo Nordisk India	2211.65
Sunitinib	Sutent 12.5 Mg Capsule	Anti-Neoplastics	Pfizer	2178.65
Long Acting, Crystalline Zinc Suspension (Ultra-Lente)	Novorapid 100 Iu Injection 10 Ml	Anti Diabetic	Novo Nordisk India	1450.00

Sources and Notes: Form 27 information submitted by companies to the Patent Office as explained in the text; price data from *Sales audit data* of AIOCD Pharmasofttech AWACS Pvt. Ltd. Out of the 24 molecules identified as products imported by MNCs, the table provides information for only those products with unit prices more than ₹1,000/-.

If patented drugs are imported rather than being manufactured, the country does not gain technologically but pays the price of higher costs of monopoly drugs and this seriously questions the propriety of having product patents in that case.

What is worse, as the attempt of Biocon to manufacture an anti-cancer drug trastuzumab and Roche's opposition shows, while MNCs may not be keen to manufacture drugs in the country they are not hesitating to take legal action against those who try to do so. Trastuzumab is a very high priced product for which Roche has been enjoying a monopoly. It sells the product under the brand name Herceptine at ₹1,10,700/- for a single 50 ml injection. Through a marketing arrangement, the product is also sold by an Indian company at ₹75,000/- for a single 440 Mg injection. This was one of the drugs which was considered by the Ministry of Health for the issue of compulsory licence because of the

high cost. Roche however decided not to pursue the patent for this drug. In addition to the first application ("mother application"), further applications ("divisional applications") are required to be made when the patent invention relates to more than one invention. Roche made three divisional applications but the Patent office treated the applications as withdrawn since Roche did not pursue these further - Roche did not file the requests for examination as required under the Patents Act for consideration and grant of patents.[9]

With no patent barrier, Biocon introduced trastuzumab in the Indian market in early 2014 after developing the product in collaboration with Mylan and after getting regulatory approval from Drug Controller General of India (DCGI). iocon claimed its product (brand name: CANMab) to be biosimilar with "the same level of safety and efficacy as the reference product", i.e., Roche's Herceptin and offered a discount of 25 per cent.[10] However though Roche does not a have a patent for trastuzumab, it filed a suit in Delhi High court against Biocon and Mylan and sought interim injunction to prevent Biocon from marketing the product. Roche's opposition relates to two points: (i) that appropriate tests and studies as prescribed under the *Guidelines on Similar Biologics* announced by the government in 2012 have not been followed and (ii) Biocon has misrepresented the nature of the product by claiming that it of the same quality and class as Roche's Herceptin. Roche has obtained an injunction on the basis of the latter.[11]

Regulatory guidelines for approving biosimilars is a controversial issue. In traditional synthetic chemical drugs which involve relatively simple small molecules, generic versions are considered to be identical to innovator products in the sense that they contain identical active ingredients. Biologic medicines such as trastuzumab however are made with or derived from living organisms and involve large and complex molecules and the generic versions are considered to be similar but not the same. The 2012 guidelines make it tougher for generic firms to enter the market. A proper consideration of the issues involved is beyond the scope of the paper. But what is relevant to point out in this context is that Roche had the option to manufacture the drug in the country. The types of skills and technical competence required for developing a biotechnology drug is different from what is required for traditional chemical drugs. The Indian generic companies at the current stage are less proficient in the former compared to the latter. Companies like Roche can contribute to the technological progress of the country by manufacturing these here. The response of Roche shows that it is more keen to enjoy monopoly markets and high prices rather than to contribute to technological progress.

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[9] "Kolkata Patent office Clarifies ITS Decision on Divisional Applications of Herceptin", Press Release, 5 August, 2013 (http://pib.nic.in/newsite/PrintRelease.aspx?relid=97629).

[10] "Biocon introduces CANMAb(TM) for Treating Breast Cancer in India", Biocon Press Release, January 18, 2014 (www.biocon.com).

[11] The text of the Order delivered on 5 February, 2014 is available from http://lobis.nic.in/dhc/MAN/judgement/06-02-2014/MAN05022014S3552014.pdf

There are also other biotechnology drugs where MNCs are sole sellers despite the absence of patent barrier. Perhaps the most prominent example is pegylated Interferon alpha 2a, a medicine used for the treatment of Hepatitis C. Roche obtained a patent for it and has been charging very high prices - ₹18,200/- for a single 180 Mcg injection 10ml for its product brand named, Pegasys. The cost of treatment is several lakhs as the medicine needs to be used for several months. It is also available at a lower price of ₹9,175/- from an Indian company, Emcure which sells it on behalf of Roche in a different brand name (Taspiance). The IAPB has revoked this patent in 2012 on the ground that the invention is "obvious" (failed the Section 2(1)(ja) test of inventive step and also the Section 3(d) test of efficacy (Harrison, 2013). But still there is no generic product in the market. The 2012 regulatory guidelines and the litigation that Biocon is facing for trastuzumab acts as a dampener for other generic companies to try to develop such products.

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