

# Challenges to India's Pharmaceutical Patent Laws

Bhaven N. Sampat,<sup>1\*</sup> Kenneth C. Shadlen,<sup>2</sup> Tahir M. Amin<sup>3,4</sup>

The Indian Supreme Court will soon hear final arguments in a challenge by the pharmaceutical company Novartis against the Indian Patent Office's (IPO) rejection of a patent for the leukemia drug Glivec. We discuss key issues, particularly the patentability of new compounds versus variants of existing compounds, and how the outcome of the case might affect patent terms and access to drugs in the developing world.

The World Trade Organization's (WTO's) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), in effect since 1995, requires all WTO countries to allow patenting of pharmaceutical products and processes. Global extension of pharmaceutical patents, which will be the effect of

until 2005. India also introduced a clause designed to restrict the number and type of pharmaceutical patents granted: Section 3(d) of the Patent Act prohibits patents on variants of existing compounds that do not show enhanced efficacy.

Section 3(d) has been extremely contentious since its introduction in 2005. The transnational pharmaceutical industry and the U.S.-India Business Council regard it as establishing an unacceptably high barrier to patenting (1, 2). Echoing this criticism, the U.S. Trade Representative regularly cites 3(d) among reasons to keep India on its list of countries whose intellectual property regimes are of concern (3). But many observers, including the United Nations Programme

An Indian Supreme Court decision about variants of existing compounds could affect access to affordable drugs.

that section 3(d) has in India's ability to supply low-cost generic pharmaceuticals domestically and abroad (6).

## Evergreening, Patent Policy, and Glivec

The core issue in this debate is not whether newly discovered molecules will be protected by patents in India or open for generic production. Rather, the main issues are whether and how countries with newly introduced pharmaceutical patent regimes limit "evergreening" of existing molecules and patent portfolios. Evergreening is a term used to describe the sequential accumulation of secondary patents on drugs, including alternative forms of active ingredients, new formulations, dosages, and uses (9). Pharmaceutical companies refer to this as "life-cycle management" (10). Because secondary patents tend to be filed later in the life of a drug than primary chemical compound patents, they can extend monopoly terms (11). Some scholars argue that innovative efforts associated with secondary patents are less substantial, although that is subject to debate (5). There is broader agreement that secondary patents are less likely to satisfy traditional patentability criteria and thus are more vulnerable legally (5, 12).

Across industries, in developed and developing countries, policy-makers wrestle with how to weed out "low-quality" patents (13). In the United States, the Hatch-Waxman Act of 1984 provides financial incentives for generic firms to identify and challenge pharmaceutical patents that they believe were improperly issued by the U.S. Patent and Trademark Office. Challenges disproportionately target secondary patents and appear to be successful: Despite the proliferation of secondary patents and expansion of nominal patent terms since Hatch-Waxman (11), the time to generic entry in the United States has remained fairly stable (9).

In the United States, then, litigation constitutes an ex post way to subject legally questionable patents to a strong second look and thus curb evergreening. India, in contrast, has adopted an ex ante mechanism: Section 3(d) attempts to scrutinize secondary patents preemptively, before they are issued (14). Apart from timing, 3(d) differs

## ... Hatch-Waxman challenge provisions and 3(d) [of India's Patent Act] ... aim to prevent low-quality patents from delaying generic entry.

TRIPS when fully implemented over various transition periods by all WTO members, has fueled concerns about drug prices and, subsequently, access to lifesaving medications.

The introduction of pharmaceutical patents in India has been particularly controversial. Indian producers have long been suppliers of low-cost medicines (including key HIV/AIDS treatments), domestically and also to other low- and middle-income countries. In amending its patent law to meet new international obligations, India, like many developing countries, attempted to take advantage of flexibilities in TRIPS to ameliorate potentially negative effects that pharmaceutical patents might have on the supply of medicines. India used its full transition period, waiting to introduce pharmaceutical product patents until 2005 (pharmaceutical process patents were already available prior to TRIPS). Applications dating from 1995 onward were received but were not examined

on HIV/AIDS (UNAIDS) and civil society groups, defend 3(d) and point to India as a model for developing countries attempting to use TRIPS flexibilities to promote public health (4–6).

In 2006, the IPO, citing 3(d), rejected Novartis's application for a patent on a crystalline form of Glivec's basic compound, imatinib mesylate. Glivec is widely recognized as having revolutionized treatment of chronic myeloid leukemia and demonstrated the potential for targeted drug development (7). As a result of the IPO's decision, Glivec is not protected by a patent in India.

Novartis appealed against the rejection, and the case has worked its way to the Supreme Court. Although the case is meant to determine whether the rejection was appropriate, the broader issues of how the IPO interprets and applies 3(d), and the validity of the provision itself, are likely to be considered by the court, making the case a referendum on 3(d). Novartis, making its case before the court of public opinion, has emphasized that the drug has received patents in more than 40 other countries, implying that if even Glivec cannot be patented in India, 3(d) must be setting unreasonable standards (8). Meanwhile, civil society groups have called on Novartis to drop the suit, emphasizing the crucial role

<sup>1</sup>Health Policy and Management, Columbia University, New York, NY 10032, USA. <sup>2</sup>International Development, London School of Economics (LSE), London WC2A 2AE, UK. <sup>3</sup>Initiative for Medicines, Access, and Knowledge, New York, NY 10016, USA. <sup>4</sup>Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA 02115, USA.

\*Author for correspondence. E-mail: bns3@columbia.edu

from the U.S. approach in that it relies on tests of efficacy in addition to the traditional “novelty” and “inventive step” standards to determine whether variants on old molecules receive patents.

Notwithstanding differences in form, Hatch-Waxman challenge provisions and 3(d) share the same goal: Both aim to prevent low-quality patents from delaying generic entry. Indeed, their effects may be similar, as Glivec itself illustrates. The same patent at issue in the Novartis case in India was the target of a Hatch-Waxman challenge in the United States in 2007 (15). Novartis does not appear to be litigating in response to this challenge, which suggests that it accepts the patent as questionable even in the United States. It is noteworthy that in the United States (and elsewhere), Novartis has an earlier patent on the drug’s basic compound, filed in 1993, which protects Glivec until 2015. This earlier application was not filed in India because India did not grant pharmaceutical products patents before TRIPS and does not recognize pre-1995 applications. In the absence of this primary patent, the only protection possible for Glivec in India would be via the secondary patents that cover alternative structural forms of the base molecule.

As a case study, Glivec is peculiar and unlikely to be representative going forward. Had it been invented a few years later (or TRIPS implemented a few years earlier), Glivec likely would be patented in India, even under 3(d) standards. Newly discovered compounds are likely to receive basic patents and to be less vulnerable to 3(d) rejections.

In the short term, whether drugs whose primary patents predate TRIPS receive any patent protection in India—and thus whether low-cost generic provision of these drugs for patients in India and abroad remains possible—may turn on whether 3(d) stands or falls. Applications for secondary patents on these drugs are vulnerable to rejections based on this provision. However, the long-term effects of 3(d) are likely to differ. Most new drugs typically have primary (compound) patents (11). For these drugs, the effects of 3(d) will be on the length of effective patent terms, not the existence of patents. Because of 3(d), consumers may benefit from generic competition on these drugs sooner, but they will not be able to count on the denial of patents altogether.

#### Laws on the Books Versus Laws in Practice

Although Novartis and its allies see a problem of false-positives, where 3(d) is applied injudiciously to deny patent protection to innovative drugs, another concern is poten-

INDIAN PATENT OFFICE OUTCOMES	
Outcome	Number
Granted	75
Pending	79
Withdrawn	35
Rejected	25
• on grounds including 3(d)	16
• exclusively on 3(d) grounds	3
• on grounds other than 3(d)	6

**Indian Patent Office Outcomes.** As of March 2012, outcomes for 214 Indian patent applications associated with drugs approved for U.S. marketing between 1996 and 2004. See the Supplementary Materials for details.

tial false-negatives: that the IPO, under severe resource constraints and pressures to clear applications (16), may not be well positioned to deploy 3(d) with sufficient robustness to block patents that perhaps should not be granted (17). Indeed, data on a set of 214 Indian patent applications associated with drugs approved by the U.S. Food and Drug Administration between 1996 and 2004 indicate that only 19 had rejections on 3(d) grounds (see the table). In 16 of the cases where there was a 3(d) rejection, the decision cited other grounds as well, which suggests that these may have faced difficulties even without 3(d). Although it is difficult to know what share of application withdrawals were responses to 3(d) rejections, or the extent to which granted patents had their scope narrowed because of 3(d), the data suggest that outright refusals based on the provision are surprisingly rare.

The issues that emerge from an assessment of 3(d) as insufficiently effective relate to broader challenges in patent policy. Arguments that applications should be rejected because of 3(d) are often brought to the attention of the IPO through third-party “oppositions” that provide a rationale for why a drug should not be patented (18). But oppositions are public goods and subject to coordination problems among and between civil society groups and generic firms.

The Supreme Court is expected to clarify exactly how and when 3(d) will be applied—and perhaps how terms such as “efficacy” should be understood (19). The IPO may need more than just clarity. Increased resources may be necessary, not only for proper implementation of 3(d) but also for improving patent examination in general. In addition to reducing the grant of low-quality patents, which would benefit generics and consumers, more resources would increase examination speed, which would benefit patenting

firms. Increased funding for the IPO implies reallocation of resources from other areas, and thus is easier said than done, but it is an area where pharmaceutical firms (patent-based and generic) and treatment advocates may find common ground.

How might limitations on secondary patents in India affect pharmaceutical innovation, generic competition, and, subsequently, prices and utilization? Accepting that restrictions on evergreening are desirable (as other countries do) raises questions of institutional design: How high should standards for patentability be? Where in the patent process should they be implemented? How much should be invested in their functioning? These issues, straightforward to enumerate although difficult to answer, are important not only in India but also in other developing (and developed) countries aiming to improve patent examination and to balance innovation and access.

#### References and Notes

1. Pharmaceutical Research and Manufacturers of America, Special 301 Submission (PhRMA, Washington, DC, 2010).
2. U.S.-India Business Council, *The Value of Incremental Pharmaceutical Innovation: Benefits for Indian Patients and Indian Businesses* (USIBC, Washington, DC, 2009).
3. Office of the U.S. Trade Representative, Special 301 Reports, 2010–2012 (USTR, Washington, DC, 2012).
4. UNAIDS, *DOHA+10: TRIPS Flexibilities and Access to Anti-retroviral Therapy: Lessons from the Past, Opportunities for the Future* (UNAIDS, Geneva, 2011).
5. C. Correa, *Guidelines for the Examination of Pharmaceutical Patents: Developing a Public Health Perspective* (WHO-ICTSD-UNCTAD, Geneva, 2007).
6. K. Grogan, *Pharmatimes*, 24 February 2012.
7. L. Pray, *Nat. Educ.* **1**, 565 (2008).
8. Novartis, Glivec Patent Case in India: Fact vs. Fiction; [www.novartis.com/downloads/newsroom/glivec-information-center/Fact\\_vs\\_fiction\\_of\\_Glivec\\_India\\_Case.pdf](http://www.novartis.com/downloads/newsroom/glivec-information-center/Fact_vs_fiction_of_Glivec_India_Case.pdf).
9. C. S. Hemphill, B. N. Sampat, *J. Health Econ.* **31**, 327 (2012).
10. M. E. Furrow, *Food Drug Law J.* **63**, 275 (2008).
11. S. Hemphill, B. N. Sampat, *J. Empir. Legal Stud.* **8**, 613 (2011).
12. R. Eisenberg, *Lewis & Clark Law Rev.* **12**, 375 (2008).
13. A. Jaffe, J. Lerner, *Innovation and Its Discontents: How Our Broken Patent System Is Endangering Innovation and Progress, and What to Do About It* (Princeton Univ. Press, Princeton, NJ, 2006).
14. Patents can be revoked using 3(d) as well, via postgrant opposition.
15. ParagraphFour.com, Gleevec (imatinib) tablets; [www.paragraphfour.com](http://www.paragraphfour.com).
16. A. Kapczynski, *Calif. Law Rev.* **97**, 1571 (2009).
17. C. H. Unnikrishnan, LiveMint.com, 10 December 2008; [www.livemint.com/2008/12/1000020/India-granting-drug-patents-fo.html](http://www.livemint.com/2008/12/1000020/India-granting-drug-patents-fo.html).
18. S. Basheer, Patent Oppositions in India: The “Efficacy” of Section 3(d); [www.spicyipindia.blogspot.com/2009/09/patent-oppositions-in-india-efficacy-of.html](http://www.spicyipindia.blogspot.com/2009/09/patent-oppositions-in-india-efficacy-of.html).
19. S. Basheer, P. Reddy, *SCRIPTed* **5**(2), 232 (2008); [www.law.ed.ac.uk/ahrc/script-ed/vol5-2/basheer.asp](http://www.law.ed.ac.uk/ahrc/script-ed/vol5-2/basheer.asp).

**Acknowledgments:** An LSE-Columbia Seed Research Grant and the Robert Wood Johnson Foundation’s Public Health Law Research Program supported this research. We thank S. Hemphill for his comments on the manuscript.

#### Supplementary Materials

[www.sciencemag.org/cgi/content/full/science.1224892/DC1](http://www.sciencemag.org/cgi/content/full/science.1224892/DC1)

10.1126/science.1224892



[www.sciencemag.org/cgi/content/full/science.1224892/DC1](http://www.sciencemag.org/cgi/content/full/science.1224892/DC1)

Supplementary Materials for  
**Challenges to India's Pharmaceutical Patent Laws**

Bhaven N. Sampat,\* Kenneth C. Shadlen, Tahir M. Amin

\*To whom correspondence should be addressed. E-mail: [bns3@columbia.edu](mailto:bns3@columbia.edu)

Published 5 July 2012 on *Science Express*  
DOI: 10.1126/science.1224892

**This PDF file includes:**

Appendix S1  
Full References

**Other Supplementary Material for this manuscript includes the following:**

(available at [www.sciencemag.org/cgi/content/full/science.1224892/DC1](http://www.sciencemag.org/cgi/content/full/science.1224892/DC1))

Table S1 as an Excel file

## Supplementary Materials

### Background

Individual drugs are typically covered by multiple patents. Mapping full patent landscapes for individual drugs is difficult. Reflecting this, entire legal proceedings are devoted to whether specific patents are infringed by a drug. The difficulties multiply when moving from one drug to many. They are especially pronounced in contexts where administrative records linking patents to drugs (such as the U.S. Food and Drug Administration's Orange Book, described below) are unavailable. These challenges are even greater in developing countries, where patent databases are often less complete and less easily accessible.

Patent searching is ideally done on a case-by-case basis, by someone familiar with the science relating to the drug as well as patent law. Since this is difficult to do for a large sample of drugs, we instead use information from commercial databases. After identifying Indian applications, we collected outcome data from the Indian Patent Office's (IPO) application status database (<http://ipindia.nic.in/ipirs1/patentsearch.htm>). The outcome data were last updated in March 2012.

The next section describes this approach in more detail. Then, we present the raw data used to compute the figures reported in our article.

### Empirical Approach

#### *The Sample and Indian Patent Applications*

We began with all non-injectable new chemical entities approved by the FDA between 1996 and 2004 that have at least one U.S. patent listed on the Orange Book, an FDA compendium of drugs marketed in the U.S. and their patents, drawing on the dataset developed by one of the authors for previous analysis (11). This set includes 159 unique active ingredients. We compiled data on all Orange Book patents for these drugs, using information from current and archival Orange Books, as described in detail elsewhere (11).

To collect Indian patent applications for these 159 drugs, we began by identifying those that are known to be associated with an Orange Book patent in our set, using patent "family" information from the Derwent World Patents Index (DWPI). We supplement this information with patent data from another database, IMS Patent Focus, which is based on expert searches of the patent literature. This is important to do both because certain types of patents are not listed on the Orange Book, and also since patent family relationships can be severed by missing or incomplete priority data in Indian patent documents, which is common.

Based on these two sources, we identified 220 Indian patent applications for the 159 drugs: 97 were in IMS only, 71 in Derwent only, and 52 in both sources. Of the 220 applications, 214 are distinct, i.e. in some cases patent applications are associated with multiple drugs. Overall, we located Indian patent applications for 70 of the 159 drugs using this approach.

#### *Indian Patent Outcomes*

We collected information on the outcomes of the patent applications in India, as of March 2012, from the IPO Application Status database. We aggregated outcomes from the searchers to four broad categories: GRANTED, PENDING (including those not yet published, those awaiting examination, and under examination), WITHDRAWN (including those abandoned), and REJECTED. This information was based primarily from the IPO database, though for three applications not available there, indicated by asterisks, we determined likely status through web sources.

In cases where patents were rejected, “Controller’s Decisions” list reasons for rejections. Based on our reading of these decisions, we coded each rejection based on whether 3(d) was a reason for the rejection, and also whether it was the sole reason for rejection, or whether or not other arguments (e.g. lack inventive step or novelty, lack of enablement) were cited as well.

*Caveats:*

The table in the paper intends only to describe this set of applications. Several issues would arise in making broader inferences.

First, for reasons noted above, ours is not meant to be a complete landscape for legal analysis or business decisions. However, under the assumption that any over-inclusion or under-inclusion of patent applications on this list is random, as we believe it to be, the data would generate unbiased estimates of the relative frequency of the different outcomes listed.

Second, note that our data on the role of 3(d) in the prosecution of these patent applications is based on rejections. As we suggest in the main text, we do not know whether withdrawals or abandonments were in response to 3(d) rejections (20), the extent to which 3(d) may have led to narrowing of claims of applications that are granted, or the extent to which 3(d) issues have been raised by the IPO (or in oppositions) for pending applications. If these were common, the figures in the text would underestimate the share of applications affected by the provision. Another possibility is that some patent applications were not filed in India in anticipation of 3(d), in which case the applications in our sample would exclude those that would generate 3(d) rejections by construction (21).

The Data

Table S1 shows each active ingredient, the Indian patent application(s) it links to, the source of the application data (DWPI, IMS, or BOTH), the status of the application at the IPO as of March 2012, and the outcome we assign the application to based on our coding. While the table includes all 220 applications, with multiple rows for the five applications (22) associated with more than one active ingredient, the figures reported in the text are calculated across the 214 distinct applications.

**References and Notes**

1. Pharmaceutical Research and Manufacturers of America, Special 301 Submission (PhRMA, Washington, DC, 2010).
2. U.S.-India Business Council, *The Value of Incremental Pharmaceutical Innovation: Benefits for Indian Patients and Indian Businesses* (USIBC, Washington, DC, 2009).
3. Office of the U.S. Trade Representative, Special 301 Reports, 2010–2012 (USTR, Washington, DC, 2012).
4. UNAIDS, *DOHA+10: TRIPS Flexibilities and Access to Antiretroviral Therapy: Lessons From the Past, Opportunities for the Future* (UNAIDS, Geneva, 2011).
5. C. Correa, Guidelines for the Examination of Pharmaceutical Patents: Developing a Public Health Perspective (WHO-ICTSD-UNCTAD, Geneva, 2007).
6. K. Grogan, *PharmaTimes*, 24 February 2012.
7. L. Pray, *Nat. Educ.* **1**, 565 (2008).
8. Novartis, Glivec Patent Case in India: Fact vs. Fiction; [www.novartis.com/downloads/newsroom/glivec-information-center/Fact\\_vs\\_fiction\\_of\\_Glivec\\_India\\_Case.pdf](http://www.novartis.com/downloads/newsroom/glivec-information-center/Fact_vs_fiction_of_Glivec_India_Case.pdf). Last Accessed 15 May 2012.
9. C. S. Hemphill, B. N. Sampat, *J. Health Econ.* **31**, 327 (2012).

10. M. E. Furrow, *Food Drug Law J.* **63**, 275 (2008).
11. S. Hemphill, B. N. Sampat, *J. Empir. Legal Stud.* **8**, 613 (2011).
12. R. Eisenberg, *Lewis & Clark Law Rev.* **12**, 375 (2008).
13. A. Jaffe, J. Lerner, *Innovation and Its Discontents: How Our Broken Patent System Is Endangering Innovation and Progress, and What to Do About It* (Princeton Univ. Press, Princeton, NJ, 2006).
14. Patents can be revoked using 3(d) as well, via post-grant opposition.
15. ParagraphFour.com, Gleevec (imatinib) tablets; [www.paragraphfour.com](http://www.paragraphfour.com).
16. A. Kapczynski, *Calif. Law Rev.* **97**, 1571 (2009).
17. C. H. Unnikrishnan, LiveMint.com, 10 December 2008; [www.livemint.com/2008/12/10000020/India-granting-drug-patents-fo.html](http://www.livemint.com/2008/12/10000020/India-granting-drug-patents-fo.html).
18. S. Basheer, Patent Oppositions in India: The "Efficacy" of Section 3(d); [www.spicyipindia.blogspot.com/2009/09/patent-oppositions-in-india-efficacy-of.html](http://www.spicyipindia.blogspot.com/2009/09/patent-oppositions-in-india-efficacy-of.html).
19. S. Basheer, P. Reddy, *SCRIPTed* 5(2), 232 (2008); [www.law.ed.ac.uk/ahrc/script-ed/vol5-2/basheer.asp](http://www.law.ed.ac.uk/ahrc/script-ed/vol5-2/basheer.asp).
20. Over half of the withdrawals are listed as Section 11B(4) withdrawals or Section 9(1) abandonments, which typically occur before examination, so are unlikely to be responses to 3(d) rejections
21. The third section of the application number indicates filing year. Two-thirds of the applications on this list were filed before 2005, i.e. before 3(d) went into effect in India.
22. Specifically, 2194/CHENP/2004 and 3102/CHENP/2006 each are associated with IBANDRONATE SODIUM and RISEDRONATE SODIUM, and 3383/DELNP/2005 and 6665/DELNP/2008 each are associated with EFAVIRENZ, TENOFOVIR DISOPROXIL FUMARATE, and EMTRICITABINE.