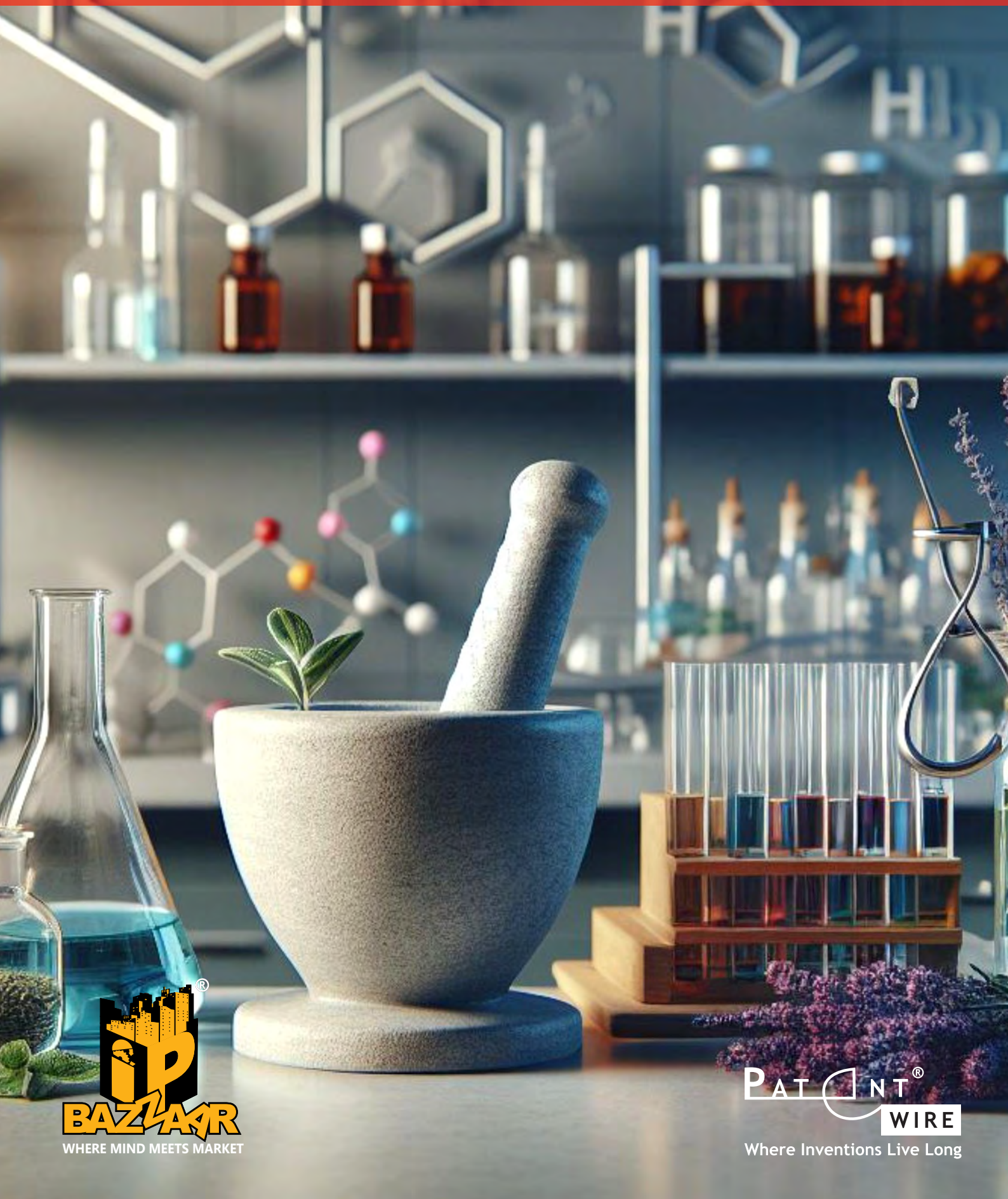
STATUS QUO



IP BAZAAR®
WHERE MIND MEETS MARKET

PATENT® WIRE
Where Inventions Live Long

PROLOGUE

India is often referred to as the "pharmacy of the world," particularly for its role in manufacturing and supplying affordable generic drugs. The country's pharmaceutical industry is a global leader in producing generic medications, contributing significantly to global healthcare by making essential medicines accessible and affordable to countries across the world.

However, it also faces several challenges and criticisms. The Indian pharmaceutical industry heavily relies on imports for its raw materials, especially Active Pharmaceutical Ingredients (APIs), predominantly from countries like China. This overdependence on imports for critical raw materials poses a risk of supply chain disruptions, as seen during the initial stages of the COVID-19 pandemic. The industry has also faced criticism and challenges related to intellectual property rights, including patent infringements, frivolous oppositions, and disputes with multinational pharmaceutical companies. This has led to a perception of a weak Intellectual Property Rights (IPR) regime, impacting India's relationship with global markets and investors.

On innovation front, the observation about India's contribution to New Chemical Entities (NCEs) highlights a significant challenge and irony within the industry, given its global stature as a leading producer of generic medicines. The Indian pharmaceutical sector is renowned worldwide for its capability in generic drug manufacturing, offering affordable medicines across the globe. However, when it comes to drug discovery, including the development of NCEs, India's track record is relatively modest, especially in comparison to its achievements in generics. Ultimately, Indian pharmaceutical industry has still opted 'Status Quo' in innovation front despite having best brains and best Research and Development (R&D) institutions.

INDIAN GENERIC MEDICINES: THE RISE

ESTABLISHMENT IN NEED

India's generic drug manufacturing history began post-independence, prioritizing self-sufficiency and public health. India's legacy of generic drug manufacturing is marked by several key developments and milestones. Before 1947, the country had a rudimentary pharmaceutical industry focused mainly on producing basic medicines for domestic use. The sector was largely dominated by multinational companies, and there was limited indigenous manufacturing of pharmaceuticals. Following independence, India's pharmaceutical industry began to expand gradually. The government implemented policies to promote indigenous manufacturing and reduce dependence on imported drugs. This period saw the emergence of several domestic pharmaceutical companies, primarily engaged in the production of generic drugs.

ESTABLISHMENT OF PUBLIC SECTOR UNITS

In the 1950s and 1960s, the Indian government established several public sector pharmaceutical companies to address the country's healthcare needs. These companies, such as Hindustan Antibiotics Limited (HAL), Indian Drugs and Pharmaceuticals Limited (IDPL), and Bengal Chemicals and Pharmaceuticals Limited (BCPL), played a significant role in producing essential medicines at affordable prices for the Indian population.

ESTABLISHMENT AS PER PATENT LAW

In 1970, India enacted the Patents Act, which allowed only process patents for pharmaceuticals and prohibited the patenting of drug molecules. This legislation encouraged domestic manufacturers to produce generic versions of patented drugs, leading to the growth of India's generic drug industry.

Reverse engineering became instrumental in India's drug manufacturing. Companies analyzed the final medication, discerning its process and ingredients to replicate it. By slightly modifying the original process while retaining the same ingredients, they circumvented patent violations, producing the same drug. The Indian pharmaceutical sector experienced exponential growth between 1970 and 1980, with the number of firms more than doubling. Over time, the gap between original innovation and India's generic production shortened, reflecting the industry's increasing efficiency. For instance, Ibuprofen debuted in 1967, with its Indian generic counterpart emerging in 1973. However, when Ciprofloxacin entered the global market in 1986, India swiftly developed its version within a mere three years.

ESTABLISHMENT OF PRIVATE SECTOR

In the 1980s and 1990s, India's pharmaceutical industry witnessed the emergence of several private sector companies, including Sun Pharmaceuticals, Cipla, Dr. Reddy's Laboratories, and Ranbaxy Laboratories. These companies focused on developing and manufacturing generic drugs for domestic and international markets.

ESTABLISHMENT IN LIEU OF HIV/AIDS TREATMENT

In the late 1990s and early 2000s, Indian generic drug manufacturers played a pivotal role in the global fight against HIV/AIDS by producing affordable antiretroviral drugs (ARVs). Companies like Cipla and Ranbaxy Laboratories significantly lowered the cost of HIV/AIDS treatment by offering generic versions of patented ARVs, making them accessible to millions of people in developing countries.

TRIPS COMPLIANCE: THE GAME CHANGER

On 1st January 1995, India became party to Trade-Related Aspects of Intellectual Property Rights (TRIPS) under the World Trade Organization (WTO). The TRIPS compliance motivated the country to introduce the culture of innovation and to foster the overall development in the era of globalization. As a result, in 2005, India amended its patent law to comply with the TRIPS Agreement. This change introduced product patents for pharmaceuticals for the first time in India.

Beyond, India implemented safeguards such as compulsory licensing and patent opposition to protect public health and promote access to medicines. Further, section 3(d) of the Indian Patents Act, 1970, is a key provision that restricts the granting of patents for incremental improvements of existing drugs unless they demonstrate significantly enhanced efficacy. This provision aims to prevent evergreening, where pharmaceutical companies make minor modifications to existing drugs to extend their patent protection. In addition, India does not provide patent term extensions for pharmaceuticals, unlike some other countries. This means that the term of a patent for a pharmaceutical product is generally 20 years from the date of filing the patent application, without extensions for regulatory review or marketing exclusivity.

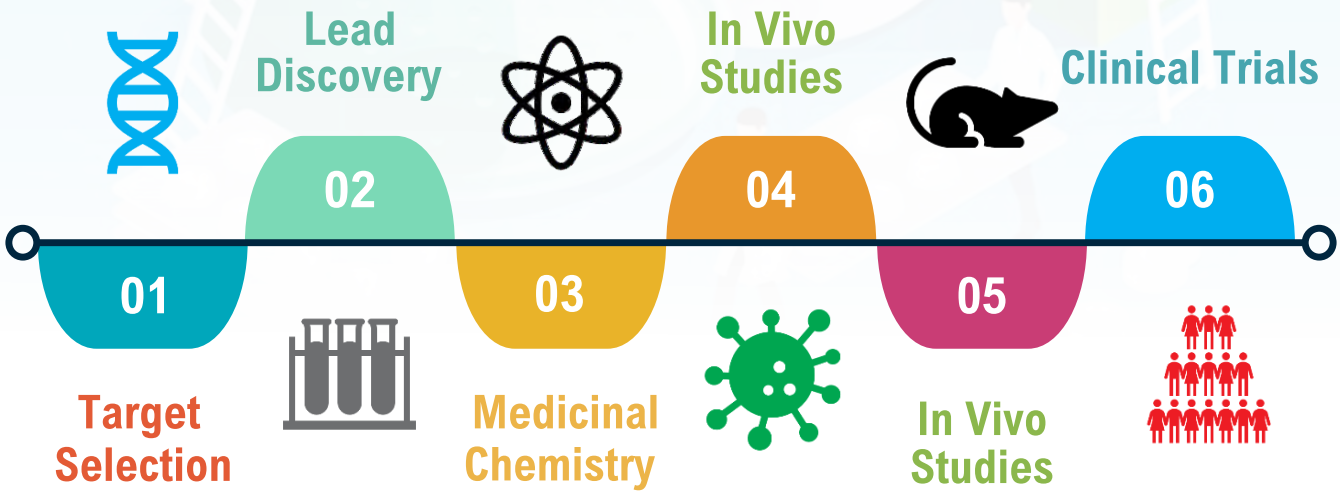
However, instead of walking on the path of innovation, the pharmaceutical sector chose to become a global generic drug manufacturer. Although, the decision is praised for supplying affordable medicines to markets around the world, however, on the other hand, India suffered a major setback in terms of innovation ecosystem development in the country. This failure not only sabotaged the growth of Indian pharmaceutical R&D sector, but also became a major hurdle in country's economic development.

NCE: THE LAGGARD

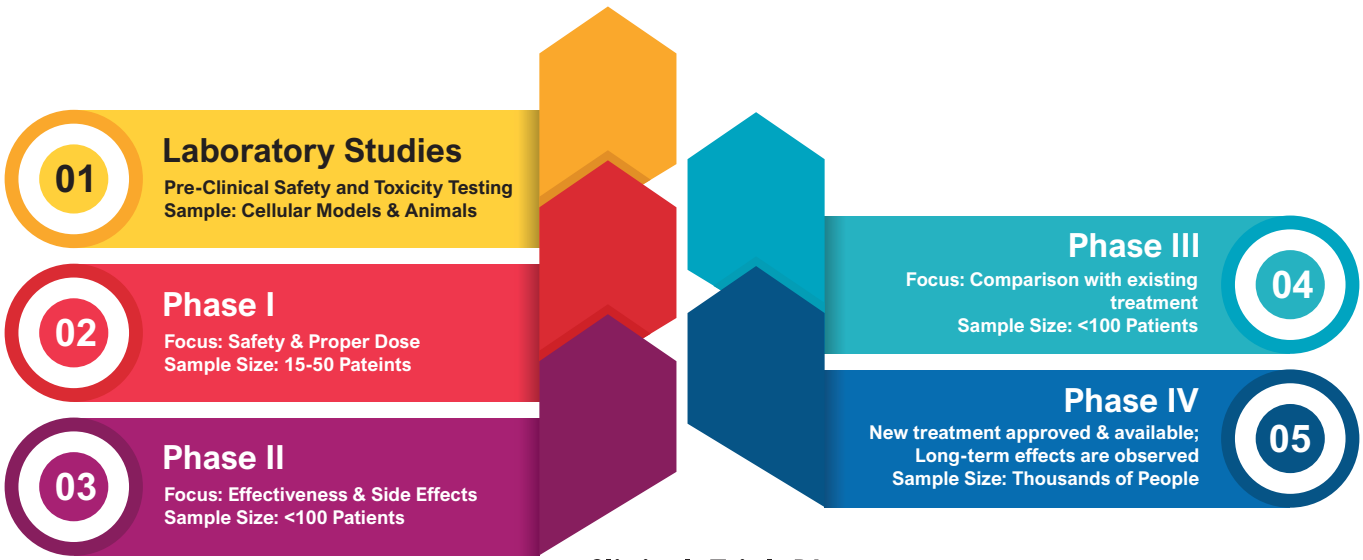
R&D for a NCE is a comprehensive and intricate process aimed at discovering and developing novel drugs to address unmet medical needs. It typically progresses through several stages. The process begins with the discovery phase, where scientists identify potential drug targets through extensive research into disease mechanisms and pathways. High-throughput screening and computational modeling aid in identifying molecules with therapeutic potential. Promising leads undergo lead optimization, refining their pharmacological properties while minimizing toxicity through medicinal chemistry techniques.

Preclinical development follows, with selected lead compounds undergoing rigorous testing in laboratory models to evaluate safety, efficacy, and pharmacokinetics. This phase provides crucial data for selecting the most promising candidate for clinical trials. Clinical development involves three phases of trials. Phase I assesses safety and pharmacokinetics in healthy volunteers, while Phase II evaluates efficacy and optimal dosing in patients. Phase III confirms efficacy, safety, and monitors adverse effects in larger patient populations.

Regulatory approval is sought after successful completion of clinical trials, with a New Drug Application (NDA) submitted to regulatory agencies for review. Post-marketing surveillance ensures continued monitoring of the drug's safety and effectiveness in real-world settings.



Stages of Drug Discovery and Development



Clinical Trial Phases

It is troubled to observe that the global innovation and invention ranking does not feature any Indian pharmaceutical industry, despite its monopoly over the global generic market. India's standing in the global market lags significantly. This is evident in the extensive time and cost associated with developing new drugs, coupled with the relatively low chances of these drugs reaching the market. Consequently, the Indian pharmaceutical sector has witnessed minimal investment in R&D due to the substantial risks and costs involved, especially when compared to generic drug development. The drug discovery process, characterized by long-term commitments, high risks, and intricate regulatory processes, has impeded the pace of new drug development in India.

RANK	INNOVATION INDEX 2023	INVENTION INDEX 2023
1	Pfizer	AstraZeneca
2	Johnson & Johnson	Johnson & Johnson
3	AstraZeneca	Regeneron
4	Roche	Eli Lilly
5	Bristol-Myers Squibb	Pfizer
6	Boehringer Ingelheim	Merck & Co
7	Eli Lilly	Novartis
8	Gilead	BeiGene
9	GlaxoSmithKline	Bristol-Myers Squibb
10	Moderna	Vertex Pharmaceuticals

Source: IDEA Pharma

GENERIC VS PATENTED DRUGS: THE REAL PAIN

New drug development takes around 7-10 years for completing its cycle before entering the market for public use. The entire process costs approximately 1-2 billion USD. In India, where the cost of clinical trials and research and development activities may be lower compared to developed countries, the cost of new drug development is generally expected to be lower. Additionally, factors such as access to a skilled workforce, lower labor costs, and a large patient population for clinical trials can contribute to cost savings in drug development.

Despite the potentially lower costs, developing a new drug in India still requires substantial investment in research, preclinical and clinical trials, regulatory compliance, manufacturing, and marketing. Companies may also incur additional expenses related to intellectual property protection, licensing agreements, and post-marketing surveillance.

Drug regulations in India are overseen at both the central and state levels. The Central Drugs Standard Control Organization (CDSCO) is tasked with approving new drugs, overseeing clinical trials, and issuing drug licenses. Approval for generic drugs necessitates Form 44 submission, along with a treasury challan of INR 15,000 for active ingredients intended for use over one year and INR 50,000 for those for use under one year in India. Additionally, alongside Form 44, applicants must provide a copy of the manufacturing license and pertinent chemical and pharmaceutical information about the active ingredients. It's worth noting that the approval process for generic drugs in India typically spans around 12 months.It's important to note that the generic drug approval process in India is generally faster and less expensive compared to the approval process for new drugs. This is because generic drugs rely on the safety and efficacy data of the RLD and do not require extensive clinical trials. As a result, considering the economic stature of India, the Indian pharmaceutical companies align their interests majorly towards generic drugs, neglecting the need for innovation and development of indigenous NCEs.

Further, the brain-drain also pose a great challenge in cultivating the innovation culture in Indian pharmaceutical industry.The phenomenon of PhDs, MPharm and MSc Chemistry students migrating from India, notably in the domain of drug innovation research, is a significant concern. Talented individuals are drawn abroad by factors like insufficient research funding, infrastructure limitations, and superior opportunities overseas. This outflow diminishes India's access to invaluable scientific expertise and impedes its capacity for pioneering drug discovery and innovation. Additionally, navigating the intricate regulatory landscape and ensuring compliance with international standards pose significant hurdles.

GENERIC MARKET: REQUIREMENT TO REMAIN STATUS QUO

Indian generic manufacturers operate within the framework of patent law provisions, including pre-grant and post-grant oppositions, which have posed challenges to the approval of numerous innovator drugs. These challenges often hinge on grounds that discourage the grant of patents for incremental innovations. In contrast, jurisdictions such as the European Patent Office, the United States, China, and Australia have been more inclined to grant patents for even minor innovations and incremental advancements.

The Patent Act of 1970 originally exclusively conferred process patents. However, upon India's accession to the Agreement on TRIPS and the subsequent amendment of the patent act in 2005, product patents became permissible in India. In alignment with its objective to bolster the generic drug sector, the Indian Patent Act includes several provisions aimed at regulating and enhancing the advantages for generics, thereby facilitating the availability of drugs at affordable prices.

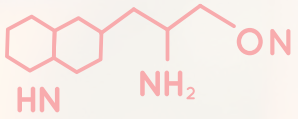
The addition of Section 3(d) of the patent system sparked mixed reactions in the pharmaceutical industry. Indian generic manufacturers praised it for countering evergreening and promoting generic drug production. However, innovator drug manufacturers criticized it for hindering patent acquisition without demonstrating significant efficacy improvements, raising concerns about TRIPS compliance.

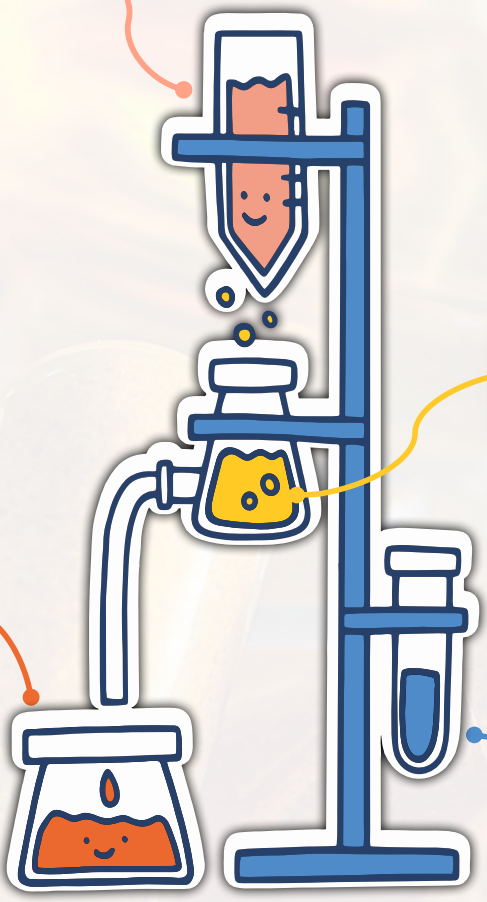
The Indian Patent Act includes provisions for pre-grant and post-grant oppositions, revocation, and compulsory licenses. These measures aim to prevent the granting of frivolous and incremental inventions and allow for monitoring even after the grant to ensure that patented innovations are effective in India. Opposition of patent of a new drug is a significant trend followed by India, reflecting the country's commitment to balancing intellectual property rights with public health interests. At the same time, being the opposition leader of innovator drug patents, Indian pharmaceutical sector poses great threat to the innovation and development of India's healthcare sector potential as well.

INNOVATION ANALYSIS

NCE

Sofosbuvir
Trikafta
Sorafenib
Sunitinib
Pibrentasvir
Daclatasvir
GSK3036656
Lenacapavir
OPC-167832
Daclatasvir
Atazanavir
Valganciclovir
Enzalutamide
Simepravir
Glecaprevir
Velpatasvir
Molnupiravir
Ledipasvir
Velpatasvir
Dolutegravir
Telacebec
Dapagliflozin





OPPONENTS

Sahara
Cipla Ltd.
Mylan Laboratories Ltd.
UPNP +& INP+
IPA
BDR Pharmaceuticals Ltd.
Mylan Laboratories India
Natco Pharma Ltd.
Poonam Singh
Fresenius Kabi Oncology Ltd
Nai Umang Positive Welfare Society
Panacea Biotech Ltd.
Matrix Laboratories Ltd.
DNP+
KNP+
PWN+

REFUSED

Tenofovir	568/MUMNP/2011
Enzalutamide	9668/DELNP/2007
Lopinavir/Ritonavir	726/MUMNP/2009
Sunitinib	IN/PCT/2002/00785/DEL
Valganciclovir	959/MAS/1995
Sorafenib	1960/DELNP/2007
Nilotinib	9322/DELNP/2007
Tenofovir Disoproxil	896/DEL/2002
Raltegravir	4187/DELNP/2007
Teneligliptin	3176/KOLNP/2007
Elvitegravir	5576/DELNP/2008
Bedaquiline	1220/MUMNP/2009
Dasatinib	4309/DELNP/2006

PATENTEE

Gilead Sciences, Inc
Bristol-Myers Squibb Holdings Ireland Unlimited Company
The Regents of the University of California
Abbott Laboratories
Sugen Inc., USA, Pharmacia & Upjohn Company
F. Hoffmann-la Roche Ag
Bayer Pharma Aktiengesellschaft
Novartis
MSD Italia S.r.l.
Mitsubishi Pharma Corporation
Japan Tobacco, Inc.
Janssen Pharmaceutica

In last 2o years,
More than 165 (45 NCEs) foreign patent applications
have been opposed by Indian entities
including individuals and NGOs using
Section 25(1) of Indian Patents Act

Disclaimer: The data presented is for the brief overview of the industry status. Some opposed drugs are not listed because of incomplete status information/refusal of patents based on application merit/demerit.

GENERIC: GOOD FOR INDUSTRY'S HEALTH

Based on the information provided, it is evident that the Indian Pharmaceutical Industry heavily focuses on generic drugs. Simultaneously, there appears to be a strategic misuse of Section 3(d) and Pre-Grant Opposition mechanisms to either delay the patent granting process or refuse/revoke NCEs submitted by international entities. Section 3(d) is a unique provision in the Indian Patent Act that prevents the patenting of new forms of known substances unless they result in enhanced efficacy. This clause was introduced to prevent "evergreening," a practice where pharmaceutical companies make slight modifications to existing drugs to extend their patent life. Misuse in this context refers to the pharmaceutical industry's criticism that Section 3(d) is overly stringent and limits innovation and the introduction of improved drugs.

Conversely, public health advocates argue that this provision is crucial for ensuring the availability of affordable generic medicines and preventing monopolies on life-saving drugs.

The controversy around these mechanisms often centers on the balance between encouraging innovation and ensuring access to affordable medicines. Critics argue that misuse of pre-grant opposition and the stringent application of Section 3(d) can hinder pharmaceutical innovation and delay the introduction of new and improved medicines. On the other hand, supporters believe that these measures are essential for public health interests, ensuring that only genuine innovations are patented and affordable generic versions of drugs are available to the public.

Understanding the balance and implications of these legal mechanisms requires a nuanced consideration of both public health goals and the incentives necessary to foster pharmaceutical research and development.


H2

INNOVATION PATH: NEED OF THE HOUR

The patent system plays a crucial role in the competitive business environment, serving multiple key functions that are instrumental in fostering innovation, securing investments, and ensuring a healthy competition among businesses. Knowing that inventions can be protected through patents, companies are more likely to invest in research and development. This investment not only leads to the creation of new products and services but also promotes continuous improvement in existing offerings, driving technological advancement and economic growth.

While generics are often seen as a means to increase market competition and reduce costs for consumers, they can also be viewed through the lens of potential anti-competitive activities, especially from the perspective of original innovators. Generics from an innovation standpoint is that they can undermine the incentives for original research and development.

While the Indian pharmaceutical industry is a critical sector for both the national economy and global healthcare, steps towards innovation and strong IP regime would strengthen to preventthe anti-competitive practices and would ensure that it operates fairly and contributes to the availability of affordable and innovative medicines. A strong and balanced IP regime is crucial for fostering a competitive and innovative business environment in India. By protecting the rights of innovators while ensuring fair competition, such a framework can contribute to economic growth, consumer welfare, and the global competitiveness of Indian industries. However, careful implementation and enforcement are key to realizing these benefits without stifling competition or innovation.

THE WAY FORWARD: ATMANIRBHAR BHARAT

Improving the pharmaceutical R&D ecosystem in India requires a multi-faceted approach, addressing both the infrastructure for innovation and the regulatory, financial, and educational frameworks supporting it. India's pharmaceutical industry has been a global leader in generics, but moving further into innovative drug development necessitates enhancing the R&D ecosystem. Improving the pharmaceutical R&D ecosystem in India is a comprehensive endeavour that requires coordinated efforts across government, industry, academia, and the regulatory framework. By increasing investment, fostering collaboration, streamlining regulations, developing human resources, focusing on innovation, and creating an enabling environment, India can enhance its pharmaceutical R&D capabilities and emerge as a leader in innovative drug development on the global stage.

It is imperative to emphasize that fostering innovation within the pharmaceutical sector is paramount for India's continued growth and competitiveness on the global stage. While India has earned acclaim as a leading manufacturer of generic drugs, there exists a pressing need to transition towards becoming a hub for NCE development. This transformation is essential for India to elevate its status from merely supplying affordable generic medications to pioneering the discovery and development of novel drugs that address unmet medical needs worldwide. By prioritizing innovation, India can not only enhance its reputation as a center for pharmaceutical excellence but also contribute significantly to advancing global healthcare outcomes and fostering economic growth. Therefore, investing in research and development, fostering a culture of innovation, and providing support for NCE development initiatives are crucial steps in propelling India towards the coveted position of a premier global NCE developer.

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https://www.ipindia.gov.in/

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