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Medical Entrepreneurship and Generic Orphan Drug Production in India: A Legal Analysis

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ABSTRACT
India is home to between 72 and 96 million persons living with rare diseases, yet it remains without a dedicated Orphan Drug Act and lacks the structured incentives, including market exclusivity, tax credits, and protocol assistance, that have catalysed orphan drug development in the United States and the European Union. This article examines how medical entrepreneurship, operating within the existing legal architecture of the Patents Act, 1970, the New Drugs and Clinical Trials Rules, 2019, and the National Policy for Rare Diseases, 2021, can accelerate the domestic production of generic orphan drugs in India. Using doctrinal legal analysis and a structured review of pharmaceutical entrepreneurship literature, the article identifies three operative legal pathways: patent challenge under Section 3(d), compulsory licensing under Section 84, and the CDSCO clinical trial waiver for orphan applications. The article further proposes a framework for targeted legislative reform to unlock generic orphan drug entrepreneurship at scale.
Keywords: Orphan Drugs, Medical Entrepreneurship, Indian Patent Law, Rare Diseases, Section 3(d), Compulsory Licensing, CDSCO, NPRD 2021, Generic Pharmaceuticals, TRIPS Flexibilities

1. INTRODUCTION

India's pharmaceutical sector supplies approximately 20 per cent of global generic drug volumes by quantity, serving over 200 countries and making it the single largest supplier of generic medicines globally. The industry's competitive character originates in the Patents Act, 1970, drafted following the recommendations of the Justice Ayyangar Committee, which abolished product patents in food and drug substances and permitted only process patents. This deliberate legislative choice, made in recognition of India's public health imperatives and the need to provide affordable medicines to a largely low-income population, allowed Indian manufacturers to reverse-engineer patented molecules and supply affordable generics both domestically and internationally for over three decades. The resulting industrial base today includes approximately 3,000 pharmaceutical companies and over 10,500 manufacturing units, many of which are approved by stringent regulatory authorities including the United States Food and Drug Administration and the European Medicines Agency.The transition to a product patent regime in 2005, compelled by India's obligations under the Agreement on Trade-Related Aspects of Intellectual Property Rights, fundamentally altered this landscape. Under the amended Patents Act, new chemical entities in pharmaceutical substances became patentable for a period of twenty years from the date of application, subject to the conditions and exclusions provided in the Act. India retained; however, the flexibility tools embedded in its amended patent law: the anti-evergreening provision of Section 3(d) and the compulsory licensing mechanism of Section 84. The former prevents secondary patents on known substances that offer no enhancement of therapeutic efficacy; the latter allows any interested person to apply for a compulsory licence where a patent is not being worked in India, is not reasonably affordable, or does not satisfy reasonable public requirements. Both provisions reflect the explicit accommodation of public health flexibilities permitted under the Doha Declaration on TRIPS and Public Health adopted by the WTO Ministerial Conference in November 2001.Against this backdrop, orphan drugs, defined under the New Drugs and Clinical Trials Rules, 2019 as medicines intended to treat conditions affecting not more than five lakhs, or 500,000, persons in India, represent an acute and largely unaddressed public health challenge. India is estimated to host between 72 and 96 million patients living with approximately 7,000 to 8,000 identified rare diseases, yet the commercial and regulatory infrastructure to serve these patients remains critically underdeveloped. Most orphan drugs available to Indian patients today are imported originator products priced at levels entirely inaccessible to most of the population. This article examines whether medical entrepreneurship, operating within the existing legal framework, can bridge this gap and what targeted legislative reform would make it possible to do so at scale.

2. REVIEW OF LITERATURE

The commercial logic of orphan drug development was substantially reframed by Meekings, Williams, and Arrowsmith (2012), who demonstrated empirically that, in regulated markets with robust exclusivity protections, the financial returns to orphan drug development had become more favourable than those for non-orphan drugs. Their analysis, drawing on data from the United States Orphan Drug Act, 1983 and its European Union counterpart under Regulation (EC) No 141/2000, established the foundational empirical argument that legal incentives do alter pharmaceutical investment behaviour in the rare disease context. This finding has since underpinned much of the comparative policy literature on why India's absence of a dedicated Orphan Drug Act constitutes a structural gap rather than a mere regulatory oversight, and it is directly relevant to any assessment of what legislative reform would be required to catalyse domestic Indian investment in this space.

In the Indian policy context, Kurian, Krishnan, and Sappani (2021) argued that rare diseases represent a sustained blind spot in Indian health policy, characterised by the absence of a comprehensive patient registry, fragmented institutional responses across central and state governments, and the near-complete absence of domestic therapeutic development. A 2024 systematic review published in the Orphanet Journal of Rare Diseases by Ranade and colleagues confirmed that Indian patients are routinely excluded from global orphan drug clinical trials, attributing this to the underdevelopment of disease registries, the absence of specialist investigator networks, and the lack of regulatory incentives comparable to those in the United States or European Union. Gokhale, Rajan, and Kamble (2020) further demonstrated that epidemiological data on rare disease prevalence in India remains severely limited, with the Indian Council of Medical Research's National Rare Disease Registry recording only a fraction of the conditions estimated to affect the population, a data deficit that itself discourages commercial investment.

The legal dimensions of pharmaceutical access have attracted concentrated scholarly attention following the Natco Pharma v. Bayer Corporation compulsory licence of 2012, the first and to date only compulsory licence granted in India under Section 84 of the Patents Act, 1970. Liu (2015), writing in the Harvard International Law Journal, analysed the Controller of Patents' interpretation of the reasonable affordability ground under Section 84(1)(b) as a potentially broad instrument for securing generic access to high-priced specialty medicines, while cautioning that subsequent rejections in Lee Pharma and BDR Pharmaceuticals demonstrated the high evidentiary threshold that Section 84 imposes on applicants. Basheer and Ayyangar (2006) provided the foundational account of Section 3(d) as a TRIPS-compatible instrument designed specifically to resist pharmaceutical evergreening, an analysis affirmed and elaborated by the Supreme Court in Novartis AG v. Union of India (2013) 6 SCC 1, where the Court held that enhanced efficacy for the purpose of the section means therapeutic efficacy and not merely improved physicochemical properties.

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On the policy and legislative reform dimensions, Dubey and Kumar (2022) provided a critical review of the National Policy for Rare Diseases, 2021, identifying the absence of statutory exclusivity incentives as the most significant structural barrier to domestic orphan drug development and contrasting India's position unfavourably with the incentive architectures of the United States, European Union, and Japan. Chaudhari, Mackintosh, and Mujumdar (2010) offered an earlier industry-level account of India's generic pharmaceutical sector as a public health asset, tracing how the process patent regime of the pre-2005 era enabled the emergence of a globally competitive industry and arguing that the post-TRIPS transition required new policy instruments to preserve the public health function of Indian generics manufacturing. From the entrepreneurship theory literature, Shane and Venkataraman (2000) argued that entrepreneurial opportunity is fundamentally shaped by the property rights structures created by legal and institutional environments, while Aldrich and Martinez (2001) demonstrated that market entry strategies in legally complex industries must account for both formal legal barriers and the informal institutional constraints that shape competitive dynamics. These theoretical contributions have not previously been applied to the specific context of generic orphan drug entrepreneurship in India.

3. RESEARCH METHODOLOGY

This article employs doctrinal legal analysis as its primary method, supplemented by a structured review of the pharmaceutical entrepreneurship and public health literature. Doctrinal analysis involves the systematic examination of primary legal sources to identify the operative legal rules and their application to the specific context of generic orphan drug entrepreneurship in India.

3.1. Research Method

The research adopts a doctrinal approach, analysing primary legal sources including the Patents Act, 1970 as amended in 2005, with particular attention to Sections 3(d), 84, and 92-A; the Drugs and Cosmetics Act, 1940; the New Drugs and Clinical Trials Rules, 2019; and India's treaty obligations under the TRIPS Agreement and the Doha Declaration on TRIPS and Public Health, 2001. Judicial decisions examined include the Supreme Court's judgment in Novartis AG v. Union of India (2013) 6 SCC 1, the Intellectual Property Appellate Board's decision in Bayer AG v. Natco Pharma (2013), and the Controller of Patents' orders in Lee Pharma v. AstraZeneca (2015) and BDR Pharmaceuticals v. Bristol Myers Squibb (2013).

3.2. Data Sources

The secondary literature review drew on peer-reviewed articles, policy documents, and working papers identified through searches of PubMed, SSRN, and Google Scholar. Primary legislative sources including the text of the National Policy for Rare Diseases, 2021, and the New Drugs and Clinical Trials Rules, 2019, were obtained from official government repositories. Sources were evaluated for methodological rigour, relevance to the Indian regulatory context, and recency, with preference given to empirical studies and legally-grounded analyses published after 2005.

4. STATEMENT OF THE PROBLEM

India confronts a structural paradox. Its pharmaceutical industry possesses the technical capability to produce complex off-patent generics at global scale, yet it has not entered the generic orphan drug market in any systematic way. The reasons are both legal and institutional. Orphan drugs approved in the United States and European Union carry overlapping intellectual property protections in India that may include composition-of-matter patents, formulation patents, and method-of-treatment patents. Even where the primary composition patent has expired or was never granted in India, secondary patents filed during a product's commercial life can delay generic entry.

The absence of a dedicated Indian Orphan Drug Act means there is no statutory data exclusivity or market exclusivity to reward the first domestic generic entrant, eliminating the commercial rationale that has attracted investment in analogous markets abroad. This gap is compounded by the absence of reliable rare disease patient registries. Without reliable prevalence data, the investment logic for orphan drug development cannot be constructed, and the cycle of neglect self-reinforces: absent registry data, no investment; absent investment, no domestic production; absent domestic production, no price competition with originator drugs; and absent competitive pricing, no affordable treatment for patients.This article proceeds from the premise that the existing Indian legal framework contains tools capable of disrupting this cycle, provided they are deployed with legal precision and complemented by targeted legislative reform.

5. DISCUSSION

5.1. Section 3(d) and Patent Challenge Strategy

Section 3(d) of the Patents Act, 1970 excludes from patentability the mere discovery of a new form of a known substance that does not result in an enhancement of known efficacy. The Supreme Court confirmed in Novartis AG v. Union of India (2013) that efficacy in this context means therapeutic efficacy, and that physicochemical improvements such as better solubility do not satisfy the standard unless they translate into improved therapeutic outcomes. A systematic freedom-to-operate analysis for any target orphan drug should identify which Indian patents cover the molecule and which are potentially vulnerable to challenge under this provision.

Pre-grant oppositions under Section 25(1) and post-grant oppositions under Section 25(2) of the Patents Act provide procedural vehicles for challenging such patents before the patent office and, on appeal, the Intellectual Property Division of the relevant High Court. An entrepreneur who successfully opposes a secondary patent reduces the freedom-to-operate risk for generic production and acquires a durable competitive advantage in the Indian market for the affected product.

5.2. Compulsory Licensing under Section 84

Section 84 permits any interested person to apply to the Controller of Patents for a compulsory licence after three years from the date of patent grant, on three grounds: that the reasonable requirements of the public have not been satisfied; that the patented invention is not available at a reasonably affordable price; or that the patented invention is not being worked in India. The sole compulsory licence granted in India, awarded to Natco Pharma in March 2012 for sorafenib tosylate, demonstrated that a price exceeding Rs. 2.8 lakh per month satisfies the affordability ground. The Controller set the generic price at approximately Rs. 8,880 per month, a reduction of over 96 per cent.

For orphan drugs, which are among the most expensively priced medicines in any market, the affordability ground is analytically compelling. However, the rejections in Lee Pharma v. AstraZeneca (2015) and BDR Pharmaceuticals v. Bristol Myers Squibb (2013) demonstrate that Section 84 requires high evidentiary preparation: a genuine prior effort to obtain a voluntary licence, demonstrated manufacturing capacity, and evidence quantifying the unmet patient need.

5.3. CDSCO Regulatory Concessions and Entrepreneurial Structuring

The New Drugs and Clinical Trials Rules, 2019 permit the CDSCO to waive the requirement for local clinical trials for orphan drug applications, allowing reliance on data generated in foreign jurisdictions. For small-molecule orphan drugs already approved by a recognised regulatory authority such as the United States Food and Drug Administration or the European Medicines Agency, the applicable regulatory pathway remains a bioequivalence-based abbreviated application, with the clinical trial waiver eliminating the most capital-intensive element of the development pathway. This concession substantially lowers the regulatory investment threshold relative to both originator orphan drug development and new drug registration more generally, and it has been insufficiently recognised in the existing literature as a commercially significant enabler of generic orphan drug entrepreneurship.

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The National Policy for Rare Diseases, 2021 designates eleven government institutions as Centres of Excellence for rare disease diagnosis and treatment, which represent clinical partnership platforms for bioequivalence studies, pharmacovigilance, and patient registry development. An entrepreneur structured to partner with a Centre of Excellence gains access to the specialist clinical networks and patient populations essential for rare disease drug development, while simultaneously building the institutional relationships required to satisfy CDSCO post-authorisation surveillance requirements. The combination of the Section 3(d) challenge pathway, the Section 84 compulsory licence mechanism, and the CDSCO clinical trial waiver creates a realistic, legally grounded entry strategy for a mid-sized Indian pharmaceutical firm with existing active pharmaceutical ingredient manufacturing capability and a dedicated rare disease legal and regulatory function.

6. FINDINGS OF THE STUDY

1. India's existing legal framework contains three operative pathways for generic orphan drug entrepreneurship: patent challenge under Section 3(d), compulsory licensing under Section 84, and the CDSCO clinical trial waiver available under the New Drugs and Clinical Trials Rules, 2019.
2. The absence of a dedicated Orphan Drug Act, the lack of statutory data exclusivity for first domestic generic entrants, and the inadequacy of the National Rare Disease Registry collectively constitute the primary structural barriers to domestic generic orphan drug production.
3. The Section 84 compulsory licensing pathway, while legally available, imposes high evidentiary standards as demonstrated by the rejections in Lee Pharma v. AstraZeneca (2015) and BDR Pharmaceuticals v. Bristol Myers Squibb (2013), requiring thorough preparatory investment from any entrepreneur seeking to deploy it.
4. The Centres of Excellence designated under the National Policy for Rare Diseases, 2021 represent underutilised institutional platforms for clinical partnership, patient registry development, and bioequivalence study design.

7. FUTURE DIRECTIONS

The most immediate legislative priority is the enactment of dedicated orphan drug provisions within the Drugs and Cosmetics Act, 1940 or through a standalone statute, establishing a defined period of data exclusivity for the first domestic generic entrant in a rare disease indication. The expansion and mandatory institutional update of the National Rare Disease Registry under the Indian Council of Medical Research is equally critical. Reliable prevalence data, disaggregated by disease, state, and patient demographics, is a precondition for rational investment decisions and for the epidemiological evidence required to support Section 84 compulsory licence applications.

A tax credit on qualifying orphan drug clinical development expenditure, modelled on the provisions of the United States Orphan Drug Act, 1983, would reduce the effective cost of generic orphan drug development and extend entrepreneurial participation to smaller pharmaceutical enterprises. Regional coordination with developing country neighbours through mechanisms such as the BRICS Medicines Initiative and the SAARC framework for pharmaceutical cooperation could also create export market volume sufficient to make generic orphan drug manufacturing commercially viable even where the Indian domestic patient population for a given rare disease is small.

8. CONCLUSION

India's legal framework already contains the tools necessary to support a domestic generic orphan drug industry. The anti-evergreening provision of Section 3(d), the compulsory licensing mechanism of Section 84, the export licence pathway of Section 92-A, and the CDSCO's clinical trial waiver for orphan applications collectively constitute a legal opportunity set that is not replicated in most other jurisdictions. The challenge is one of deployment rather than availability: legal tools must be applied with precision, evidentiary standards must be met rigorously, and the regulatory pathway must be navigated in partnership with the Centres of Excellence designated under the National Policy for Rare Diseases, 2021.

Three targeted reforms would materially accelerate this process: dedicated data exclusivity for the first domestic generic entrant in a rare disease indication; the expansion and mandatory update of the National Rare Disease Registry; and a tax credit on qualifying orphan drug clinical development expenditure. India's generic pharmaceutical sector has demonstrated across four decades that affordable medicines can be produced and distributed at scale when the legal framework supports entrepreneurial action. What is required is legally informed medical entrepreneurship, supported by incremental but well-targeted legislative reform.

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