

Challenges to India's Pharmaceutical Patent Laws

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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

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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

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

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

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

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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.

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Supplementary Materials

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