Open Innovation in New Drug Research:
The Case of the Indian Pharmaceutical Sector

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Declaration of Authenticity and Author's Rights

This thesis is the result of the author's original research. It has been composed by the author and has not been previously submitted for examination, which has led to the award of a degree.

Signed: Bhawani Bhatnagar

Date: June 6, 2017

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"In life you will realise there is a role for everyone you meet. Some will test you, some will use you, some will love you and some will teach you. But the ones who are truly important are the ones who bring out the best in you. They are the rare and amazing people who remind you why it's worth it"
Unknown

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Abstract

The legislative environment in India underwent changes in 2005 leading to product patent protection for pharmaceuticals. Equipped with superior process capabilities acquired for generic manufacturing, the pharmaceutical sector embarked on a journey to undertake radical innovation. The aim of the research is to explore how changes in the national environment and asset profile of firms have influenced openness for research of novel drugs. The review of literature, synthesis of conceptual framework and data analysis is shaped by the theoretical approaches of national innovation systems (NIS), dynamic capabilities and open innovation. The theoretical lens of *national innovation systems* enables our understanding of what shapes innovation behaviour of a firm, *open innovation* approach provides a description of how firms adopt open innovation and *dynamic capabilities* concept supports the interpretation of why firms differ in opening up their boundaries. The answers are examined through nine cases of established and start-up pharmaceutical firms in India.

New drug research is challenging and requires collaborative effort predominantly at the drug discovery stage. However, in the Indian setting, research networks are minimal and there is little cohesion within the ecosystem among firms, research institutes and universities. Firms are opening up their R&D innovation process to foreign partners through open innovation strategies; in-licensing, out-licensing and collaborative innovation that vary by stage of drug research. The open innovation pathways adopted by firms are influenced by four 4Rs - *resource supplementation* and *risk mitigation* that initiate open innovation, *retention of control* and *revenue maximization* that impel closed innovation. The insights into the strategic trends of these firms unveil an open innovation framework that is relevant to the open innovation theory and praxis.

1 Introduction

The Agreement on Trade-Related Aspects of Intellectual Property (TRIPS) signed in 1995 by all the members of the World Trade Organisation (World Trade Organisation), to harmonise patent protection laws in pharmaceuticals, has created many opportunities for developing countries to innovate and develop new medicines, under a high patent protection environment. One of the objectives of the TRIPS agreement is to provide incentives for developing countries to invest in research and development (R&D) for new medicines and in this way stimulate meaningful innovation. The most important concern of TRIPS has however been to restrict imitation of patented drugs in developing countries and increase exports of drugs from developed countries, raising widespread concerns on availability of low priced generic medicines and sustenance of generic drugs industry in developing countries (Smith Richard et al., 2009). Developing countries with manufacturing capabilities like India were given a time period of ten years to achieve transition to the stringent intellectual property protection.

The legislative environment in India for the pharmaceutical sector underwent changes from a process patent environment to a product patent environment with the implementation of Patent Amendments Act 2005. This marked a significant transition point for the pharmaceutical industry, heavily dependent on generics business. The generic drugs industry in India evolved under the process patent law prevalent during the period 1970-2005. The process patent regime restricted foreign direct investment and supported domestic firms to learn capabilities for reverse engineering of drugs in a protected environment (Feinberg and Majumdar, 2001; Iyer, 2012: 57). The Indian pharmaceutical industry achieved burgeoning growth during this period and currently ranks third largest in the world (IndiaPharmaSummit, 2015).

The change in patent regime brought about important changes in the innovation landscape in India. It has led to initiation of research for novel drugs by Indian pharmaceutical firms and growth of new small companies for drug discovery research. The government also brought about important changes in the public sector such as increased availability of funds for public research, initiation of public private partnership schemes, subsidized loans and incentives for pharmaceutical firms. The terrain of research for novel drugs is difficult and complex. It

requires abnormally high investments in R&D costs (estimated costs of a new chemical entity is approximately more than one billion dollar) and is marked by high attrition rates of molecules during the clinical development stage. The success achieved by the Indian pharmaceutical sector in the generics business has equipped firms with manufacturing capabilities, regulatory knowledge, vast network of sales & distribution channels and business acumen to enter new markets. Despite this, it's a tough proposition for any Indian pharmaceutical firm to carry out the process of research and development singularly from drug discovery to drug development stage.

The pharmaceutical sector of India evolved under the aegis of a weak patent protection environment, supportive policies, massive science & technology infrastructure, large number of scientific workforce and entrepreneurial spirit. The success of the generic drugs business exemplifies the willingness of the firms to exploit commercial opportunities available in the selection environment to propel it forward. India is responding to the challenges at the macro level by pursuing open innovation pathways to steer the new drug innovation process. Ranbaxy and Zydus Cadila have launched two new drugs 'Synriam' and 'Saroglitazar', which are innovative therapies for malaria and cardiovascular disorder. With few successes and many failures witnessed by India in the domain of new chemical entity (NCE) research, the question remains can India re-create the magic of generics business in the field of research for novel drugs too?

The shift in patent regime in India is marked by extraordinary changes at the environmental and firm level and provides an interesting research setting to explore the different facets of open innovation. The aim of the research study is to explore how changes in the national environment and firm's asset profile have influenced openness in firms for research of novel drugs. The answers are examined through cases of established and SMEs in India engaged in innovation of new drugs. The data is gathered through research interviews with academics, public research scientists, key public department officials and experts in the field of pharmaceutical research and secondary research. The conceptual framework draws from three theoretical perspectives: national innovation system (Freeman, 1987; Lundvall, 1992; Mowery, 1992; Nelson and Rosenberg, 1993), open innovation (HW Chesbrough, 2003) and dynamic capabilities (Teece and Pisano, 1994; Teece et al., 1997) which form the theoretical basis for this study. Firstly, the national innovation system (NIS) enables the understanding of *'what influences behaviour of a firm?'* in a changing selection environment.

The literature on NIS provides an explanation of the manner in which institutional and regulatory factors blend together to influence the rate and direction of innovation and enable formation of open innovation networks within the local innovation system. Secondly, open innovation literature informs *how firms adopt open innovation to their advantage?* Finally, the dynamic capabilities perspective provides a clarification on *'why firms differ?'* in the adoption of open innovation approaches. The 'asset profile' and 'dynamic capabilities' of a firm explain the differences in the open innovation strategy adopted by established and SMEs.

The pharmaceutical industry is one of the few industries strongly driven by scientific innovation. Investments in research and development for novel drugs, process improvements, improvements of existent drugs are of critical importance to the industry. The pharmaceutical innovation process is a complex phenomenon with only one out of 10,000 substances becoming a marketable product. A typical R&D process of a new drug takes up to 13 years and the cost of discovery and development is estimated to be a staggering US$ 1 billion (Gassmann and Reepmeyer, 2005). In spite of incorporating new technologies in the drug discovery process, there has been a gradual decline in R&D productivity, continued increase in R&D costs leading to decline in innovation (Correa, 2012).

In current times, the traditionally closed innovation model that endorses innovation in isolation is fast losing ground and open innovation in pharmaceutical research is becoming a pivotal innovation strategy (H Chesbrough, 2003a; Gassmann and Reepmeyer, 2005). Open innovation in pharmaceutical industry has gained currency for three reasons: First, *inbound innovation* allows firms to capture knowledge and capabilities from external actors and sustain innovation (HW Chesbrough, 2003; Laursen and Salter, 2005b). Inbound innovation is more relevant for high R&D intensive industry such as pharmaceuticals, as they have the built up absorptive capacity to assimilate and exploit scientific knowledge generated through external sources (Cohen and Levinthal, 1990). Second, *outbound innovation* allows exploitation of firm resources by selling or licensing-out ideas (HW Chesbrough, 2003). Thirdly, the *unification of patent policies* by Trade Related Aspects of Intellectual Property Rights (TRIPS) agreement in developed and developing countries has led to globalization of patent protection. This has opened up new market opportunities for trade and globalization of R&D (Kiriyama, 2011).

The link between appropriability regime and innovation sketched by (Arrow, 1962) and explored by many scholars asserts that a strong patent system provides incentive for firms to innovate and is imperative for the technological progress of the nation (Levin et al., 1987; Nelson and Winter, 1982). Teece (1986) outlined two important components of appropriability regime as *legal system* and *nature of technology* that determine the strength of appropriability regime. If intellectual property environment is insufficient to protect and the nature of technology is easy to imitate then the appropriability regime is *'weak'* and spurs imitation. Conversely, a *'strong'* appropriability regime that is determined by the strength of patent protection and difficult nature of technology stimulates innovation. These two factors have important implications on a firm's strategy to affect R&D and the rate and direction of innovation (Teece, 1986).

Appropriability regime is of fundamental interest to organisational scholars because it makes it easier for firms to capture R&D value (West, 2006) and support broad networks of innovation (Pisano, 2006). A strong appropriability regime enables open innovation (West, 2006) and allows an interface between inside and outside the firm in a secure environment (HW Chesbrough, 2003). When intellectual protection is guaranteed, inventors use multiple pathways to gain economic returns of their invention (HW Chesbrough, 2003; West, 2006). Pharmaceutical industry with high levels of appropriability mechanisms show high degree of openness in opening up to external knowledge sources (Laursen and Salter, 2005b). In fact, public research has been an important source of basic knowledge and occasionally industrially relevant technology for innovation (Mowery and Sampat, 2005). The biotechnology industry has its roots in the discoveries made in university laboratories (Owen-Smith et al., 2002). Several influential studies have linked collaboration between public research, large pharmaceutical firms and biotechnology firms to innovation of novel drugs (Arora and Gambardella, 1990; Cockburn and Henderson, 1996; Owen-Smith et al., 2002). A noteworthy example is the establishment of Open Innovation Drug discovery programme by Eli Lily to engage the academia in the pharmaceutical innovation process.

Governments have recognized the importance of science based interactions between public and private research sectors and have launched various initiatives since the 1970s in an effort to improve national economic performance (Mowery and Sampat, 2005; OECD, 2002). The broader national innovation system literature provides insights regarding the importance of public intervention in grooming an industrial sector. Policy intervention has enabled to

absorb the effects of changes in selection environment and has lent support in the form of financial support, education and training facilities, R&D institutions, infrastructure facilities, and regulations to enable growth of an industry (Gregersen, 1992; Hall, 2002). This has been especially true in case of developing countries such as India, Cuba, where public intervention enabled building of research capabilities, promoted education and shaped incentives to stimulate innovation & manufacturing capabilities to meet domestic healthcare needs (Mytelka, 2006).

At the firm level, the broad strategic management literature provides insights into how firms carry out adaptive processes and seek innovative ways to balance organisational resources, structure and strategy (Prahalad, 2006; Teece and Pisano, 1994). The dynamic capabilities of a firm lies in its ability to sense and adapt to external opportunities through configuration of assets and processes to attain competitive advantage (Teece and Pisano, 1994). In the context of developing countries, a mix of small budgets, and pressure of keeping prices low has led to companies exploring new ways to manage businesses. In various other sectors, India has been able to successfully leapfrog over the challenges of scarce resources and capabilities and has devised creative business models to develop affordable and sustainable innovative products in different sectors (Prahalad and Mashelkar, 2010). It is a matter of academic and industry relevance to see how the Indian pharmaceutical sector has responded to the myriad challenges of internal and external forces to innovate new drugs. Indian pharmaceutical firms balance a tightrope between in-house R&D and open innovation to combat the challenges in the national innovation system and the internal complexities of the innovation process. The open innovation pathways adopted by the Indian pharmaceutical sector and the factors that influence open innovation is the focus of this research study.

1.1 Research aim, Research questions and Objectives

The purpose of this study is to explore how changes in the national context have influenced innovation and openness in the Indian pharmaceutical firms sector. This leads us to our main research question - **How does national innovation system and asset position of a firm influence openness in the Indian pharmaceutical sector for innovation in novel drugs?** This research study uses cases of established and SME pharmaceutical firms to understand the phenomenon of open innovation in pharmaceutical setting. In this study, the patterns of

innovation in firms are studied through patent data and openness in the sector is explored using primary and secondary data from diverse sources. The research findings in this dissertation are presented as three central themes:

a) Role of national innovation system in shaping the innovation ecosystem
b) Open innovation networks within the national innovation system
c) Open Innovation strategies used in new drug innovation process

In Table 1, the three central themes have been mapped to the primary research questions and embedded research objectives.

Table 1: Key themes, research questions and research objectives used in the study

Themes	Primary Research question	Objectives
a) Role of national innovation system in shaping the innovation ecosystem	RQ1: How have changes in the institutional and regulatory level influenced the innovation ecosystem for pharmaceutical innovation?	In order to answer this question, the following objectives were pursued: • Identify the important public policy initiatives in the two patent regime and describe the positive changes and challenges in the innovation ecosystem for new drug research • To explore and understand the nature of innovation through patenting patterns and secondary data in the two appropriability regimes (Pre-2005 and Post-2005) • To develop a suitable method to undertake analysis of patent documents • To understand firm strategy through patenting patterns of international patent applications
b) Open innovation networks within the national innovation system	RQ2: How does national innovation system and asset position of a firm influence adoption of open innovation networks between firms and public sector labs & universities?	The following objectives were pursued: • Types of innovation networks formed • Role of asset profile of a firm in influencing formation of open innovation networks • Factors that influence formation of innovation networks • Factors that mitigate formation of open innovation networks
c) Open Innovation strategies used in new drug innovation process	RQ3: How does national innovation system and asset position of a firm influence adoption of open innovation strategies for novel drug research in the Indian pharmaceutical sector?	The following objectives were pursued: • Examine open innovation strategies pursued by established and SMEs • Examine open innovation strategies by stage of drug research • Identify key influencing factors which affect strategic choice

Empirical data was collected from five established pharmaceutical companies of India and four SMEs engaged in the research of novel drugs. The data was collected at two levels: sector level and firm level. The sector level data enabled to understand the broad trends in the industry and important policy initiatives by the government. The firm level data enabled to understand the business activities, nature of innovation, information about research partnerships and open innovation approaches used by firms. Table 2 shows the type of data and sources of data used in the research study.

Table 2: Data sources used in the study

Level of analysis	Type of data	Data source type	Source
Sector level	Secondary data source	Public Policy initiatives, Public Private Partnership schemes, Industry report	• Government websites • Five year plans • Reports by consultancy companies • Government published reports • Academic papers
Firm level	Secondary data source	Patent data	• Patent data from three patent offices- WIPO, US and India
		Research based partnerships, company activities, event timelines	• Press releases online magazine – Pharmabiz, Express Pharma • Annual reports • Company websites
Sector and firm level	Primary data source	Semi structured interviews	• Pharmaceutical industry professionals • University professors • Public research scientists • Senior government department officials • Experts in pharmaceutical industry

1.2 Significance of the study

Most of the open literature work on pharmaceutical R&D has been analysed in the context of developed countries (Bianchi et al., 2011; Gassmann and Reepmeyer, 2005; Hunter and Stephens, 2010; Schuhmacher et al., 2013). New drug research is a recent phenomenon in developing countries and there is sparse literature available on open innovation especially in

the pharmaceutical industry in a developing country setting. There is hence a need to focus research in open innovation in developing countries using different research settings to develop this field. The approach of this dissertation is to explicitly analyze open innovation used by Indian pharmaceutical firms for advancement in innovation of new drugs against a backdrop of changes in the Indian environment. The research findings of this study in this way contribute to theory, method and practice.

1.2.1 Contribution to Theory

The shift in patent regime generated a lot of interest among the academic scholars to examine the effect of TRIPS agreement on drug prices, access to essential medicines in India (Lanjouw, 1998), R&D intensity and innovative output of firms (A. Arora et al., 2009; Chowdhary, 2010), and patenting in India (Abrol et al., 2010; Chaudhuri, 2007; Ganguli, 1999; Kamble et al., 2012; Mueller, 2007; Simonetti et al., 2007). The contentious elements of the Indian Patents Amendment Act 2005 such as Section 3D and compulsory licensing (Ganguli, 2003) garnered much attention due to conflicting interests between innovator companies to make profit and the governments of developing countries to use the medicines for public health use. However, a systematic analysis of the relationship between institutional and regulatory forces and open innovation in the pharmaceutical sector is largely missing in the Indian setting.

This study expands on previous catching up literature (Fu et al., 2011; Mike Hobday, 1995; Michael Hobday, 1995; Patel and Pavitt, 1994; Perez and Soete, 1988) by examining the transition process of Indian firms. The exploratory study on the Indian pharmaceutical sector elucidates the understanding of factors that play an important role to aid the transition from process to product innovation in pharmaceutical research. The adoption of open innovation pathways to circumvent many of the challenges within the national innovation system is a good learning lesson for other firms in developing countries that face similar challenges to innovate a product as complex as new drug innovation.

The theoretical framework built on prior literature and empirically tested using cases of Indian pharmaceutical firms provide an explanation of why certain open innovation pathways are preferred over others. Researchers on openness have suggested that firms keep some aspects of innovation process closed (Dahlander and Gann, 2010; Laursen and Salter, 2005b) more specifically if the innovation is technologically complex (Almirall and Casadesus-

Masanell, 2010). The research findings enable to understand at which stages of the new drug R&D process firms pursue closed innovation and what factors impel firms to open up their boundaries to seek open innovation strategies and networks. In the new drug innovation process, Indian firms follow a closed innovation model in the initial discovery stage and focus more on ownership of research and intellectual property assets to enable open innovation in subsequent stages of drug development. The weak innovation networks between firms and public research institutions in the Indian context support the contention that a strong intellectual property regime is not enough to inculcate science industry networks within a national system. A strong IP regime also brings with it barriers to open innovation in the form of *paradox of openness* and *paradox of disclosure* which prevents firms and public research institutions to open up for research based collaborations. The paradox of openness comes into play when firms restrict openness to preserve their research assets from opportunism and preclude possibility of profiting from innovation (Pisano, 2006; Teece, 1986). On the other hand, the tendency of public research institutions to disclose their research through publications rather than patent leads to weak appropriability of their research and make them wary of collaborations and partnerships. In empirically testing these results in the Indian pharmaceutical sector, the research findings add to the growing literature of national innovation system, appropriability regime and open innovation and tries to integrate macro level changes to the changes at the entity level of the ecosystem.

Why do firms differ in their adaptive choices to environmental change is an intriguing question that has bothered management scholars for long. Indian firms use open innovation as an adaptive mechanism to respond to changes in the selection environment, technological complexity associated with innovation of new drugs and constraints related to resources and competence. The capability to sense and seize opportunities and shift towards a transformative mode lies within the firms and is a reflection of their dynamic capabilities. Of the nine Indian pharmaceutical companies used as case study, not all the firms exhibit the same strategic response. Firms differ not only in their open innovation approaches but also to the extent they open up to the external environment to their advantage. *An important conclusion of this study is to attribute firm differences in open innovation to their dynamic capabilities.* In this way, this study lends support to the dynamic capabilities theory by providing empirical evidence from Indian pharmaceutical sector.

The comparative differences in the strategic choices of established and SMEs help to gain an understanding of the underlying factors that influence the strategic choices. The resource profile of firms to understand firm action in response to external environments has been neglected in academic research (Priem et al., 2013). In their reflection on future directions for strategic research (Priem et al., 2013), emphasised on the need for research studies linking the resource side of the firm to environmental contexts. This study identifies resource supplementation as an important factor that propels open innovation. The comparative assessment of established and SMEs further ascertains that asset position of a firm accounts for different strategies employed at different stages of drug research. However, the asset position of a firm has little influence on the local innovation networks formed in the Indian setting. This learning is a useful contribution to the strategic management literature.

The central contribution of this dissertation is a *framework for open innovation* that links the changes at the macro environment and internal tensions at firm level to the type of innovation pathways pursued. The empirical findings of this research identify a) the key drivers of open innovation b) the 4R factors that account for differences in openness at firm level and c) the open innovation pathways adopted. The 4R factors developed in this study enables to identify the tensions at firm level to balance closed innovation with open innovation. The open innovation pathways show the distinct paths adopted by firms differentiated by open innovation strategy, local innovation networks and stage of research. In this way, this study makes an important contribution to the open innovation literature.

1.2.2 Contribution to Method

This thesis offers a methodological contribution in proposing a *unique* patent analysis method to count and segregate patents by patent type. Patent analysis is not straightforward. It is complicated by the legalities in different countries, different patent offices, their corresponding databases and the propensity of the companies to file the same patent applications in different countries. The use of patent counts as a measure of innovative output is used in various studies and upheld to be a relevant indicator of the technological activities undertaken by a firm (Acs et al., 2002; De Rassenfosse et al., 2013; Griliches, 1990; Pavitt, 1985). The abundance of data sources, different counting methods, use of reference date, level of aggregation and several other dimensions can lead to different patent counts (De Rassenfosse et al., 2013). A patent analysis hence involves important considerations such as a) how to identify pharmaceutical patents filed by a particular company b) which

patent office and database to use for patent search c) how to segregate different patent applications to identify product patents d) how to tackle duplication issues when a same patent is filed in different patent offices and e) what should be the unit of analysis – granted patents or filed patent applications? These initial deliberations, readings and process of seeking answers to these questions led to the finalisation of the patent analysis approach.

The method follows the guidelines specified in OECD patents statistics manual (Zuniga et al., 2009) and used various referential material such as academic papers (Grupp and Schmoch, 1999; Lanjouw et al., 1998; Martinez, 2010; Roehrs, 2003: , ; Scherer, 1984) and written documents in patent office websites (WIPO, 2007, 2013). Further, a certified patent professional with extensive experience in pharmaceutical industry has validated this approach. The method detailed in this study is not new per se but the uniqueness of the approach lies in combining different existing approaches to solve data related issues to extract a meaningful dataset and use text analysis to identify different patent types.

This paper undertakes count of unique, active, priority patent applications by different patent types (basic patents, secondary patents and method patents) using 20-year data from PCT, Indian and US patent offices. Two steps are significant for this patent analysis approach. First, it involves workable adjustments to the patent dataset and secondly, it employs text analysis of claims to segregate process-based patents from product patents using the method specified by (Scherer, 1984). In this way, this patent analysis method details a patent analysis approach that can be used by other researchers and practitioners.

1.2.3 Contribution to Praxis

Open innovation is adopted by many organisations in many different sectors and the learning gained about different innovation pathways has practical implications in technically complex innovation. By referencing to the practices of open innovation in Indian pharmaceutical, this research has examined how the Indian companies have mobilised external sources for funds, to speed up innovation and mitigate risk through different open innovation routes. The barriers and the limitations of open innovation practices in this setting are important insights for practitioners and managers.

This study also advances an open innovation framework that identifies the key drivers that influence open innovation at macro and micro level. The framework also explains how the 4R factors: Resource supplementation, Risk mitigation, Revenue maximisation and Retention of control guide firms to select the open innovation pathways carefully. The four open innovation pathways currently in praxis show how open innovation can be used in different ways to combat the various challenges in innovation and leverage the opportunities in the macro environment. In this way, this study is useful for managers to know how open innovation pathways can be used to exploit outside knowledge, supplement resources, reduce risk and maximise revenues. The experience and strategies of the Indian pharmaceutical firms serves as useful role model for local firms in other developing countries. Understanding the innovation pathways the Indian firms will enable them to devise their strategies and provide learning on how to exploit their advantages.

The findings presented in this research have important implications not just for understanding open innovation practices at firm level but also for policy debates on how to revive the declining public private interactions between science and industry for mutual benefits. This study brings together different perspectives of academics, public research scientists and firms and provides a holistic view of the common problems inherent in the sector. By highlighting the issues prevalent in the local innovation system, the results are useful to fuel a debate to make policies more context specific to bring about contemporary changes in the areas of innovation.

The findings of this research in a developing country setting is a useful insight for policy makers who try to imitate the policies of developed countries for achieving success. The governments of developing countries such as Taiwan and Korea have implemented supportive policies that enabled to make the semiconductor industry successful. In contrast to this, the Indian government is focusing on lacklustre funding initiatives implemented through various schemes, which is not enough to support the transition from a generics drug industry to a product innovation industry. There is hence a need for the government to step in with a unique customised innovative approach to tackle the underlying problems in the system.

1.3 Scope and structure of the dissertation

This dissertation on hand is divided into eight chapters with the following content: Chapter 1 Introduction: The current chapter provides the background context, research purpose, and significance of the study along with a structure of the dissertation. Chapter 2 Literature Review: This chapter introduces the key concepts of open innovation, national innovation system and dynamic capabilities theory, which form the theoretical part of the study. The literature on national innovation system introduces the key concepts of selection environment, science industry linkages and their link to innovation. The open innovation literature reviews the recent changes in strategy, structure and networks taking place in the pharmaceutical innovation process. The dynamic capabilities literature provides an explanation for differences in strategy response to the external changes based on its own asset profile and capability. Chapter 3 Conceptual Framework: The conceptual framework is an amalgamation of theoretical concepts and outlines the scope and research questions of the study. Chapter 4 Methodological Considerations: This chapter introduces the research framework of this dissertation by discussing the study's philosophical foundation, research design, research participants, sources of data, methods of data collection and rigor of the qualitative research study. The methods for data analysis section describes the methods used to analyze different data types. Three different methods have been used in this study a) Patent analysis approach to analyze patent documents, b) Gioia approach used to decode interview data and c) Analysis of other secondary data to compile information in a systematic manner. The patent analysis approach describes the logic of data extraction from the patent office databases and explains the text analysis approach used to categorize patent applications into different patent types. The Gioia approach (Gioia et al., 2013) was used in this study for a systematic assessment of interview data for research use. The analysis and compilation of secondary data from various sources to prepare case profiles and undertake classification of formal research partnerships into different categories is described in this section. Chapter 5 Evolution of Indian pharmaceutical industry under distinct appropriability regimes: This chapter reconstructs the evolution and development of the Indian pharmaceutical industry in the two important appropriability periods – the process patent regime from 1970 to 2005 and the product patent regime from 2005 onwards. The chapter lays out important policy initiatives undertaken by the government in both the periods and uses patent data analysis and secondary research information to show the technological progression of case firms during

both the appropriability regimes. Chapter 6 Open Innovation in Indian pharmaceutical industry: This chapter presents the empirical findings and the key themes that emerged through descriptive qualitative analysis. The first section 'Open Innovation networks within the national innovation system' explores the formation of networks between firm-university-public research labs for research of new drugs and describes the key issues, which acts as a barrier to innovation networks. The second section 'Formulating Open innovation strategies and pathways' explores the open innovation approaches pursued by case firms at different stages of new drug research. A comparative analysis is undertaken between established firms and SMEs to show the influence of firm assets and competence on the strategies adopted. Chapter 7 Discussion: This section links the conceptual framework to research findings to explain how convergence of selection environment and strategic decisions at firm level influence the nature of innovation and openness in the pharmaceutical sector. The findings of the study lead to a framework for Open Innovation that combines the local open innovation networks formed and open innovation strategies at firm level to describe the drivers and key influencing factors that affect openness in Indian pharmaceutical firms. Chapter 8 Conclusion: The closing section of the dissertation presents the conclusions that can be drawn from this contribution. This chapter outlines the limitations of the study and summarizes the main and ancillary findings by proposing future research directions.

2 Literature Review

The goal of this chapter is to review relevant academic literature that addresses an important question - How open is pharmaceutical innovation and what are the important factors in the external environment and internal environment that influences the openness of an organisation? This literature review focuses on three streams of literature: national innovation systems, open innovation and dynamic capabilities theory, each of which make a significant contribution to the conceptual framework used in this study. The literature review is divided into three parts. The first part focuses on the role of selection environment in influencing the local innovation system and harbouring innovation at an entity level. The second part examines the role of open innovation in pharmaceutical sector more specifically in the research for novel drugs. Recent academic literature on open innovation has established its growing importance in pharmaceutical research and the different ways in which firms are embracing openness in their research and development work. The third part examines how firms respond differently to the open innovation approaches using the lens of dynamic capabilities.

A key theoretical perspective highlighted in this study is the role of appropriability in influencing open innovation patterns. The presence of tight or weak appropriability regimes shapes the behaviour of firms to patent and make profits (Cohen et al., 2002; Levin et al., 1987; Teece, 1986). A strong appropriability environment is crucial in shaping the development of an industry more specifically a patent intensive industry like pharmaceuticals which heavily moulds firm incentive to undertake research and development (Levin et al., 1987). A general consensus exists in the literature regarding the 'profiting from innovation' framework that the extant appropriability regime and appropriability mechanisms are important factors that significantly influence a firm's ability to profit from innovation (Arora and Ceccagnoli, 2006; Hurmelinna-Laukkanen and Puumalainen, 2007; Teece, 1986). However, too much appropriability can introduce a myopic view in emphasizing more towards exploitation of current research assets than exploration for new ones. Such overprotectiveness may foster an inward focus for firms and restrict liasioning with external partners for innovation (Laursen and Salter, 2005a). The concept of dynamic capability provides a key theoretical basis to explain differences in firms' ability to make use of

opportunities and profit from innovation. The differences in open innovation behaviour of firms can be traced back to differences in their dynamic capabilities. This theorizing leads to important research questions with practical implications that are articulated in the conceptual framework.

2.1 National innovation system - influencing innovation ecosystem

The literature on national innovation systems (NIS/NSI) has evolved since the 1980s and attests to the importance of government policy and supporting institutions such as universities/research institutes in shaping technological advancement in a country (Gregersen, 1992; Lundvall, 1992; Mowery, 1992; Nelson Richard, 1993). The broader definition of innovation system encompasses firms undertaking industrial innovation, supporting institutions such as universities, government agencies and policies, which may shape or constrain innovation based on national characteristics (Nelson and Rosenberg, 1993). Four sets of institutions constitute the core of national system of innovation a) business firms, b) universities and similar institutions, c) public and private institutions and d) governments (Patel and Pavitt, 1994).

Technology gap and imitation lag in developing countries is ubiquitous (Freeman, 1995; Perez and Soete, 1988; Posner, 1961). Constraints, such as investment, infrastructure, knowledge & skill faced by developing countries are formidable enough to keep the gap widened between developed and developing countries (Perez and Soete, 1988). As Perez and Soete (1988) quotes:

> *"Previous capital is needed to produce new capital, previous knowledge is needed to absorb new knowledge, skills must be available to acquire new skills, and a certain development is required to create the infrastructure." (Perez and Soete, 1988: 459)*

This reflects the vicious cycle of developing countries that leads to catch up strategies and continues to keep the gap between developing countries and developed countries wide open for income, productivity growth and international differences in economic performance (Patel and Pavitt, 1994; Perez and Soete, 1988). In this vein, technological innovation is seen as a solution to bridge the gap and catch-up with developed countries (Fu et al., 2011; Perez and

Soete, 1988). Innovation is considered vital for the growth and productivity of national output and has been the central theme of discussions in the management literature (Baumol, 2002; Schumpeter, 1934; Tidd and Bessant, 2011).

Literature on latecomer innovators in East and South East Asia show how firms have emerged from being mere technology users to front end players for launching new products and processes (Mike Hobday, 1995; Michael Hobday, 1995; Hobday et al., 2004). An explaination lies in their process of innovation models pursued. The firms follow a reverse product life cycle (RPLC) theory that is based on learning, assimilation, and adaptation from the mature stage of the product life cycle and shift to creators of products in early stages of product life cycle. Through a staged transition process these latecomer firms evolve from adopters to creators of technology (Choung et al., 2014). The case of electronics sector is an excellent example to show how firms in South Korea, Taiwan, Singapore and Hong Kong emerged from being low cost assembly manufacturers of consumer goods to manufacturers of new product innovations generated in developed countries through reverse engineering. In the late 1990s, the firms made the transition towards manufacture of advanced electronics and information technology systems and managed to bridge the gap between process engineering to developing product innovation capabilities (Mike Hobday, 1995; Michael Hobday, 1995).

In the pharmaceutical sector, the technology lag has been reduced in the past through a set trajectory. The companies in developing countries typically adopt the route of manufacturing and export of reverse engineered generic drugs (Mytelka, 2006). Countries like Brazil, India and China have well developed pharmaceutical industries but technological innovation has been limited to reverse engineering of drugs (Henry and Lexchin, 2002). Thailand and Brazil have shown remarkable success in the production and export of antiretroviral generic drugs under the process patent regime (Ford et al., 2007). The World Trade Organization led Trade Related Aspects of Intellectual Property Rights Agreement of 2005 signed by most developing economies to bring in intellectual patent protection and unify patent laws, threatens the generic drugs industry in these economies (FM't Hoen, 2002). In his seminal paper, Mashelkar (2005) classifies countries based on their economic strength and innovation capability. Countries such as US, Japan and other European countries have been ranked high in both economic strength and innovation capability while countries such as India, China, Brazil, Argentina, Chile, South Africa have been categorised as innovating developing

countries (IDC). These IDCs have relatively low economic strength but are distinguished by their strengths in indigenous science and technology capacity, increased patenting and publishing activities and investments in technology in both the public and private sectors (Morel et al., 2005). In this vein, it would be interesting to understand how these economies which have predominantly focused on reverse engineering of drugs cope up with the challenges of new drug innovation in a product patent regime.

2.1.1 Vagaries of selection environment

Every sector has its own selection environment constituting its own set of demanders which monitor, mould and constrain behaviour of firms (Nelson and Winter, 1977). Technological innovation is predominantly guided by market related considerations 'demand pull', or by technological feasibility considerations 'capabilities push' (Dosi, 1982; Nelson and Winter, 1977). There are two important forces in the selection environment a) market element and non-market element, which work together to impel or hold back innovation. Market element comprises of commercial and profitability considerations and influences motivation of firm to spend on R&D for commercial exploitation. Non market forces on the other hand encompasses public agency, financing sources, policy issues, political constraints and regulatory issues and work to constrain behaviour of firms (Nelson and Winter, 1977). Dosi (1982) emphasises that the emergence of new technological paradigm is an interplay of scientific advances, economic factors, institutional variables and technological difficulties. Thus, a mix of demand-pull and capability push factors in the selection environment influences the rate and extent of innovation (Dosi, 1982; Nelson and Winter, 1977).

In the pharmaceutical industry, commercial considerations have played a very important role in driving innovation in the industry. The drug discovery industry has been criticised for developing drugs for global diseases and for failing to develop drugs for neglected diseases, which mainly afflicts the developing countries. On the other hand, the focus of the pharmaceutical industry has largely been on global diseases such as cardiovascular, neurological disorders and cancer that affect large number of countries and has high commercial market (Kyle and McGahan, 2012). An analysis of returns on R&D for new drug introductions shows, that top decile of new chemical entities (NCEs) ranked by global sales, generates six times revenues of the average R&D cost (Grabowski and Wang, 2006). Despite the lucrative commercial potential, pharmaceutical innovation is constrained by technical and commercial considerations that influence the progress of a drug compound through various

stages. Commercial considerations like market size, competition and commercialization capabilities are influencers in the early stage of drug development, but in the later stages, it is the technical considerations like safety, effectiveness and potential side effects that play a deciding role in the progress of the drug compound (Ashish Arora et al., 2009).

Regulation plays a very important role in innovation as it entails safety related regulatory encumbrances before getting the approval to enter the market (Baldwin and Von Hippel, 2010). There has been a considerable decline in the number of new drugs approved by regulatory bodies. More drugs are failing due to lack of clinical efficacy or safety issues. The number of new drugs new molecular entity (NME) approved each year by US Food and Drug Administration (USFDA) have ranged between 15 to 31 during the period 2001 to 2011 (Mullard, 2012) with the number of new applications not increasing significantly each year (USFDA, 2014). The two important regulatory mileposts a new drug must meet are a) Investigational New Drug Application (IND)[1] and b) New Drug Application (Enyinda et al.)[2]. During the regulatory approval process, a new drug must get approval at the beginning of clinical trials, which is referred to as the Investigational New Drug Application. The regulatory approval at the end of clinical trials is referred to as New Drug Application (Ashish Arora et al., 2009; Enyinda et al.). In this way, regulation makes innovation less viable and tends to decrease the value of innovation opportunities (Baldwin and Von Hippel, 2010; Gregersen, 1992).

The vagaries of the selection environment may stifle technological progress by applying selection at the level of technology and market (Dosi, 1982). Historically, the field of aerodynamics, applied thermodynamics, agriculture and medicines has advanced with

[1] Any new drug, which needs to be commercialised in US needs to get a regulatory approval from US Food and Drug Administration USFDA (2014) Novel New Drugs 2013 Summary. In: Cder CfDEaR (ed).and is subject to the specific requirements of the drug regulatory system. The new drug approval process requires regulatory approval at two stages – before initiation of clinical trials and after conducting the clinical trials. When the sponsor (usually the manufacturer or potential marketer) has screened the molecule for pharmacological activity and acute toxicity potential in animals and has a justification for commercial development, the sponsor will submit an application to initiate testing of the drug in humans for diagnostic or therapeutic potential. The necessary data and information submitted to the USFDA to seek approval to conduct clinical trials is referred to as Investigational New Drug application (IND) ibid..

[2] New drug application is the application filed with USFDA to get approval for sale and marketing of the new drug in US. The documentation required for an NDA involves the complete details about the drug development process including the data gathered during the animal studies and human clinical trials of an investigational new drug. The decision to approve is mainly based on provision of sufficient information to assess safety and efficacy of the drug, meeting the labelling criterion and the ability of the manufacturer to demonstrate good manufacturing practices.

government support. Governments in different countries have played a significant role in setting up public institutions and providing funds for expanding scientific knowledge base. Effective policy hence plays a key role in advancing the natural trajectory of science and ensuring that it is not constrained by selection issues (Nelson and Winter, 1977).

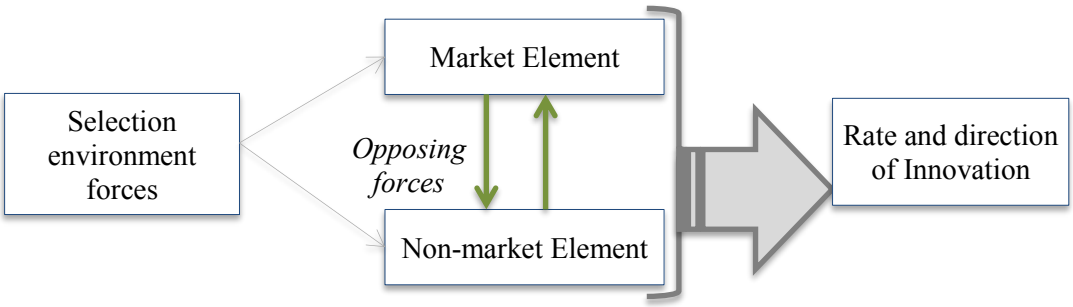


Figure 1: Vagaries of selection environment

Road mapping: role of institutional factor in selection environment

An important question posed by Nelson & Winter decades ago, which still holds relevance in the context of pharmaceutical sector, is

> *'To what extent are the directions in which science advances inevitable and to what extent can these be moulded by conscious policy?' - (Nelson and Winter, 1977: 73)*

Arrow (1962) has reasoned that in an ideal free enterprise economy, there is likely to be underinvestment in invention and research, due to uncertainty, and difficulty of appropriating information in early stages of research (Arrow, 1962). This line of reasoning has warranted intervention from policymakers who stimulate innovation through technology programmes and public procurement policies. The traditional role of public sector and government has been to support private domestic firms through taxes, direct subsidies, education and training facilities, R&D institutions and infrastructure facilities (Gregersen, 1992). Such policies have enabled to mitigate market uncertainty and prompted R&D institutions to serve as a bridging gap between pure research and applied research (Dosi, 1982; Freeman, 1992; Gregersen, 1992; Nelson and Winter, 1977).

Policies are significantly important in developing countries to strengthen the knowledge base, stimulate production capacity, provide incentives for innovation and foster start-ups

(Mytelka, 2006). The success of the semiconductor industry in Korea and Taiwan is due to the co-evolution of national and industrial innovation systems (Hwang and Choung, 2014). The role of government in case of Korea was significant not only in terms of providing financial support but also in providing tariff reductions for capital investments, technological development loans, technological and human resources development to develop the semiconductor industry. Similarly in Taiwan, the government played a vital role in supporting technological development and enabling diffusion to local SMEs (Hwang and Choung, 2014). Centralised public departments like the Ministry of Science and Technology in Korea encouraged the economic development by facilitating innovation and promoting the nascent industry (Spencer et al., 2005).

In India, post independence (after 1947), the Government supported development of tertiary education in science and set up research institutes for medicine and science. Government policies were designed to incentivise innovation and to ensure investment by private firms to set up manufacturing capacity for drug production (Mytelka, 2006). From 1947 to 1990, the Indian government followed an interventionist strategy by pursuing policies to support development of capabilities in select industries (Lall, 1992). Brazil also implemented many similar strategies like India, which enabled the development of a huge industrial base. The industrial and technology policies of Brazil government promoted large public research organisations and public enterprises and followed a strategy to intervene in technology imports thus supporting development of local capabilities (Lall, 1992). Both Brazil and India used a license mechanism to control the start of a new firm or business by giving license permit and controlling new business creation in different sectors (Hasenclever and Paranhos, 2009).

Post 2005, the TRIPS initiated change in patent laws (as elaborated in Section 5.2) caused the government to step up measures to support innovation by increasing funds for research, providing fiscal incentives to conduct R&D and initiating public private partnership schemes to propel innovation (Department of Science and Technology, 2013). The framework in India which shapes the innovation in pharmaceutical sector has the following components a) policy framework towards the development of the industry b) intellectual property rights c) price regulations and d) product and quality regulations (Mani, 2006). The role of public policy and government regulation has a positive as well as negative role to play in the development of innovative pharmaceuticals. Policies that affect research funding, intellectual

property protection, price controls, and regulations for drug approvals have a marked influence on new drug discovery and development (Miller and Henderson, 2007).

Roadmapping: role of regulatory factor in selection environment

Academic literature has stressed that the interplay of regulation and innovation either stimulates or restrains the rate of innovation. Regulatory standards, patents act and other regulatory procedures may either impact the innovator (patents law) or may affect the user (regulations regarding drugs and pharmaceuticals) or the availability of resources (environmental regulations regarding quotas or emission rates). The mode of enforcement of these regulations also influences the outcome of innovation. While taxes and fines dampen corporate incentive to innovate, subsidies and contracts stimulate innovation (Gregersen, 1992). An important mechanism through which governments try to control the regulatory environment is through intellectual property laws.

In recent years, the pharmaceutical industry has been influenced by a change in patenting policies in different parts of the world. The decision of the Trade Related Aspects of Intellectual Property Rights (TRIPS) to unify the patent protection in developed and developing countries has globalized patent protection (Correa, 2007). Compliance with TRIPS mandates all World Trade Organization members to adopt the significant features of the patent systems of wealthy developed countries, such as a 20-year term, non-discrimination in different technology fields and effective enforcement system (Cockburn and Slaughter, 2010).

The quest for profits by innovator companies through high prices of patented medicines has led to debates against implementation of strong patent policies in developing countries. The existence of loose patent protection in developing countries has given rise to burgeoning generic drugs industry in few developing economies. Though it has hit the profitability of innovator companies, it proved beneficial to developing and least developed countries by providing access to cheap generic medicines where access to treatment and affordability are bigger concerns.

Critics argue that the objectives of the TRIPS agreement are lopsided (Mueller, 2007) and stands to advantage the developed countries by preventing generics competition, supplying patented drugs at higher prices and raising profitability. The TRIPS agreement brought about

a major change in IP rights and in this way affects the regulatory environment in several developing and least developed countries raising serious concerns on the availability of drugs in developing countries.

India, South Africa, Brazil and Mexico are among the few developing economies that have well-developed generic drugs industry and signed the TRIPS agreements in 1995. All these economies share similar characteristics in having minimal patent protection before 1995 leading to evolution of a pharmaceutical industry based on imitation of patented drugs. The countries are characterised by existence of huge base of scientific infrastructure, presence of educational skills and less R&D investments for innovation (Albuquerque, 1999). The table below lists the dates when these countries adopted the TRIPS compliant agreement (Kyle and McGahan, 2012).

Table 3: List of top generic drugs producing countries that have adopted TRIPS agreement

Country name	Year of WTO Membership	Year of pharmaceutical patents enforcement using Ginarte-Park Index*[3]
Argentina	1995	2000
Brazil	1995	2000
Chile	1995	2000
China	2001	2005
India	1995	2005
Malaysia	1995	1985
Philippines	1995	2000
South Africa	1995	1985
Mexico	1995	2000

Source: Adapted from (Kyle and McGahan, 2012)

[3] Ginarte JC and Park WG (1997) Determinants of patent rights: A cross-national study. *Research Policy* 26(3): 283-301. have computed an index of patent strength ranging from 0 to 5 (IPI). The maximum value corresponds to the highest level of protection of intellectual property rights. The index is composed of five categories, each having a maximum score of 1. The categories are a) the coverage of subject matters that can be patented b) mechanisms for enforcing patents rights c) the restrictions on the use of patents rights d) membership in international patent treaties and e) length of protection from the priority date.

In case of high-income countries, innovation and strong intellectual property laws have led to huge investments and profitable innovations (Kyle and McGahan, 2012). One of the objectives of TRIPS agreement is to stimulate innovation in less developed economies. In that context, there is evidence to support that post 2005 pharmaceutical patenting activity and R&D investment has increased in the Indian pharmaceutical sector (Abrol et al., 2010). However, empirical evidence supports that a stronger IP protection has not resulted in significant research activity for discovery and development of new therapeutic options for neglected diseases in developing economies (Kyle and McGahan).

Linking appropriability regime, patenting and innovation

The link between appropriability regime and innovation sketched by (Arrow, 1962) and explored by many scholars asserts that a strong patent system provides an incentive for firms to innovate and is imperative for the technological progress of the nation (Levin et al., 1987; Nelson and Winter, 1982). Building on this thread, two important issues highlighted by Nelson are the 'template externality' problem and the 'oil-pool effect'. The 'template externality' problem arises when appropriability conditions are weak, which leads to externalization of technology through imitation. The externality problem dissuades innovators to innovate, as there is no incentive to profit. A separate set of problem arises when appropriability conditions are strong and it induces a race for first to patent among firms. Such a scenario referred to as 'oil pool effect' leads to secrecy and misallocation of resources (Nelson and Winter, 1982). Laws and policies related to patents that detail which actions are acceptable and which are not, influence the activities of firms with regards to innovating and imitating (Nelson and Winter, 1982).

> *"The objective of intellectual property protection is to create incentives that maximize the difference between the value of intellectual property that is created and used and the social cost of its creation, including the cost of administering the system." (Besen and Raskind, 1991: 5)*

Teece (1986) elaborated these underlying issues to define appropriability regime. Appropriability regime is defined as a set of environmental factors, which determines a firm's ability to capture profits from an innovation. The two important components of appropriability regime are *legal system* and *nature of technology*. The interplay between these two components determines whether an appropriability regime is weak or strong. If the

appropriability mechanisms are insufficient to protect intellectual property and nature of technology is easy to imitate, then the appropriability regime is 'weak' and spurs imitation. Conversely, a 'strong' appropriability regime determined by the strength of patent protection and difficult nature of technology stimulates innovation. These two factors have important implications on a firm's strategy to affect R&D and the rate and direction of innovation (Teece, 1986). An appropriability regime assures that "new knowledge remain naturally excludable and appropriable" (Zucker et al., 2002: 138) and ensures an innovator is able to profit from innovation (Teece, 1986).

At the firm level, appropriability[4] is a serious concern in the production of scientific knowledge (Arora and Gambardella, 1990) and appropriability conditions determine the level of profits a firm can generate through its innovative activity (Cohen and Levinthal, 1990). Patents, copyrights, trademarks, trade secrets, restricted access, contracts, passwords, secrecy are all different forms of appropriability mechanisms which enable an inventor to protect an invention. Intellectual Property rights (IPR) specially patents are the most evident and formal means of protection among all the other prevalent forms of appropriability (Hurmelinna and Puumalainen, 2005).

> *"A patent is a set of exclusive rights granted to applicants for inventions that meets the standards of novelty, obviousness and industrial applicability." WIPO (2013b: 43)*

Patents grant exclusive rights to inventors for a period of 20 years from the date of filing. The patent system is designed to reward innovators by giving exclusive rights to appropriate returns from their innovation. It also stimulates innovation, as inventors are obliged to disclose their invention to the public to enable replication (WIPO, 2013). The importance and effectiveness of patents vary largely among industries (Cohen et al., 2000). In the early

[4] Appropriability is an innovator's ability to capture return on its invention. This definition is influenced by the works of Arrow K (1962) Economic welfare and the allocation of resources for invention. *The rate and direction of inventive activity: Economic and social factors.* Princeton, NJ: Princeton University Press, 609-626, Cohen WM, Nelson RR and Walsh JP (2000) Protecting their intellectual assets: Appropriability conditions and why US manufacturing firms patent (or not). National Bureau of Economic Research, Levin RC, Klevorick AK, Nelson RR, et al. (1987) Appropriating the returns from industrial research and development. *Brookings papers on economic activity* 1987(3): 783-831, Teece DJ (1986) Profiting from Technological Innovation: Implications for Integration, Collaboration, Licensing and Public Policy. *Research Policy* 15(6): 285-305. who discussed and elaborated on the nature of conditions which govern the economic returns/rents an inventor may derive from the invention and the effectiveness of various mechanisms to protect their inventions.

1980s, patent protection was found to be vital for the development and introduction of 30 per cent or more of the inventions in the pharmaceutical and chemical industry. Patenting was found to be relatively insignificant in case of other industries such as petroleum, machinery and fabricated metal product where only 10-20% of inventions were protected by patents. Additionally, in the pharmaceutical industry it was also found that 80% of the inventions which can be patented are patentable (Mansfield, 1986).

Incentives for innovation in a strong patent regime

When intellectual protection is guaranteed, inventors use multiple pathways to gain economic returns on their invention (HW Chesbrough, 2003; West, 2006). Patents grant exclusive rights to inventors for a period of 20 years from the date of filing, and are designed to reward innovators by giving exclusive rights to appropriate returns from their innovation (Roehrs, 2003). A strong appropriability regime makes it easier for firms to capture R&D value (West, 2006) and support broad networks of innovation (Pisano, 2006). Patenting supports exploitation of innovation in three ways: a) it enables protection of invention and can also be used to block rivals from patenting related inventions, also referred to as 'patent blocking' (Cohen et al., 2000), b) it safeguards intellectual property and facilitates licensing deals which require information disclosure between buyers and sellers in a secure environment (Gallini, 2002; West, 2006) and c) it provides opportunity for firms to commercialize their inventions in new territories, thus facilitating globalization of innovations (Archibugi and Michie, 1995).

Strong patent laws also open up licensing and commercialisation opportunities for public research institutes (Teece, 1986). The landmark Bayh Dole Patent and Trademark Amendments Act of 1980 implemented by US completely revamped innovation and licensing in US universities. The Bayh Dole Act provided blanket agreement for researches in public institutions to file for patents and grant licenses to third parties. This helped the university/public institutions research in two ways: First it made patenting easier by removing a web of patent agreements between universities and government; secondly the act, endorsed government support for the license transactions between universities and firms. This also increased avenues for raising funds through licenses (HW Chesbrough, 2003; Mowery and Sampat, 2005).

Secure environment for innovation networks

The modern dynamic theory of patents attests to the benefit of patents in promoting information disclosure. A patent document discloses necessary information about an invention which otherwise would have been kept secret. It also provides free access to information after the patent expires and in this way avoids duplication of research efforts and redirects research into unexplored areas (Gallini, 2002). Another benefit of patenting is that it renders it possible to solve the problem of information exchange during licensing, which requires information disclosure between buyers and sellers in a secure environment (Besen and Raskind, 1991). Intellectual protection provides a secure way of protecting information and in this way encourages external interactions with competitors and other entities in the innovation system to trade knowledge and other assets. The argument in favour of a strong patent protection is that it encourages disclosure, technology transfer and shapes degree of openness to external sources (Laursen and Salter, 2005b).

The appropriability problem as discussed by (Arrow, 1962) emphasises the point that without a legal protection, invention is likely to be stifled especially in early stages of basic research, which provides informational output to other inventive activities (Arrow, 1962). The restriction on information transmission and uncertainty in realising the economic value of invention is more likely to act as a disincentive to a firm to engage in research (Arrow, 1962). An underinvestment in new technology may stall technological progress and this is the reason why patent systems have been the central focus of national policies for technological innovation (Cohen et al., 2000; Levin et al., 1987; Mansfield, 1986).

Patents reward the inventor for a limited period of time and enables diffusion of innovation after the patent expiry and in this way balances the tension between returns from innovation and diffusion of innovation (Levin et al., 1987). However, a contrasting view also prevails in the literature which states that a strong appropriability regime brings in increased patenting for exploitation of commercialisation opportunities, encourages secrecy and restricts follow-on research (Gallini, 2002; Hurmelinna et al., 2007). A strong emphasis on patenting by firms is complemented by increased efforts to capture returns to innovation and this in turn leads firms to be less open to external sources for fear of theft or leakage (Laursen and Salter, 2005b).

This literature review concentrates on three central tenets to the national innovation system a) institutions b) policies and c) regulatory environment. The national innovation system has historically been important in influencing the rate and direction of innovation. The set up of public research institutions (universities, public research labs) and private firms have contributed to the growth of the economy in most countries of the world. Scientific research performed in academic and governmental research institutions has been the driving force behind high technology innovations. The important dimensions, which make this work are institutional set-up, polices and intellectual property laws in an economy. The pharmaceutical sector in different countries has evolved due to a confluence of these factors. In case of the Indian pharmaceutical sector, this is more evident as the industry has taken sharp turns whenever the patent laws were revised.

2.1.2 Innovation networks

A considerable body of research illustrates the different roles university, public research labs and firms play in the innovation ecosystem and the importance of these linkages for basic and applied research (Cockburn and Henderson, 1996). The history of 'linear model of innovation', wherein firms take advantage of basic research done in universities and research institution and use in-house research to develop new products and processes, can be traced back to the German dyestuff industry in 1870 (Freeman, 1995; Johnson, 1992). The success of Germany's chemical industry based on innovation of new products and processes in specialised R&D labs housed within the company led to the adoption of this approach in other industries and other countries too, with professional R&D labs emerging as the main source of innovation. Over the years, mobilising academic research, government and industry for large R&D projects became the norm in large science based R&D projects (Freeman, 1995). The local sources of innovation began to play an efficient function in contributing towards breakthrough innovation specifically in early stages of research and enabling diffusion of innovation. (Freeman, 1992).

The role of public policy has been to coxswain linkages and mobilize competencies between public and private research sectors (OECD, 2002: 15). It is now well grounded that innovation is directly rooted in scientific and technological progress and is increasingly becoming dependent on science based industry linkages with academic work more than ever. Mowery and Rosenberg (1979) have emphasised the role of government policies towards

increasing knowledge and improving interactions between basic research institutes and private sector (Mowery and Rosenberg, 1979).

Across economies, the role of university and public labs is varying and dynamic in each of the national innovation systems. A number of polices have been brought into place in developed countries since 1980s to make linkages strong between universities, public research organisations and industry. Policies have been directed at establishing high technology agglomerations like Silicon Valley science parks. Though the productivity of these technology parks is still debatable, what is proven is the fact that effective interlinks between universities, public research labs and firms are important for technological advancement of a sector (Mowery and Sampat, 2005). Partnerships with universities provide firms with access to basic research in a particular field and opportunity to acquire license of new discovery in the initial stages of an innovation cycle (Arora and Gambardella, 1990) which in turn influences the productivity of downstream activities (Cockburn and Henderson, 1998).

The importance of public research is particularly important in high technology areas such as drugs, agriculture, computers, semiconductors, medical equipment and aeronautics (Arrow, 1962; Cohen et al., 2002). Mansfield (1986) provides empirical data to show that the percentage of new products and processes based on academic research is highest in the drug industry. The role of universities and public research institutions is particularly important in the early phases of new product development (Perez and Soete, 1988). Public research in universities and research institutes have primarily been associated with basic research oriented towards the discovery of basic scientific principles while the application of this research into products and processes rested with the private firms (Cockburn and Henderson, 1996).

In difficult learning environments, the amount of technical knowledge in basic and applied sciences shapes the technological opportunities and determines R&D spending by firms in industries (Cohen and Levinthal, 1990; Lane et al., 2006; Levin et al., 1987). Technological opportunities are a measure of technical advancement in a given industry and represent the impact of university research (Levin et al., 1987). The determinants of the technological opportunity are extra industry technical knowledge which can be research output from government or university labs or knowledge which resides with the suppliers (Cohen and Levinthal, 1989). The role of collaboration with firms and university is particularly decisive

for radical innovation as it is marred with different types of technical, market, organisational and resource uncertainties (Leifer et al., 2001). Collaborative networks hence play an important role to reduce development time and promote learning and capacity development at a comparatively lesser cost (Bessant and Tsekouras, 2001; Chesbrough et al., 2008; Freeman, 1995; Hagedoorn, 1993).

The resources of a firm also have an important influence on the formation of networks as evidenced from the rise of biotechnology industry. Biotechnology has its roots in university laboratories and research institutes fuelled by upstart biotechnology companies and funded by venture capitalists. When these small scale firms struggled to move beyond the drug exploration stage to drug development stages due to lack of experience in getting regulatory approvals and requirement of massive funds, large cash rich pharmaceutical firms entered the scene with various kinds of partnerships. These circumstances of mutual need developed a base for innovation networks (Arora and Gambardella, 1990; Powell et al., 1996).

The leading position of the United States in the commercialisation of biotech products as compared to Europe can be tied to strong industry-university relations which flourished in the US under the patronage of federal policy initiatives like the Bayh-Dohl Act of 1980 (Owen-Smith et al., 2002). Positive changes in the university industry collaborations in US can be tied to change in intellectual property regime through the Bayh-Dole Act that propelled increased patenting of university research and encouraged licensing to industry, thus earning licensing revenues and reducing dependency on public funds for research. Other factors which played an important role in forging collaborations was the proliferation of technology transfer offices in universities, rise of biotechnology sector, development of IT industry and insufficient public funds for research that necessitated long term changes in the system (OECD, 2002).

The high productivity and technological advancement witnessed in Japan can be attributed to strong social, economic and technical linkages, high R&D intensity and an incentive at firm level to innovate (Freeman, 1995). The Industrial Revitalising Law of 1999 in Japan established a legal structure similar to that created in Bayh-Dole Act in the US. Of significance is the law that was passed in 2004 that altered the legal status of national universities from a government institution to an independent administrative entity. These changes coupled with other reforms undertaken in Japanese national universities positively affected the attitude and mind-set of the university researchers enabled to increase

collaboration with the industry and also promoted spin offs from university laboratories (Nezu, 2005). Networks formed on the premises of learning and knowledge exchange has enabled to accelerate innovation and is thus high on the agenda of policy makers (Bessant et al., 2012; Bessant and Tsekouras, 2001).

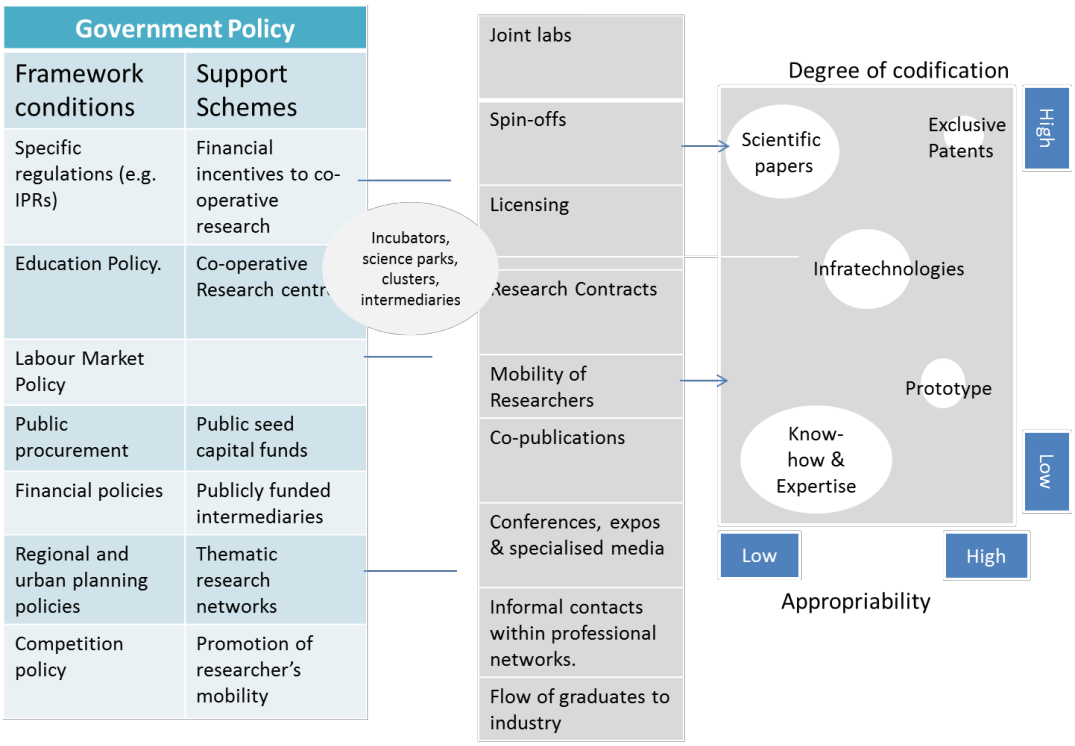
Apart from the institutional factors affecting the productivity of the linkages, a literature has since evolved highlighting the importance of social, technical and economic factors in playing a critical role in the formation and maintenance of networks (Freeman, 1995). It has been well established in prior literature that relationship between university, industries and public research laboratories has always been influenced by historical and cultural background of the country (Nezu, 2005). Another important factor, which plays a major role, is trust. Fukuyama (1995), the well-known American political scientist states that

> *"A nation's well being as well as its ability to compete is conditioned by a single pervasive cultural characteristic: the level of trust inherent in the society." Fukuyama (1995: 7)*

Trust also plays a critical role in forming relationships between two entities and is associated with high levels of co-operation and organisational performance (Gulati, 1995). Studies have established two important components of trust – calculative component and non-calculative component. The calculative component reflects the confidence placed on a partner's reliability and dependability. Non calculative component encompasses identification about a partner based on shared values and aligned goals (Gulati and Sytch, 2008). There are many studies that focus on behavioral certainty, moral hazards and unwillingness to share information as key limitations in the formation of inter-organisational collaborations. Trust hence plays a central role in shaping these relations between organizations (Arrow, 1974; Bessant et al., 2012; Gulati and Sytch, 2008). The lagging behind of industry-university relations in Europe can be traced to legal prohibitions and cultural disposition in some countries against collaboration of faculty with industry (Owen-Smith et al., 2002).

Figure 2 below depicts the mechanisms through which science industry interactions take place and sums up how policy and related support schemes/measures encourage research and network formation between academia and industry. Knowledge codification in the form of patents, scientific papers, prototypes, knowhow forms the basis of technological opportunities for the industry and spurs various collaborative networks in the form of licensing,

agreements, co-publications and setting up of joint labs. The interactions of public research institutions with industry varies in different countries by institutional setup, regulatory framework, patent regime, financing and mobility of researchers (OECD, 2002).



Source:(OECD, 2002)

Figure 2: Formal mechanism for Industry-Science Interactions

To sum up, the stream of national innovation system literature stresses the significance of institutional, policy and regulatory settings that make up the business environment and accounts for significant differences at country level. The interactions of public research institutions with industry varies in different countries by institutional setup, regulatory framework, patent regime, financing and mobility of researchers (OECD, 2002). The important tenets of national innovation system present in the literature are summarized in Table 4. These definitions and terms form the core of the conceptual framework and are used throughout the study.

Table 4: Salient features of National Innovation System relevant to pharmaceutical sector

Salient features of NIS	Description	Empirical and Theoretical Research examples
Innovation system	National communities encompassing firms, supporting institutions such as universities, research institutes enabling technological innovation in a country.	(Gregersen, 1992; Lundvall, 1992; Mowery, 1992; Nelson Richard, 1993)
Selection environment and institutional factor	Institutional policies play an important role in – mitigating uncertainty – help bridge the gap between basic and applied research – catching up with developed countries to make the transition from imitators to innovators	(Dosi, 1982; Freeman, 1992; Gregersen, 1992; Mike Hobday, 1995; Michael Hobday, 1995; Hobday et al., 2004; Nelson and Winter, 1977; Perez and Soete, 1988)
Selection environment and regulatory factor	Patents act and other regulatory procedures effect the regulatory environment. Patent laws and nature of technology influence the appropriability regime	(Gregersen, 1992; Teece, 1986)
Appropriability regime in developing countries	TRIPS agreement aims to unify patent laws making intellectual property protection mandatory in developing economies. One of the objectives of TRIPS is to promote firms to invest in R&D for innovation.	(Albuquerque, 1999; Cockburn and Slaughter, 2010; Correa, 2007)
Patent laws and appropriability regime	Appropriability regime important for two reasons – allows firms to profit from innovation – provides a secure environment to network	(Besen and Raskind, 1991; Laursen and Salter, 2005b; Teece, 1986)
Innovation networks – institutional policies – culture and trust	Linkages important between public institutions and firms for basic and applied research. Policies, laws, culture, trust influence the formation and productivity of these linkages	(Bessant et al., 2012; Cockburn and Henderson, 1996; Fukuyama, 1995; Gulati and Sytch, 2008; Mowery and Sampat, 2005; OECD, 2002; Zaheer et al., 1998)

Policies, patent regime influence the public and private system in the local setup and they both reinforce each other to enhance technological capabilities in the innovation system. The theory of national innovation systems (Freeman, 1987; Gregersen, 1992; Lundvall, 1992; Mowery, 1992; Nelson Richard, 1993) which gained currency in the 1990s provides a good ground to study the actors and linkages in the backdrop of policy decisions and provides a rich perspective of an industrial setting in the study. The institutional set up, an important dimension of the system of innovation underlines the role of supporting institutions in uncertain innovative activity (Lundvall, 1992).

In the context of developing countries, national policies and interactions within the national system is of utmost importance (Freeman, 1995). Within the ambit of institutional and regulatory factors, governments use various mechanisms to bridge the technological gaps between developed and developing countries and support innovation. Furthermore, the review of the literature discussed the importance of intellectual property protection in propelling research and innovation in high technology industry like pharmaceuticals. Empirical findings from the literature supports that a strong patent regime opens up commercialisation opportunities for science and industry and provides a secure environment to exchange ideas and information thus facilitating network between public research institutes, academia and industry.

In an era of globalisation when countries are transcending borders to seek international sources of innovation, many authors have questioned the relevance of National Innovation System (NIS) in the wake of globalisation and the pervasiveness of transnational companies (Nelson and Rosenberg, 1993; Ohmae, 1990). However, the usefulness of the theory lies in enabling a better understanding of national idiosyncrasies and its effect on the innovative capability of national systems (Lundvall, 1992). In the context of developing countries and high technology innovation like pharmaceuticals, NIS provides a useful theory to investigate

> *"How firms and countries catch up, forge ahead, and then leapfrog other firms and countries in economic performance." (Majumdar and Bhattacharjee, 2014: 523)*

2.2 Opening up of firm boundaries[5] - enabling innovation

The preceding section described the intensity of environmental factors in constraining or promoting business activities of firms and underpinned the role of technological innovation as the key solution for progress in a developing country. The section also deliberated on the importance of public private interactions in increasing national innovation output. Within this context, the effect of selection environment as a change driver at the national level with its influence at the firm level has been the centre stage of discussion in the literature on organizational studies. In the strategic management literature, it has been recognised that management must develop strategies and new organisational forms to achieve success amidst external changes such as technology explosions and globalisation (Helfat et al., 2009; Higgins and Maciariello, 2004). Strategic decisions must take into account new patterns of relationship, behaviour and evolution of new systems, risk mitigation (Prahalad and Krishnan, 2008) and seek opportunities to survive and prosper under conditions of change (Helfat et al., 2009). Just as nature immunizes against the environmental risks, by constantly creating new genetic material through sexual recombination and mutation, firms adopt the management principles of adaptability (variety, competition, flexibility in resource allocation, devolution and activism) to be on the path of continuous strategic renewal (Hamel, 2006). Recent years have witnessed phenomenal change in macro environment and one of the changes that have taken place at firm level is the phenomenon of open innovation. This section of literature review will examine some of the recent trends and shifts taking place in the business of R&D in relation to use of open innovation for product innovation in pharmaceutical industry.

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[5]The importance of 'firm boundaries' originated with Coase RH (1937) The nature of the firm. *economica* 4(16): 386-405. when he discussed about price as a determinant to undertake transactions within the firm or outside the firm in his seminal paper. With this the boundaries of the firm became the center of discussion for 'make' vs 'buy' decision in studies related to transaction costs economics theory Williamson OE (1979) Transaction-cost economics: the governance of contractual relations. *Journal of law and economics* 22(2): 233-261. Barney JB (2012) How a firm's capabilities affect boundary decisions. *Sloan Management Review*. discussed the role of firm capability as influencing its boundary decisions while Pisano identified technology change as a major influencer in determining R&D boundaries of firms Pisano GP (1990) The R&D boundaries of the firm: an empirical analysis. *Administrative Science Quarterly* 35(1): 153-176. Teece emphasized the role of capability, complementary assets and appropriability regime in influencing boundary decisions and elaborated various governance mechanisms through which a firm may undertake boundary decisions Teece DJ (1986) Profiting from Technological Innovation: Implications for Integration, Collaboration, Licensing and Public Policy. *Research Policy* 15(6): 285-305.. Recently the term 'boundary' gained resurgence when Chesbrough HW (2003) *Open innovation: The new imperative for creating and profiting from technology*: Harvard Business Press. used the porous boundary concept to differentiate between open and closed innovation concept.

2.2.1 The phenomenon of open innovation

Traditionally, firms have adopted a closed approach for innovation leveraging internal research and design capabilities (Peter et al., 2010). Innovativeness in the past has been associated with strong internal R&D capabilities. A firm's research lab was considered to be the breeding ground for ideas and inventions which was further developed by the firm's engineering department into commercial products (Hamel, 2006). Commercialisation of innovation rested solely with the firm's own marketing and sales department and innovative results were rarely disclosed (Gassmann, 2006; Hamel, 2006). Exemplars of closed innovation model are Edison's Menlo Park, AT &T Bell Labs, and Xerox's PARC who brought in many inventions and innovations during the twentieth century (Chesbrough et al., 2008).

The open innovation approach (HW Chesbrough, 2003; Chesbrough, 2006) rests on the underlying argument that the traditional in-house R&D structure is losing ground in the wake of revolutionary factors like globalisation of technology, resources, knowledge, and funds defining new ways in which innovation is taking place (HW Chesbrough, 2003; Chesbrough, 2006; Gassmann, 2006; Gassmann and Enkel, 2004) and making way for rapid growth of single user and open collaborative innovation (Baldwin and Von Hippel, 2010). The boundaries of the firm have emerged as an important strategic variable for innovation (Teece, 1986) and the porous boundary of firm in an open innovation model allows for an interface between inside and outside the firm (HW Chesbrough, 2003). Connections made by firms across boundaries contribute to idea sharing and combination of ideas between groups lead to new concepts or products (Hargadon and Sutton, 1997).

The decades of 1970s and 1980s saw greater dispersion of technological and organisational resources, global competition through liberalisation of trading and investment regimes, and growth in venture capital steering the way for a global industry competence (Teece, 1992). Advanced information and communication technologies have facilitated global networks and made foreign talent more accessible resulting in few centralised stand-alone R&D labs (Jelinek et al., 2012; Persaud et al., 2002). In the 1960's, R&D partnerships in high tech industries (pharmaceuticals, information technology, aerospace and defence) was between 20% and 40% of the overall R&D partnerships in North America, Europe and Asia and this reached new levels between 1980 to 1998 where it increased from about 50% to over 80% (Hagedoorn, 2002).

Within the pharmaceutical sector, key factors responsible for the increase in partnerships were identified as advancement in information technology, need to generate new products, ability to share costs for overall R&D budget and precedence set by successful partnerships in biotechnology sector (Hagedoorn, 2002). The biotechnology industry provides a perfect illustration, as the roots of the evolution of the industry are deep-rooted in network formation. At the nascent stages, start-up biotechnology firms relied on venture capital firms for finance. As the industry set in its growth path, these biotech start-ups attracted new partners for diverse set of activities and large multinational firms for commercialisation. Over a period of time, biotech firms deepened their position in the market through collaborations with multiple partners as the firms became larger and older (Koput and Powell, 2000; Powell et al., 2005).

An analysis by Kneller on a sample of 252 new drugs approved by the US Food and Drug Administration (USFDA) between 1998 and 2007 indicate the increasing involvement of different innovating organisations (pharmaceutical companies, academic or not for profit research organisations, and small biotechnology companies) in the new drug development process. The analysis reveals that approximately 40% of the FDA approved new drugs were transferred to the firms by universities and biotechnology companies (Kneller, 2010). Table 5 summarises the analysis of 252 drugs approved by the US regulatory authority (USFDA) by discovering organisations. The numbers in the table indicates whole drug equivalents and the percentages in brackets indicate the proportion of the drug discovered by the type of discovering organisation.

Table 5: New drugs approved by the FDA CDER from 1998 to 2007 by discovering organization

Number of New drugs	Pharmaceutical company	Biotechnology company	University first transfer to a pharmaceutical company	University first transfer to a biotechnology company
252	147.2 (58%)	44.1(18%)	20.4(8%)	40.3(16%)

Source: Adapted from (Kneller, 2010)

In current times, the focus of innovation has moved a long way from the individual inventor to R&D labs to networks of firms (Teece, 1996). A research paper published in Nature, February 9, 1995 on the development of an animal model for Alzheimer's disease was co-authored by 34 scientists who were affiliated with two biotech companies, one pharmaceutical company, a research university, one government research laboratory and a

research institute. This example shows the number and diversity of people involved in such research projects (Powell et al., 1996). The increasing importance of 'connectedness'; active involvement of researchers with public sector researchers in new drug discovery research (Cockburn and Henderson, 1998) and the escalating demand for intellectual and scientific skills to enable research breakthroughs (Powell et al., 1996); all point to the fact that the locus of innovation has shifted from centrality of the firm to a network of inter-organisational relations (Arora and Gambardella, 1990; Powell et al., 1996).

In recent times, open innovation emerges as a plausible solution; as networks provide access to resources, technologies, market and information along with minimizing risk and outsourcing value chain activities and organisational functions (Hamel, 1991; Zaheer et al., 2000). Complementary networks driven by strategic motives to fill in gaps in value chain or gain access to new knowledge leads to successful firms. Networks reinforce one another in interesting ways – funding through networks fuels research efforts while success in research progress attracts partners and more funds (Powell et al., 2005). On similar lines, a lack of competitive resources induces firms to form linkages while availability of resources makes a firm attractive to other partners for collaboration (Ahuja, 2000).

In times when open innovation is gaining new grounds in its applicability in different sectors, Almirall and Casadesus-Masanell (2010) provide a compelling argument that open innovation may not be superior in all cases of product innovation. Open innovation has the following downside effects especially when product complexity is high: - a) when innovation process is open to partners, firms tend to lose control of the development trajectory and b) if the goals of innovator firm and partners are not aligned, it may not be beneficial to the innovation process. In such cases, where the downside effects of open innovation outweighs the benefits, open innovation may not be superior to closed innovation (Almirall and Casadesus-Masanell, 2010). The open behaviour of a firm is also dependent on its appropriability strategy and its ability to protect its research ideas and assets. While a strong appropriability strategy solves the problem of protection and provides a secure environment for firms to open up their boundaries for innovation, too much reliance of appropriability also limits the flow of innovation (West, 2006). Firms also face a paradox of openness when they face the tension of sharing knowledge in open innovation but are also wary of misappropriation and threat that might limit their potential to profit from innovation (Bogers, 2011; Laursen and Salter, 2005b; Laursen and Salter, 2014).

An interesting study carried out in Japanese pharmaceutical industry shows that the industry has made significant discoveries in the area of new drugs using the closed innovation route. The initial stages of drug discovery are carried out in an autarkic (closed innovation) manner. Their innovative drug development often depends upon a single insightful, dynamic and iconoclastic lead scientist who builds his own team and carries out in-house research referred to as autarkic innovation. Japanese companies tend to open up for collaboration and other partnerships only at the drug development or commercialisation stage (Kneller, 2003). This manner of drug discovery research is in stark contrast to the developed economies of US and Europe where pharmaceutical companies engage with university start-ups for new drug candidates and technology (Cockburn and Henderson, 1997; Kneller, 2003).

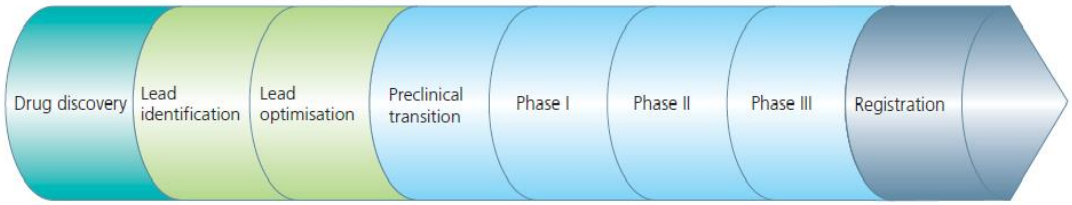
Academic literature points towards existence of open innovation for years even before this concept gained popularity in early 2000s. Literature is replete with examples of firms forming external linkages for innovation (Allen, 1983; Rothwell, 1994; Tidd and Bessant, 2011). The community based innovation model (Shah, 2005) and use of contractual strategies (Teece, 1986) are exemplars of firms seeking help outside their boundaries to fulfil their strategic objectives. Allen's study which dates back to 18th century found that firms in the iron industry cooperated and shared knowledge to improve blast furnace design technology (Allen, 1983; Shah, 2005). Thomas Edison's laboratory scientists extended their knowledge of electromagnetic power gained from the telegraph industry to find technological solutions for other industries like telephone, phonograph, railways and mining industry (Hargadon and Sutton, 1997). Thus, the concept of open innovation has also been criticised in the academic literature as 'old wine in new bottles' (Trott and Hartmann, 2009).

In the past, external knowledge played a supplemental role to the internal R&D activities of the firm, which was the central focus for innovation. In recent times, external knowledge has assumed greater importance and plays an equal role to that afforded to internal R&D (Chesbrough et al., 2006). What is compelling and interesting is the fact that factors have become more conducive than ever before for firms to consciously take a decision to adopt an open innovation model for innovation. In the past decade, there has been an unprecedented trend witnessed by Fortune 500 companies to license out their core technology assets to other companies (even competitors) for economic benefits, competitive advantage, mining of R&D investments, creation of new market opportunities etc. Companies had previously restricted themselves to license out their non-core technologies or core technologies to non-rivalling

industry but in recent years there has been a shift in strategy to open up their technology to everyone (Kline, 2003). Open innovation is now so pervasive that companies are using integrated roadmaps for strategic technology planning. These roadmaps enable to analyse and make use of strategic opportunities to generate adequate value and strengthen their competitive position (Lichtenthaler, 2008).

2.2.2 Stage of research important in pharmaceutical R&D

Globally, pharmaceutical innovation is becoming more modularised with specific competencies for each stage of drug discovery and development process being outsourced (London School of Economics and Political Science, 2005; Sampath, 2008). Pharmaceutical research and development for new drugs has two prominent stages - drug discovery and drug development. The drug discovery stage focuses in discovering a chemical compound with desirable effects in a screen; which mimics the disease state in humans (Henderson and Cockburn, 1996). New compounds generated in the laboratory (initial discovery stage), progress to animal testing (preclinical research stage) and if successful, move to clinical trials (clinical development) in humans (Ashish Arora et al., 2009). Figure 3 below depicts the different stages involved in the drug discovery and development for new drug research.



Source: (Nwaka and Ridley, 2003)

Figure 3: New drug R&D process

Firms enter alliances with different motivations and different goals at different stages of product development process (Arora and Gambardella, 1990; Koza and Lewin, 1998; Lichtenthaler, 2007; Rothaermel and Deeds, 2004). In the pharmaceutical industry too, new knowledge is located primarily upstream in the value chain within the research community (Cockburn and Henderson, 1998; Rothaermel and Hess, 2007). In early stages of product development when uncertainty is high, universities and smaller number of key sources work closer with firms and as success comes into picture with the research progress, more partners are attracted in the subsequent stages of development (Laursen and Salter, 2006; Owen-Smith

et al., 2002). Open innovation allows capturing the knowledge of diverse partners and considering new approaches that a lone innovator may not consider. In this way, open innovation aids the new drug discovery process (Almirall and Casadesus-Masanell, 2010).

A more specialised literature on collaborations for research for new drugs provides a dichotomy of alliances. The upstream downstream lens (Hess and Rothaermel, 2011; Rothaermel and Deeds, 2004) built on exploration–exploitation model of organizational learning (March, 1991; Rothaermel and Deeds, 2004) has been applied to differentiate these alliances based on strategic intent. To elucidate this further, Levinthal and March (1993: 105) defined exploration as 'the pursuit of knowledge, of things that might come to be known', and exploitation as 'the use and development of things already known' (Levinthal and March, 1993: 105). This dichotomy was used by (Rothaermel and Deeds, 2004) to categorize alliances formed along the pharmaceutical value chain as upstream and downstream alliances based on strategic intent and research stage (Rothaermel and Deeds, 2004).

Upstream research alliances are exploration alliances undertaken by firms that focus on upstream activities of the value chain (basic research, drug discovery and development) (Rothaermel and Deeds, 2004). These types of alliances are usually undertaken with universities and other research institutions for exploratory search in an attempt to discover something new. Downstream alliances occur at the drug development stage and focus on downstream activities of the value chain such as access to manufacturing capabilities, regulatory know-how, market knowledge and access (Hess and Rothaermel, 2011). Finance is an upstream activity as it fuels R&D, licensing and other R&D activities while commercialisation, the last stage in the product life cycle is a downstream activity (Powell et al., 2005).

The pharmaceutical industry in recent years is facing a decline in R&D pipeline and continual increase in R&D costs. Pharmaceutical innovation is complex and this necessitates open innovation at early stages of research to access discoveries in the universities, small biotech firms and public research organisations to speed up research (Gassmann and Reepmeyer, 2005). It has been well documented that young, small and medium sized research firms that are often resource constrained, form more extensive linkages with external partners (Baum et al., 2000; Koput and Powell, 2000). On the other hand, established successful firms with necessary experience, financial resources and complimentary assets obviates the need for outside assistance (Koput and Powell, 2000). Firms are opening up the

innovation process through diverse modes–: a) internationalisation of R&D to access markets and resources b) outsourcing of R&D for cost saving c) involvement of suppliers and/or users in the innovation process and d) external commercialisation of intellectual property (Gassmann, 2006).

As Rothwell (1994) summed it up, the 5th generation innovation process has arrived which sees a marked strategic shift in innovator companies. The linear dichotomous model of public sector performing basic research and private sector concentrating on applied research is blurring significantly (Cockburn and Henderson, 1996). Companies in the 1950s to mid-1960s predominantly took the linear progression route to innovate and followed the sequential development phases from scientific discovery to technological development to commercialisation phase. The mid 1990s marks the era of fifth generation process where firms are getting increasingly engaged in a variety of strategic practices such as strong inter-firm vertical linkages, external horizontal linkages marking a shift towards systems integration and networking (Hobday, 2005; Rothwell, 1994). Latecomer firms in developing countries create new strategies and new innovation models to deal with technological and market disadvantage to enter new international markets (Hobday, 2005). The pharmaceutical industry of 21st century is witnessing major shifts in strategy and structure for new drug development. The new ways of achieving R&D efficiency and greater return on investment are consolidation, partnerships, outsourcing, innovation networks, expansion into emerging markets, globalisation of drug development process and academic alliances (Kaitin and DiMasi, 2010).

2.2.3 Opening up the R&D process

Across a range of companies and industries, open innovation is a verity with R&D corporations embedded in a complex maze of collaborations. Corporations engage in collaborations across geographies, disciplinary areas and the emergent picture is that of a dynamic innovation ecosystem (Jelinek et al., 2012). A variety of networks mark the business environment with profound implication on how companies innovate (Dhanaraj and Parkhe, 2006). Such networks include strategic alliances, joint ventures, long term buyer supplier relationships, and similar other alliances (Zaheer et al., 2000). Based on a study with 27 R&D organisations (Jelinek et al., 2012) has categorised the following three types of emergent R&D structures.

Table 6: Emergent network based R&D structures for open innovation

R&D Structure	Description
Centralised R&D with outsourcing activities	This structure is the closest to the classic model of centralised corporate model (hub) where the central lab has networks with their own divisional labs, subsidiary labs or outsider labs such as universities or government research labs or institutes (spokes). This is also termed as the firm centric network with offshore outposts arranged in a 'hub and spoke' structure.
Collaborative Innovation	When firms participate in industry focused research consortia to leverage technical expertise and share financial costs.
Virtual network of resources	In this R&D structure, relational innovation networks are formed for sharing information, knowledge to reduce uncertainty and for mutual benefit.

The following section seeks to elaborate on these major types of network based organisational forms from the existing innovation literature.

Centralised R&D with outsourcing activities

This R&D structure is the most common structural arrangement traditionally used by firms for R&D and innovation. While the core traditional model relies on internal development and commercialisation of products by the firm, this structure extends its nodes to reach out to external partners to gain strategic advantage whilst maintaining a centralised lab structure (Jelinek et al., 2012). Such an organisation stands to benefit by forming networks and alliances to capture the new technologies, learn new ideas, process and products outside the firm's boundaries and allow exploitation of assets. (Teece, 1996). It is typical in the pharmaceutical organisation to concentrate their R&D efforts in-house and outsource select activities to service providers *who have no stake in the outcome* (Melese et al., 2009). This allows a company to retain control of the R&D projects, get external support and reduce time and cost.

The outsourcing business has boomed in the past years due to predominance of this type of business model. Rising R&D costs and decreasing profit margins have forced multinational companies to outsource activities to cheaper sources (Chowdhary, 2010) like China and India which have emerged to be destinations for high skill low cost centres (London School of Economics and Political Science, 2005). Noteworthy trend in this respect is the outsourcing

of clinical trials to India due to its huge population, diversity of patient pool & diseases, high enrolment rates, well developed medical infrastructure and availability of inexpensive English speaking medical professionals. Lax regulations in developing countries are adding to the attractiveness of India emerging as a destination for clinical trials (Cekola, 2007). Activities related to new drug development process may be outsourced at preclinical, clinical research and/or manufacturing stages (Chowdhary, 2010). Increasingly, the contract research organisations are entering the integrated[6] partnership mode an exemplar being the TB alliance group contracting out the entire development chain from preclinical to Phase 1 (London School of Economics and Political Science, 2005).

Collaborative Innovation

In such a structure, the company has research agreements with a network of partners each one of which has a *stake in the outcome* (Melese et al., 2009). Such organisational forms are commonplace in pharmaceutical industry, where alliances are imbued as a way to tap into the drug development capabilities of biotech firms. Such a structure is also essential to biotech firms to access resources and capabilities available with the larger firms (Teece and Pisano, 1994).

In recent years, pharmaceutical firms have increased research partnerships with scientists of universities and research labs to get access to research discoveries. Large US based pharmaceutical companies such as Merck, GlaxoSmithKline, AstraZeneca and Pfizer have all established multimillion-dollar, multiyear collaborations with academic institutes for a number of therapeutic areas. Different forms of research partnerships include firms providing research funding to a) a sole investigator b) university, research institute or university consortium or c) to multiple parties to focus on one research problem. The firms may also undertake fee for service projects with universities. Higher levels of engagement between company and academia involve either a company supporting a university consortium or participating in an industry consortium. A firm may also enter into venture capital funding by providing seed money to start a research venture (Melese et al., 2009).

[6] Integration by definition involves ownership, is distinguished from pure contractual modes in that it typically facilitates incentive alignment and control Teece DJ (1986) Profiting from Technological Innovation: Implications for Integration, Collaboration, Licensing and Public Policy. *Research Policy* 15(6): 285-305.

By and large, R&D activity for new drug research has mostly been confined to United States, Europe and Japan. In recent years, the principle of comparative advantage has resulted in global re-allocation of activities by the companies to relatively large low-cost countries (Sampath, 2008) such as India and China. These countries offer prospects to tap new sources of human capital and infrastructure at cheaper costs offering significant potential to bring down R&D costs (Cockburn and Slaughter, 2010).

Another example of collaborative innovation formed by firms for discovery of new medicines is 'Public-Private Partnership'. Such partnerships stimulate R&D investments in two ways, one by supporting funding of applied R&D industrial projects in industry and secondly by facilitating government and industry scientists to work together. Most of these partnership programmes require private sector to contribute towards a sizeable portion of funds in the project. In recent years, government has used public private partnership programmes to initiate research in areas, which are commercially not profitable for the private industry to take up, but has high social benefits (Stiglitz and Wallsten, 1999).

One such example is the proliferation of public partnership projects for research in neglected diseases. Noteworthy public partnership examples are Medicines for Malaria Venture (MMV), the TB Alliance, Drugs for Neglected Diseases (DNDi), the Institute for One World Health (iOWH) and the World Health Organisation Special Programme for Research and Training in Tropical Diseases (TDR) which have been formed to discover new drugs for neglected diseases (diseases afflicting the developing country). Such partnerships involve engagement with academics, contract research organisations and pharmaceutical firms and are examples where the public sector provides funds and companies engage in development work (London School of Economics and Political Science, 2005).

Virtual Labs

Another deviant of the linear model R&D structure is the formation of virtual networks of collaborators who get involved in product development by sharing resources, components, technical solutions and expertise (Jelinek et al., 2012). Many upstart companies based on this R&D structure have mushroomed and these companies engage in little or no in-house research, develop products externally and commercialise them. Such corporations designated as 'hollow corporations 'are suitable to exploit rich technological opportunities and acquire diverse capabilities through contractual mechanisms, (Teece et al., 1994). Hollow

corporations are ascribed this name as such a firm is primarily a nexus of contracts and possess no specific firm competence within the firm; the competence of the firm being primarily shaped by the capability of the allying partners and multiplicity of contracting partners (Teece et al., 1994). Due to their alliance with competent corporations, virtual structures are very innovative and have the ability to excel in early stage innovative activities and reflect a dynamic innovation system (Jelinek et al., 2012; Teece, 1996). In the pharmaceutical innovation, some of the projects of Medicines for Malaria venture (MMV) were conducted successfully using the virtual drug discovery route. A lead optimisation project on anti-malarial peroxide achieved success with the efforts of a virtual team of scientists from USA, Australia and Switzerland (Nwaka and Ridley, 2003).

InnoCentive; a company based on open innovation model connects companies seeking solutions to scientific problems to a virtual global community of highly qualified scientists. Client companies are called 'seekers' and scientists providing solutions are called 'solvers'. A global community of over 50,000 scientists and scientific organisations provide solutions to problems posted on website by anonymous seekers (Allio, 2004). Such an open source approach innovation in software industry has already gained popularity and is used frequently in the contribution of software code (Von Hippel, 2002).

There is however a fundamental difference between open source software model and organisation's openness to new ideas, patents and products, from outside its boundaries (Baldwin and Von Hippel, 2010; HW Chesbrough, 2003; Raymond, 1999). While a firm may open up its boundaries to get new ideas and collaborate with other firms (HW Chesbrough, 2003), it may still retain control to appropriate returns on innovation. In this way, networks formed for new product or process development may be confined to members with a claim on intellectual property and commercial rights and not open to all (Bessant and Tsekouras, 2001). On the other hand, an open source software model works on the premise that 'all information related to innovation is public good, non-rivalrous and non-excludable' (Baldwin and Von Hippel, 2010: 4), eliminating manufacturer's direct path to appropriate returns (Von Hippel, 2002).

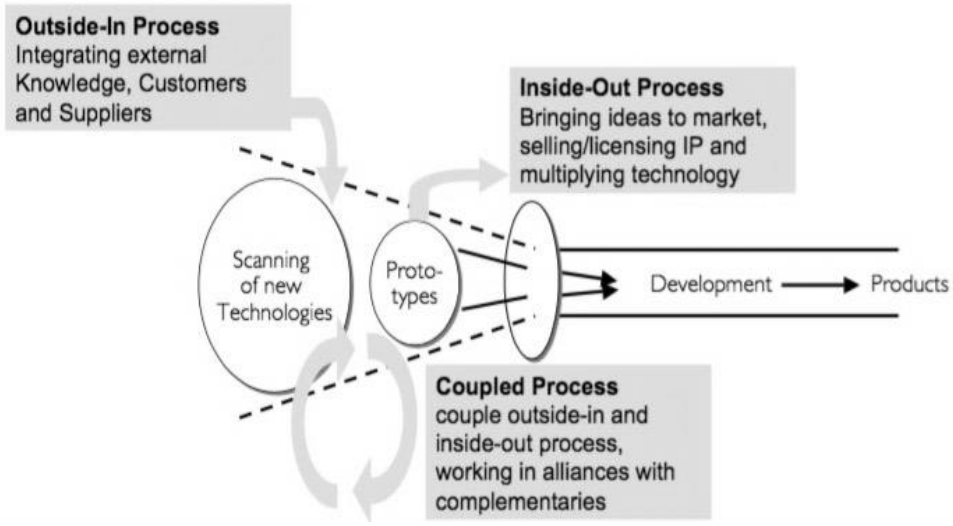
Potential ideas to integrate all the potential stakeholders in the drug innovation process includes funding of a 'fee-for-service website' by users and government to provide a platform for collaboration among academics, biotechnology and pharmaceutical professionals. Drug companies such as Pfizer has shared 12,000 compounds with scientists affiliated with the

WHO's Special Programme for Research and Training in Tropical Disease and allowed these scientists to work in their R&D labs to develop lead candidates (Nathan, 2007). Other examples of open source innovation includes the Council for Scientific and Industrial Research Team India Consortium's 'Open Source Drug Discovery' project (CSIR OSDD) and 'The Synaptic Leap's Schistosomiasis' (TSLS) project that operates through virtual networks (Årdal and Røttingen, 2012).

The underlying pattern observed in all these R&D structures is the propensity of firms to open up their boundaries to form a complex web of alliances for pharmaceutical R&D. The drivers for open innovation are many and the concept is gaining prominence in recent years due to confluence of many factors like strengthening of patent protection due to TRIPS, technological advancement, globalisation, increasing R&D costs, uncertainty and risk in new drug development. Constraints in new drug innovation coupled with the need to increase speed of innovation, at reduced cost is boosting the formation of network based R&D structures. The closed in-house R&D structure stands challenged in today's circumstances.

2.2.4 Adaptive Open Innovation Strategies

A central core theme of the open innovation concept is the *inbound open innovation* strategy that allows firms to exploit discoveries of others in their own R&D labs and the *outbound open innovation* strategy that allows firm to opt for external pathways to exploit their innovation (Chesbrough and Crowther, 2006; HW Chesbrough, 2003). This classification was extended to include the *coupled process* or the *collaborative R&D* in the open innovation framework in latter studies. The open innovation strategy can be classified into three archetypes a) outside-in process (inbound) b) inside-out process (outbound) c) coupled-process (collaborative R&D) (Enkel et al., 2009; Gassmann and Enkel, 2004). This archetype is important to categorise and understand the different strategic options which firms consider while opening up their innovation process. The figure below summarises the three open innovation strategies.



Source: (Gassmann and Enkel, 2004: 7)

Figure 4: Three archetypes of Open Innovation

Inbound strategy

The 'outside-in' process or the inbound strategy develops the company's knowledge base by accessing external sources like suppliers, customers (HW Chesbrough, 2003). The inbound strategy can be executed through two important processes – a) *sourcing* and b) *acquiring*. Sourcing refers to scanning and absorbing existing knowledge and mechanism from external environment and making them fit with internal processes. Acquiring refers to buying in external ideas, expertise or knowledge through pecuniary exchange (Dahlander and Gann, 2010). Common ways in which a technology or knowledge can be acquired are: a) in-licensing b) funding external research programmes c) acquisition of technology and d) investing in start-up ventures. The strategic considerations for each of the decision points involves evaluation of time, risk, and rewards (HW Chesbrough, 2003). The make or buy decisions in turn are impacted by the core competency of the firm, learning capabilities of the firm, new market entry strategy and the need to combat survival pressure (Kogut and Zander, 1992). Non-pecuniary exchange mechanism for sourcing of knowledge includes networks with universities, public research organisations, consultants, customers and suppliers to access wide variety of ideas and knowledge and find solutions to problems (Dahlander and Gann, 2010).

The outside-in strategy enables transfer and development of ideas and knowledge (Gassmann and Enkel, 2004) and supports a company's growth strategy as new capabilities drive innovation and impede imitation (Kogut and Zander, 1992). In current times, speed to innovation and cost effectiveness are the key drivers for competitive advantage (Tidd et al., 2001). Japanese firms have gained significant competitive advantage in high technology industries like computers, chemicals, electronics and equipment industry as compared to their US counterparts, by capitalising external technology at a much faster pace and lower cost (Mansfield, 1988).

In the field of pharmaceutical research, some of the examples of inbound innovation are in-licensing of anti-malarial technology by Sanofi Aventis from Amyris, a start-up company (Chesbrough, 2011) and in-licensing deal of Pfizer of novel drug for gout and hyper-uricemia from Kissei Pharmaceutical, Japan (Pfizer, 2013). Of the path breaking discoveries in genetic engineering, such as recombinant DNA method, cell infusion technology, gene sequencing have been done in universities and the spill overs have enabled the pharmaceutical industry to benefit from these research outputs (Powell, 1998). Despite these successes, in-licensing suffers from the not invented here syndrome (NIH). The notion that a technology or research asset cannot be relied upon for its quality and performance if not produced inside a company is referred to as NIH (HW Chesbrough, 2003). Increase in open innovation activities and benefits accrued would serve to reduce this syndrome and enable open innovation to be an integral part of firm strategy.

Outbound innovation

The 'inside-out' process or the outbound strategy includes technology transfer, selling IP, out-licensing to outside environment (HW Chesbrough, 2003). In the open innovation literature, outbound innovation occurs in two ways: selling/out-licensing and revealing. *Selling* or *out-licensing* involves commercialisation of innovation by firms for pecuniary benefits. *Revealing*, on the other hand involves selective revealing of internal resources to seek indirect benefits from an external partner (Dahlander and Gann, 2010). The software industry benefited immensely through the non pecuniary mode as in open source software that involved collective involvement of a group of individuals to contribute towards innovations (Von Hippel, 2002). The revealing mode is non pecuniary based and aims to benefit from the exchange of ideas and resources to further the innovation process (Dahlander

and Gann, 2010). In the pharmaceutical industry, the open source drug discovery initiatives try to leverage this concept for public health benefits (Nwaka and Ridley, 2003).

Companies commonly use the modes of out-licensing, franchising and technology transfer to exploit its innovative products and technology outside the firm. In a study carried out to understand firm motivation to engage in technology out-licensing, the motives included strengthening of product base, or technological position or gain benefits like access to knowledge, enhancing reputation or strengthening network position as important reasons. In contrast to the common perception, 'revenue generation' did not emerge as the most important factor for firms to undertake this strategy. Instead out-licensing deals also used to guarantee freedom of operation through cross licensing arrangements was of utmost importance to the strategy of firms. In this strategy, intellectual property rights are used as bargaining chips to avoid potential patent infringement lawsuits (Lichtenthaler, 2007: 118).

In pharmaceutical innovation, Eli Lily has suitably used open innovation practices to maintain its pace and scale of innovation. It indulges in regular scanning of opportunities for exploitation of research work and explores the out-licensing route at every stage. In order to ascertain the therapeutic and business value of drugs under development the company also uses initial market reaction to assess project value. This aids the company in decision-making and enables to raise cash, retain talent and reduce uncertainty in the long drawn R&D process for new drug innovation (Rigby and Zook, 2002). Out-licensing strategy also enables a firm to manage its portfolio of drugs compounds under limited resources and time constraints. It is specially a useful strategy to offset additional financial expense a) if a firm has more prospective compounds in pipeline ready for development while the in-house capacity is limited and b) if the market potential of pipeline compounds is less than the set threshold level (Danzon et al., 2005).

A firm equipped with complementary assets such as distribution systems, manufacturing plant, equipment and complementary technologies might find it strategically beneficial to exploit its technology internally rather than out-licensing (Teece and Pisano, 1994; Teece, 1986). Out-licensing of innovation is also contingent on other factors like speed of imitation, first mover advantages and rents from innovation. If the speed of innovation is slow then the firm can benefit from first mover advantage by developing it in-house and profiting from the innovation. In cases when the innovation is imperfectly immobile, out-licensing might increase the risk of revealing proprietary information and result in loss of potential profits.

On the contrary, if speed of imitation is high, it is better for the firm to license the technology to prevent from locking into a technology that will be rapidly replaced (Hill, 1992; Peteraf, 1993).

Despite the recent increase in out-licensing activities by firms, the inside-out strategy involves risk as it may enable competitors to ably equip themselves with know-how and may result in loss of market exclusivity (Kline, 2003; Lichtenthaler, 2008). Proponents of out-licensing advocate it to be a sensible strategy as it yields financial and strategic benefits and is a rational way of maximising returns on investments (HW Chesbrough, 2003; Kline, 2003; Lichtenthaler, 2008). However, it is a critical strategic decision for firms to make, whether to out-license and manage projects or to develop and commercialise the project through their own channels. The timing of the project, control over the product/technology, presence or absence of complementary assets, development costs and patenting decisions all influence and add to the complexity of decision making (HW Chesbrough, 2003).

Collaborative R&D

When companies blend inside-out and outside-in practices to form alliances with complementary partners it is referred to as coupled process. Firms might engage in any of the open innovation strategies or might integrate these strategies (Gassmann and Enkel, 2004). The different modes of coupled process are joint ventures, alliances with specific partners such as industry consortia etc. In the past decades, the pharmaceutical industry has witnessed intensive cooperation with biotechnology companies. An example is the development of recombinant human insulin by Eli Lily in collaboration with Genentech (Gassmann and Enkel, 2004).

Collaborative R&D networks involve active learning, knowledge exchange addressing specific applications of knowledge and involvement of diverse partners for a specific product or process development (Bessant and Tsekouras, 2001). Collaborations on pharmaceutical research are also influenced to a great extent by the size of firms. Small firms primarily engage in collaborative deals because of the insufficiency of funds and lack of experience in complex stages of clinical trials. Large firms may form development and marketing alliances to share marketing expense and diversify risk. It has been empirically validated through several studies that drugs developed in alliances are more likely to achieve success in R&D (Danzon et al., 2005; DiMasi, 2001).

The phenomenon of non-equity R&D partnerships such as joint R&D pacts and joint development agreements have become more important modes of inter firm collaboration in recent years than joint ventures. While joint ventures require long term commitments and high organisational costs, R&D partnerships on the other hand require commitments for a limited time horizon and provides significant benefits in sharing resources, costs and knowledge. In 1960s, R&D based partnerships in high tech industries such as pharmaceuticals constituted only 20% to 40% of the total number of partnerships. Influenced by biotechnology and progress in information technology systems, R&D partnerships increased from 60% to over 80% in the 1990s (Hagedoorn, 1993, 2002).

Literature is replete with why firms enter alliances. The common reasons include funding (Powell, 1998), access to resources (Prahalad, 1998), learning (Bessant and Tsekouras, 2001; Bruns, 2013; Khanna, 1998), external knowledge (Rothaermel, 2001), utilisation of complementary assets, lack of expertise technology (Arora and Gambardella, 1990; Powell, 1998) and reducing uncertainty in high risk areas of R&D (Hagedoorn, 2002; Teece, 1992) . Effective inter-organisational networking has enabled knowledge transfer and capacity building in various sectors (Bessant and Tsekouras, 2001). Collaborative R& D for innovation offers beneficial effects and enables firms to gain competitive advantage (Ordover and Willig, 1985).

In scientific R&D projects, collaboration is particularly useful as scientists from diverse disciplines build on their knowledge and contribute for a collective task. In this way, collaboration allows to seamlessly connect contributions across disciplines asynchronously, facilitate co-ordination across and within domains and enable innovation (Bruns, 2013). Furthermore, horizontal linkages with other competing firms may help to overcome appropriability problems, as the firms would have collectively contributed to the R&D costs. Additionally, collaboration helps in reducing wasteful duplicate expenditures on research and development (Teece, 1992).

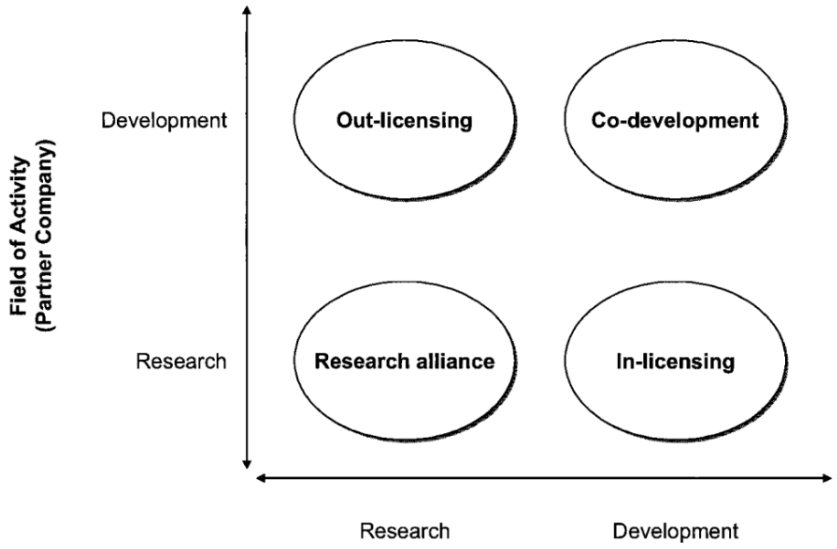
In the pharmaceutical industry setting, two types of collaborations are prevalent: a) research alliances and b) co-development (Reepmeyer, 2006).

- Research alliances are formed when two firms form partnerships for early stage risk sharing. This allows companies to share research costs and share risks. The joint

research leverages competencies of both the companies, increases the possibility of getting positive research results and the probability to progress to subsequent stages.

- Co-development alliances are usually formed during the drug development stages and allow leveraging the development and marketing capabilities of the other company. Such agreements are usually characterised by revenue sharing or profit sharing agreement (Reepmeyer, 2006).

The open strategies existent in the pharmaceutical industry by their drug research stage is summarised in the figure below:



Source: (Reepmeyer, 2006)

Figure 5: Open innovation strategies in pharmaceutical industry

A salient feature in all these cases is complementing each of the open innovation strategies with in-house R&D for performance. To sum up, the review of the literature shows how open innovation and its relevance have increased in pharmaceutical industry. Out-licensing of technology or in-licensing from external sources have increased in the past decade (H Chesbrough, 2003a; Ernst, 2003; Kline, 2003; Lichtenthaler, 2007, 2008) and cooperation with external entities is core to reduce uncertainty in R&D, improve success and reduce time to market. Firms need to strike a right balance between open and closed innovation activities to achieve success in innovation. Too much openness can negatively impact the chances of long-term success as it can lead to loss of control and knowledge. On the other hand, closed innovation tend to increase a firm's innovation cycle time (Enkel et al., 2009). In current

times, the traditionally closed innovation model that endorses innovation in isolation is fast losing ground and instead open innovation in pharmaceutical research is becoming a pivotal innovation strategy (H Chesbrough, 2003a; Gassmann and Reepmeyer, 2005).

Table 7 summarises the open innovation approaches followed by the pharmaceutical industry as evidenced in the literature.

Table 7: Open innovation approaches used by firms for pharmaceutical innovation

R&D Structures	**Open innovation approaches and strategies**	**Industry/Sector**	**Study**
Centralised R&D with outsourcing activities	– Internationalization of R&D – Outsourcing of R&D – External commercialization of intellectual property	Companies with R&D Labs	(H Chesbrough, 2003a; Chesbrough and Crowther, 2006; Gassmann, 2006)
	– Low risk partnering options for multinationals	Biotech Pharmaceuticals Fine chemicals	(Rosebush et al., 2012)
Collaborative Innovation	– Firm-centric network with offshore outposts	Across range of R&D companies	(Jelinek et al., 2012)
	– Bidirectional information exchange between public funded institutions and firms – Extensive co-authoring between researchers of industry and public sector	Pharmaceutical firms	(Henderson and Cockburn, 1996)
	Innovation networks between academia and industry o One company-one investigator o One company-one university o One company supports a university consortium o One company supports a university institute o Industry consortium (pre- or non-competitive) o Competition o Venture capital investment o Fee-for-service	Biopharmaceutical innovation	(Melese et al., 2009).
	– Industry wide, targeted, collaborative innovation efforts	Across range of R&D companies	(Jelinek et al., 2012)
	– Academic patenting – Licensing – Technology transfer office	Medical technologies and drugs	(Sampat, 2010)
	– Open approaches to R&D – Pooled funds – Grants to companies in developing countries – Prizes for milestones and end prod-	New drugs	(Correa, 2012)

	ucts – Patent pools		
	– Alliances for resources learning	Biotechnology	(Koput and Powell, 2000)
Virtual Labs	– Virtual, ad hoc networks of resources	Drug R&D	(Jelinek et al., 2012)
	– Public private partnerships for neglected diseases – Modular approach to R&D	Neglected diseases	(London School of Economics and Political Science, 2005)
	– Open Source Model in drug discovery	New drugs	(Årdal and Røttingen, 2012)

The recent trends in the pharmaceutical industry milieu are suggestive of changes happening in the new drug development landscape and provide an understanding of the factors influencing the changes. The complexity for pharmaceutical innovation warrants openness to leverage available knowledge and expertise that may reside outside firms' boundaries. It allows exchanges of ideas, resources and allows capturing the knowledge of diverse partners and considering new approaches that a lone innovator may not consider. In this way, open innovation aids the new drug discovery process. (Almirall and Casadesus-Masanell, 2010).

The nature of external forces which mediate firm actions have been a matter of serious analysis more predominantly in the management literature of 1990s (Chandler, 1990; Porter, 1990). An important question raised by Nelson in his seminal paper 'Why firms differ?' is an introspective question raised to stress the point that though firms in a particular set of industry face the same environment and similar choice sets, they still differ in their behaviour and strategic choices (Nelson, 1991). A plausible explanation lies in the concept of dynamic firm capabilities which evaluates the role of firm capability in charting the course of firm's behaviour (Nelson, 1991; Teece et al., 1997). It's in this realm that the concept of dynamic capabilities will be examined in the next section to seek an answer to an important question: *What guides firm's behaviour?*

2.3 Why firms differ[7]?

The previous section elaborated on how firms are experimenting with a range of open innovation strategies and models for pharmaceutical innovation. An underlying point emphasised by open innovation scholars is that firms these days do not follow a pure closed innovation or pure open innovation approach, rather open innovation is used to augment the traditional R&D based practices (HW Chesbrough, 2003). The diverse pathways adopted by firms make them different from one another and leads us to the question – why do firms differ? In this section, the lens of dynamic capabilities theory has been used to understand why firms differ in their strategic response to external conditions and openness.

Dynamic capabilities approach include the ability to identify needs or opportunities, formulate a response to such a need or opportunity and implement a course of action (Helfat et al., 2009). The two important aspects of dynamic capabilities which enable understanding of firm actions are –a) ability of a firm to undertake a strategic change and b) asset profile of the firm which influences strategy formulation. These two interrelated aspects influence the dynamic capabilities of a firm.

2.3.1 Firm level dynamic capabilities

How organisations change in response to environmental threats and opportunities? This is a question which has evinced academic interest for long and has resulted in scholarly contributions such as prospect theory (Kahneman and Tversky, 1979), ecological theory (Hannan and Freeman, 1977, 1984), sense making (Weick, 1993; Weick, 1995), and threat rigidity hypothesis (Staw et al., 1981). These studies have focussed on two divergent views of organisational change. One line of research explores changes at organisational level and focuses on multiple factors such as inertia of firms, sense making and adaptation of firms to external environment (Levinthal and Rerup, 2006; Weick, 1995; Weick and Sutcliffe, 2006). Weick (1993) emphasised that organisations falter not because of poor decision-making but because of deficient sense making. Sense making is what appears rational to an organisation in the event of complex problems which may lead to vague questions and murky answers in unfamiliar situations (Weick, 1993). While the outcome of sense making may be success or

[7] This title was used by Cohen WM, Nelson RR and Walsh JP (2002) Links and Impacts: The Influence of Public Research on Industrial R&D. *Management Science* 48(1): 1-23. in their seminal paper.

failure, rigidity in organisational response in the event of a major threat due to environmental changes is a more serious threat and has higher likelihood of organisational collapse (Staw et al., 1981). The literature above supports the argument that it is critical for organisations to adapt in the event of adverse changes in the environments. Rigidity (lack of flexibility in conditioning an appropriate response) and deficient sense making (lack of making sense of the gravity of situation) in firms influences their behaviour and may lead to organisational success or failure.

While most of the literature has focused on how firms adapt to changing environment, a parallel line of research has focused on the differential birth and death rates within a population of firms (Hannan and Freeman, 1977; Utterback and Suárez, 1993). Later writings have tried to combine the two perspectives and conclude that these studies at the firm and industry level are indeed complementary (Astley and Van de Ven, 1983; Levinthal, 1991; Scott, 1987). In this view, Levinthal (1991) explains the organisational adaptation and selection are interrelated processes and links models of organisational learning with ecological analysis of firm survival. A firm's competence has its roots in organisational learning and experience, which leads to organisational inertia and shapes the selection process. Thus selection and adaptation cross paths in the journey of organisational change (Levinthal, 1991).

Organisations face difficulty in adapting to change in uncertain conditions. The ambiguity around making strategic choices and uncertainty involved to predict future preferences makes it complex for organisations to change (March, 1991). In a dynamic environment, firms need to resolve tensions at many different levels – industry context, interdivisional dynamics and corporate level (Galunic and Eisenhardt, 2001). The conflict and tension, which an organisation faces in the event of environmental changes, affect its response and can amplify or diminish the potential of success or failure.

> *'If the environment changes rapidly, so will the responses of stable organizations; change driven by such shifts will be dramatic if shifts in the environment are large' (March, 1981: 564)*

Organisations adapt and evolve to the larger environment (March, 1991) through learning, conflict resolution (March, 1981), evolution of new organisational forms (Lewin et al., 1999) and effective selection of exploration or exploitation strategies (March, 1991). A change in

strategy is often necessary if an old firm needs to survive in a new environment. Nelson (1991) states that just as environmental forces have a constraining effect, firms also use their own discretion on how the environment really affects them.

The concept of dynamic capabilities provides a convincing framework to assess a firm's ability to modify strategies to adapt to a rapid changing environment. Dynamic capabilities are the subset of competencies/capabilities which allow the firm to create new products and processes and respond to changing market circumstances (Teece and Pisano, 1994). The term 'dynamic' refers to the changing environment caused due to changes in technology market, uncertainty in competition and future markets and increased emphasis on speed to innovation. The term 'capabilities' refers to firm's ability to *sense* and shape opportunities and threats, to *seize* opportunities, and to *maintain* competitiveness through enhancing, combining, protecting, integrating and reconfiguring assets (Teece, 2007).

Various authors have defined the theory of dynamic capabilities in different ways. Nelson (1991) identifies *strategy, structure* and *capabilities* as important components of dynamic capabilities. A firm exhibits dynamic capabilities by changing its strategy and structure to mould organisational capabilities (Nelson, 1991). In defining dynamic capabilities, (Eisenhardt and Martin, 2000) emphasises on organisational and strategic routines which enable a firm to achieve resource reconfiguration. Teece and Pisano (1994) explicate dynamic capabilities by emphasising on three components that shape the capabilities of a firm – *processes*, *position* and available *paths*. Processes constitute organisational routines, current practices and strategic decisions while a firm's asset position constitutes its current technological, financial and complementary assets. The processes and position of firms collectively shape its capability to choose strategic alternatives (Teece and Pisano, 1994). Figure 6 shown below is a graphical illustration of the important components of dynamic capabilities and how these components influence each other to gain competitive advantage.

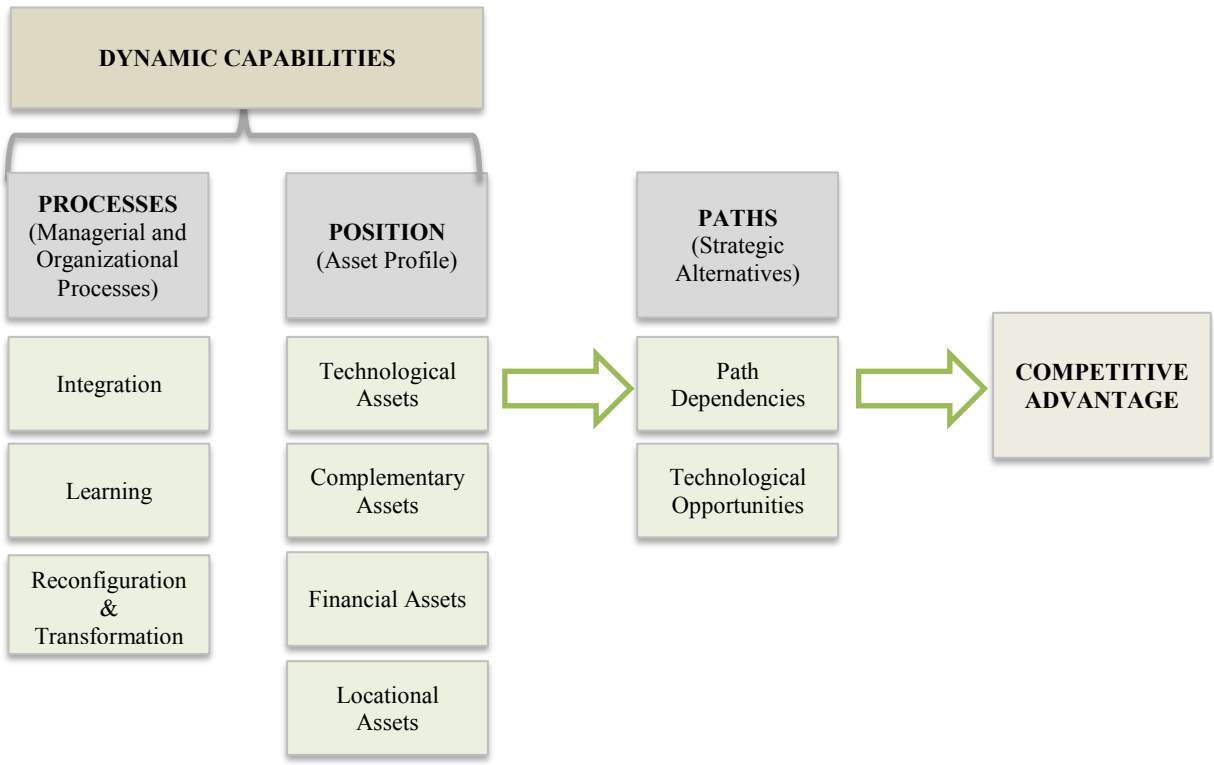


Figure 6: Dimensions of a firm's dynamic capabilities

The micro foundations of dynamic capabilities of a firm lie in its skills, processes, procedures, structure and can be encapsulated as a firm's capability to 1) sense and shape opportunities and threats 2) seize opportunities and 3) maintain competitiveness through reconfiguring assets (Teece, 2007).

The effectiveness of dynamic capabilities can be measured in different ways. Nelson (1991) defines a firm's capability to innovate and its ability to profit from innovation as two key metrics of a firm's dynamic innovation capabilities while Teece et al. (1997) emphasises on competitive advantage as a measure of success. Helfat et al. (2009) proposed two measures to assess the dynamic capabilities of firms a) evolutionary fitness and b) technical fitness. Evolutionary fitness is a measure of the ability of the firm to reconfigure or modify its resource in a changing environment while technical fitness is a measure of a firm's technical ability to develop in a cost effective manner.

Other writings by authors (Athreye et al., 2009; Eisenhardt and Martin, 2000; Helfat and Peteraf, 2009) described how dynamic capabilities provide strategic logic to change in view of opportunities and allow firms to adapt to business ecosystem. In the study on pharmaceutical industry, Athreye et al. (2009) assessed the influence of regulatory changes in the external environment on the dynamic capabilities of four large Indian pharmaceutical

firms. The study concluded that the firms responded to the changes in the environments by formulating various strategies that enabled development of capabilities and exploitation of opportunities thrown up by regulatory changes (Athreye et al., 2009). In other studies, dynamic capabilities have been assessed to enable change in organisational processes (Lee and Kelley, 2008) or to investigate the role of managerial practices in reconfiguration of resources (Eisenhardt and Martin, 2000). Another research study shows the importance of innovation in enabling firms to configure their strategies and exhibit dynamic capability (Tsekouras et al., 2011). These theoretical and empirical work show that dynamic capabilities concept provides an appropriate framework to assess strategic response of organizations in a given context.

To recap, uncertainties in external environments cause organisations to mould their dynamic capabilities as it affects their ability to profit from innovation (Nelson, 1991). When firms adapt their internal structure, processes, strategies to adapt to environmental changes, it is referred to as dynamic capabilities. The concept of dynamic capabilities holds relevance in the wake of globalisation and open economy, which has brought about massive changes in the business environment. It assumes even more importance in case of developing countries that grapple with limited resources and budgets. Firms in these countries face resource constraints and pressure from the markets to make available quality products at affordable prices (Prahalad and Mashelkar, 2010). External constraints have compelled firms in emerging economies to display internal creativity to adapt structure and strategy to do business and create innovative business models (Prahalad, 2006). Within this view, dynamic capabilities serves as a guide to understand differences in strategic approaches adopted by firms and to understand how firms have responded to changing external environment.

2.3.2 Asset position

The resource perspective as key element in strategy formulation and attainment of competitive advantage has various endorsers in the strategic management literature (Barney, 1991; Barney, 2001; Hansen and Nohria, 2004; Peteraf, 1993; Wernerfelt, 1984; Wright, 1994). Resource based view put forth by (Penrose, 1959) and extended by various other scholars posits that firms differ in their resources which offers them competitive advantage in important ways (Barney, 1991; Bates and Flynn, 1995; Chandler, 1992; Peteraf, 1993). Central to this perspective is the notion that a firm's resource bundle offers unique competitive advantage if the resources possess heterogeneity, imperfect imitability and

immobility. If resource mobility is high or entry barriers do not exist, then it can be easily acquired by competitors or new entrants and thus cease to be a source of advantage (Barney, 1991).

Wernerfelt (1984) analysed the resource base of firms with diversified business to develop resource-product matrix tool, which can be used to identify the resource position of the firm and chalk strategic actions. This tool intended to enable firms to manage their resource position and maximise profitability through an optimum allocation of resources (Wernerfelt, 1984). The underpinning statement in this stream of literature is the importance of firms' resource endowment as a source of competitive advantage.

The resource based view as the sole element to attain competitive advantage has been criticised on various grounds. An important critique is the concept of 'resource immobility' that is questionable in changing times. In this increasing networked world, when mobility barriers are low, it's unlikely that all critical resources lie within a firm's boundary. Scale of research and development, new opportunities and distant geographic markets are all contributing to shifting firms' boundaries (HW Chesbrough, 2003; Hamel and Prahalad, 1996). The resource based view also suffers from a myopic view as it includes only tangible and intangible assets and fails to account for capabilities; a key element for competitive advantage (Priem et al., 2013; Priem and Butler, 2001). The theory also fails to capture a dynamic view of firm assets in a changing environment. In this light, dynamic capabilities approach, an extension of resource based view, holds more relevance as the underlying tenet is reconfiguration of firm capability to address changing environment (Teece et al., 1997).

Dynamic capabilities framework defines a firm's *position* as firm specific endowments of technology, intellectual property, complementary assets, reputational and relational assets (Teece et al., 1997). A firm's competence is a bundle of distinctive technological skills, complementary assets, organisational routines and capacities which enable it to solve technical and organisational problems and renders competitive advantage (Teece et al., 1994). Companies have realised over time that a firm's organisational capabilities determines its competitive strength and weakness. The success of American firms in industries like chemicals, pharmaceuticals computers, aircraft, aerospace, oil refining and food processing and their ability to retain their global leadership position has been due to their organisational capabilities which gave them distinct competitive advantage (Chandler, 1992).

Teece and Pisano (1994) introduced four categories of assets as technological, complementary, financial and locational in his original paper on dynamic capabilities. Latter writings, expanded the asset categories to include reputational, structural, institutional and market assets (Teece et al., 1997). The table below shows the key definitions of the different assets types.

Table 8: Definition of asset types

Types of assets	**Definition**
Specific assets	Specialised plant and equipment
Technological assets	Current endowment of technology usually protected by intellectual property
Complementary assets	Related assets required to produce and deliver new products and services.
Financial assets	The cash flow or cash position of a company and degree of financial leverage
Reputational assets	An intangible asset which signifies a firm's standing in the market and shapes the responses of customers, suppliers and competitors
Structural assets	Formal and informal structure of organisations and their external linkages
Institutional assets	Public policies, institutions, regulatory environment such as intellectual property regimes, antitrust laws that shape the business environment and serve as institutional assets
Locational assets	Uniqueness in geographical location resulting in firm advantage

Source: (Teece et al., 1997)

The following section focuses and elaborates on three types of assets –technological, financial and complementary.

Technological assets

Technological assets are defined as current endowments of technology, which provide a differentiating factor for firms (Teece et al., 1997). The knowhow of a firm may be tacit knowledge inherent with the firm or may be codified in the form of patents, publications etc. In pharmaceutical research, pipeline of new compounds and new drug applications filed with regulatory authorities for registration of new molecules are a measure of technical competence of a firm (Henderson and Cockburn, 1994). Various studies have used R&D and patent data to provide a plausible picture of technological activities at a national or global

level (Patel and Pavitt, 1994). Because of the increasing importance organizations place on patenting their innovations, patents are important indicators for pharmaceutical innovation (Zuniga et al., 2009). For universities and related institutions, number of research papers published and citations are important indicators of their technological assets (Patel and Pavitt, 1994).

Technical competence involves a firm's learning ability and its ability to develop and design new products and processes (Ahuja, 2000; Teece et al., 1994). Without a strong base in organisational learning, and industry specific capabilities in R&D, production and distribution, a firm cannot develop the necessary competitive strengths (Chandler, 1992). Organisational learning allows a firm to translate its experience and routines into core organisational capabilities (Chandler, 1992; Teece et al., 1994). Routines imply "regular and predictable patterns of firm behaviour" (Nelson and Winter, 1982: 14). Learned routines like basic market understanding, regulatory procedures to comply for quality and safety tests, and the capability of firms to integrate knowledge in new ways for product development have enabled companies like Merck, Abbott, Pfizer, Eli Lily, Upjohn (now a subsidiary of Pfizer) and Parke Davis (also a subsidiary of Pfizer) to enter prescription drugs market in 1940s and 1950s and retain market leadership for decades (Chandler, 1992). These potential strengths enable to ward off new entrants and keep existing competition at bay (Chandler, 1992; Teece et al., 1994).

Two forms of competence have been identified to be particularly important to gain competitive advantage in pharmaceutical research. One being the ability to access new knowledge from outside the organisational boundary and the other being the ability to integrate knowledge across disciplines and therapeutic classes within a firm (Conner, 1994; Henderson and Cockburn, 1994; Powell et al., 1996).Companies also engage in technological acquisitions to improve competency and this was found to have a positive effect on innovation output. The size of the knowledge base acquired or the number of patents also has a positive effect on firm innovation (Ahuja and Katila, 2001).

In pharmaceutical research, local competence is in the form of expertise in a unique discipline or a particular disease area leads to significant impacts on productivity of drug discovery research (Henderson and Cockburn, 1994). The competence of a firm is particularly crucial in pharmaceutical innovation as it determines a drug's progression in different stages of clinical development. A study conducted on more than 1900 compounds

developed by US pharmaceutical and biotech firms between 1988 and 2000 shows that experience of a firm has a significant influence in the success of a drug compound specially in late stage clinical trials. The likelihood of drugs passing successfully through complex phase 2 and phase 3 trials was higher with experienced firms, which requires perfection in dosage and efficacy studies in large patient samples. A firm's experience in a particular therapeutic area also makes it more competent and likely to complete phase 3 of drug development than a firm which has a broader scope and experience in many therapeutic areas (Danzon et al., 2005).

Financial assets

A firm's financial resources and cash flow position constitutes its financial assets and has important implications on the strategy of a firm (Teece et al., 1997). In pharmaceutical research, the process of drug discovery and development is capital intensive. New entrants and small firms are specifically constrained for resources and find it difficult to finance the R&D process (Hall, 2002; Rothaermel and Hill, 2005). In the biotechnology industry, the lack of resources in small innovative biotech firms provided opportunities for the incumbent firms to in-license biotechnology drugs and commercialise them using their own sales force (Rothaermel and Hill, 2005). Financial resources which include debt, equity, retained earnings have a bearing on the firm's capacity to support R&D activities (Canto et al., 1999). Financial strength is an important determinant in R&D spending and allows incumbent firms to engage in R&D investment in start-up companies or to enter alliances with other firms (Rothaermel and Hill, 2005).

Evidence from theory, survey and empirical findings show that R&D investment in firms is dependent on positive cash flows (Hall, 2002). R&D expenditures and sales are also an important metrics to know the firm's investment in research. Though R&D spending is not guided by its financial position alone but also by other factors such as spill over knowledge, strategic decisions, technological certainty and previous R&D investment (Helfat, 1997), access to capital is still a main parameter for driving innovation process (Teece, 1996). R&D intensity measured as R&D expenditure as percentage of sales and transfer is used commonly as an indicator to analyse inter firm differences (Cohen and Levinthal, 1989).

Complementary assets

Commercialisation of technology requires access to assets that range from manufacturing, distribution, service and/or access to other complementary technologies. These are collectively referred to as complementary assets (Teece, 1992; Teece et al., 1997). Empirical studies demonstrate that complementary assets have played an important role in forging many inter-firm alliances between large and small sized firms (Arora and Ceccagnoli, 2006; Rothaermel, 2001). Teece (1986) differentiates between three types of complementary assets: generic, specialised and firm specific. Generic assets are easily accessible and less tailor made for the innovation whereas specialised complementary assets have a unilateral dependence of the asset on innovation (Teece, 1986). Firm specific assets include specialised plant, equipment and marketing specialised for innovation (Arora and Ceccagnoli, 2006; Teece et al., 1997).

Ownership of complementary assets also has a conditioning effect on the boundary decision of firms. If firms possess specialised complementary assets to enter the product markets, they are more likely to opt for in-house drug development over licensing or collaborative decisions. However, if firms lack the necessary complementary assets to commercialize new technology, they tend to look for options outside the companies (Arora and Ceccagnoli, 2006). Small sized firms align with large pharmaceutical firms to gain access to capital and market, extend their value chain and gain reputational effects.

To recapitulate, the dynamic capabilities framework provides a useful approach to determine a firm's specific *asset position* by evaluating its technological, financial and complementary assets. The asset position of a firm along with its processes plays a significant role in contouring the future actions of a firm. The responsive action, which a firm formulates as a result of the changing environment, based on its *asset position* and *processes* is reflective of its *dynamic capabilities*. Such a framework not only allows understanding a firm's behavioural response to environmental changes but also deepens our understanding on why firms, which face the same set of environmental factors, differ in their firm actions. Two important facets of dynamic capabilities that are fundamentally important to support our understanding of Indian pharmaceutical industry are: a) strategic change and b) asset position in Indian firms.

2.4 Summary

This chapter reviewed relevant academic literature in order to acquire a better understanding of the dimensions of institutional/regulatory settings, open innovation and dynamic capabilities that allows firms to take appropriate strategic action to maximize leveraging external opportunities and internal capabilities. The literature review aimed to develop a conceptual framework that guided data collection and analysis.

The following areas were covered and discussed in detail. The section on national innovation system showed that institutional and regulatory environment play an important role in shaping the current selection environment and influences action of firms to undertake research and innovation. The national environment encourages local innovation networks between science and industry either by shaping pull mechanism such as technological opportunities through R&D funds/grants or through push mechanism such as public private partnerships schemes and laws such as Bayh-Dohl Act[8]. Such mechanisms have proved to be beneficial in the developed countries in promoting research and innovation in a country.

The regulatory aspect of national innovation system is critical for open innovation as strong patent laws encourage innovation, patenting and licensing and provides a suitable environment for open innovation (Teece, 1986; West, 2006). Literature also supports that pharmaceutical innovation is technologically difficult, risky, cost intensive and a mix of in-house and open innovation pathways provides options for firms to bring down R&D costs and increase chances of success in pharmaceutical innovation (Almirall and Casadesus-Masanell, 2010; Gassmann and Reepmeyer, 2005). However, firms differ in their strategic response. The dynamic capabilities (Teece and Pisano, 1994) concept enables the understanding of important components that come into play when a firm faces critical changes in the environment. The focus on firm's asset position enables to understand the influence of resources in charting a suitable course of action for firms and provides an explanation for the idiosyncratic pathways adopted by firms (Teece, 2007).

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[8] The Bayh Dole Act implemented in 1980 allowed the patenting and licensing of inventions by academic institutions to third parties OECD (2002) Benchmarking Industry Science Relationships. Paris, France: Organisation for Economic Co-operation and Development, 193..

This literature review was helpful in establishing a conceptual framework that guided the methodological considerations for this study. The review of literature has tried to integrate the innovation and strategic management literature and provides an umbrella framework that highlights important concepts from national innovation system, open innovation and dynamic capabilities. A traditional literature review approach has been used to review critique and summarise the body of literature. The key words used to conduct the literature search using electronic search and database strategy were 'innovation', 'open innovation', 'pharmaceutical industry', 'Indian pharmaceutical industry' and 'new drug innovation'. This resulted in a comprehensive list of articles, the examination of which would have been a difficult task considering the duration of the study. The review of literary works was hence restricted to key authors who had made significant contributions in the field of open innovation, national innovation system and dynamic capabilities. Frequent references and works of significant authors in leading journals relevant to the study were also included along with other academic authors. Non-academic authors and sources were also studied to identify key innovation trends in pharmaceutical innovation. The next section presents the conceptual framework of the study and the line of inquiry, which this study aims to pursue.

3 Conceptual Framework

The pharmaceutical industry presently operates in an uncertain environment affected by changes at the national and global level. The sustenance of the industry depends on innovative medicines with genuine therapeutic value. Pharmaceutical innovation is difficult, risky and takes place under considerable constraining conditions. At the *macro* level, shifting policies, changing patent regimes, stringent regulatory standards add to the difficulties of pharmaceutical companies. At the *firm* level, there is a need to realign strategy to meet the challenges in the external environment and combat increasing R&D costs and reduce non-productive outcomes. During these times, open innovation emerges as a plausible strategy to look for solutions outside the boundaries for innovation.

The Indian pharmaceutical industry has traditionally been a generic drugs industry with R&D confined to generic and incrementally modified drugs. The low end of research carried out during this regime provided little incentive for firms to open up the innovation process to outside partners. The change in the patent regime in 2005 with the amendment of patent law triggered research for novel drugs and necessitated firms to open up their boundaries of R&D labs to external partners. Open innovation is used in this study to understand the strategic choices used by Indian pharmaceutical firms within and outside the local innovation system for new drug innovation. In this dissertation, the role of public sector and appropriability regime is considered at macro level to understand the impact of national policies and patent laws to nurture innovation at firm level. In this way, the study aims to gain perspectives from macro level and firm level to understand the factors that enable firms to open up to outside sources. The dynamic capabilities approach enables to understand why firms differ in their strategic response to external environment.

The conceptual framework is a congruence of three streams of literature: national innovation systems, open innovation and dynamic capabilities approach. This study explores answers to the research questions along three important themes – Firstly, the role of national institutional context in influencing the local ecosystem to enable innovation during two distinct appropriability regimes is explored. Secondly, the study assesses the type of open innovation networks formed between public and private science within the innovation ecosystem and factors that influence and mitigate the formation of such networks. Thirdly, the study assesses

the open innovation strategies pursued by firms and the factors that influence the strategic choice. The open innovation practices of firms are investigated through the inbound and outbound innovation activities undertaken by firms and the interactions formed within the local innovation system for new drug discovery and development. The setting for this investigative study is the pharmaceutical sector of India. In this respect, this study aligns more with organisation-environment co-evolution theory, that underpins that industry co-evolves with the changes taking place in the institutional environment (Lewin et al., 1999).

3.1 Linking National context to firm action

A major underpinning of the NIS theory is the dynamics between universities, public research institutions and firms in providing the necessary scientific and technical input to firms and hence propelling research and innovation. This study aims to employ the underlying tenet offered by NIS theory to gain an understanding of the Indian pharmaceutical sector and the role of policy framework in spurring transformative processes leading to inter-organisational networks and affecting outcomes (Laumann et al., 1978). This study utilises this concept to understand interactions between firms, universities and public research institutions for research of novel drugs.

Within the National Innovation framework, political, cultural, social factors also contribute to the efficacy of innovation system. However given the scope and limits of the study, only institutional and regulatory factors are considered to understand the effectiveness of national system in the Indian context. Figure 7 identifies the important factors of National Innovation system in literature and shows the two factors used in this study.

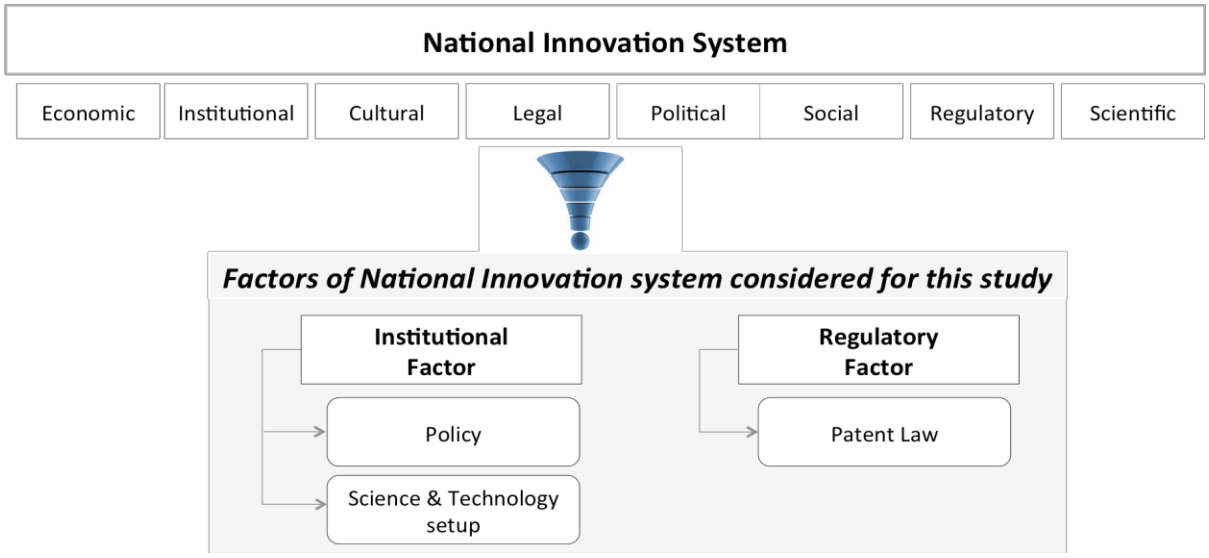


Figure 7: Representation of factors of NIS of interest in this study

3.2 Linking Firm asset profile to firm action

There are a variety of studies in the strategic management literature that support our understanding of firm level adaptation in a changing environment (March, 1991; Nelson and Winter, 1982; Teece and Pisano, 1994; Teece, 2009). The theoretical work of dynamic capabilities underpins the role of resources and competence in enabling firms to adapt in a changing environment (Teece et al., 1997). A firm may possess resources/competencies but may lack dynamic capabilities or the ability to reconfigure itself. The understanding of how firms open up their boundaries and adopt a particular strategic pathway can be assessed using the lens of dynamic capabilities. This dissertation study uses the dynamic capabilities approach (Teece et al., 1997) to investigate the strategic flexibility of firms with respect to changing national environment of India and to understand differences in their strategic actions.

Within this view, this study borrows the following concepts from dynamic capabilities (Teece et al., 1997)

a) the 'position' of the firm; a reflection of resources and competencies to assess the asset profile of the firm
b) the dynamic capabilities of the firm; which is a determinant of flexibility of the firm to change.

Using the definitions provided by (Teece, 1986; Teece et al., 1997), the firm's *asset position* is evaluated through its technological, financial and complementary assets. Technological assets are measured through the number of product patent applications filed and pipeline of new chemical entities. Financial assets are measured through consolidated net revenues and R&D intensity. The presence of a manufacturing facility, number of R&D labs, and marketing capability as reflected in the strength of sales force are used as indicators of complementary assets of a firm.

The conceptual framework in Figure 8 is a result of review of literature and adoption of important concepts from the theoretical domain of national innovation system, dynamic capabilities and open innovation. The figure shows the main issues and the research questions explored in the study.

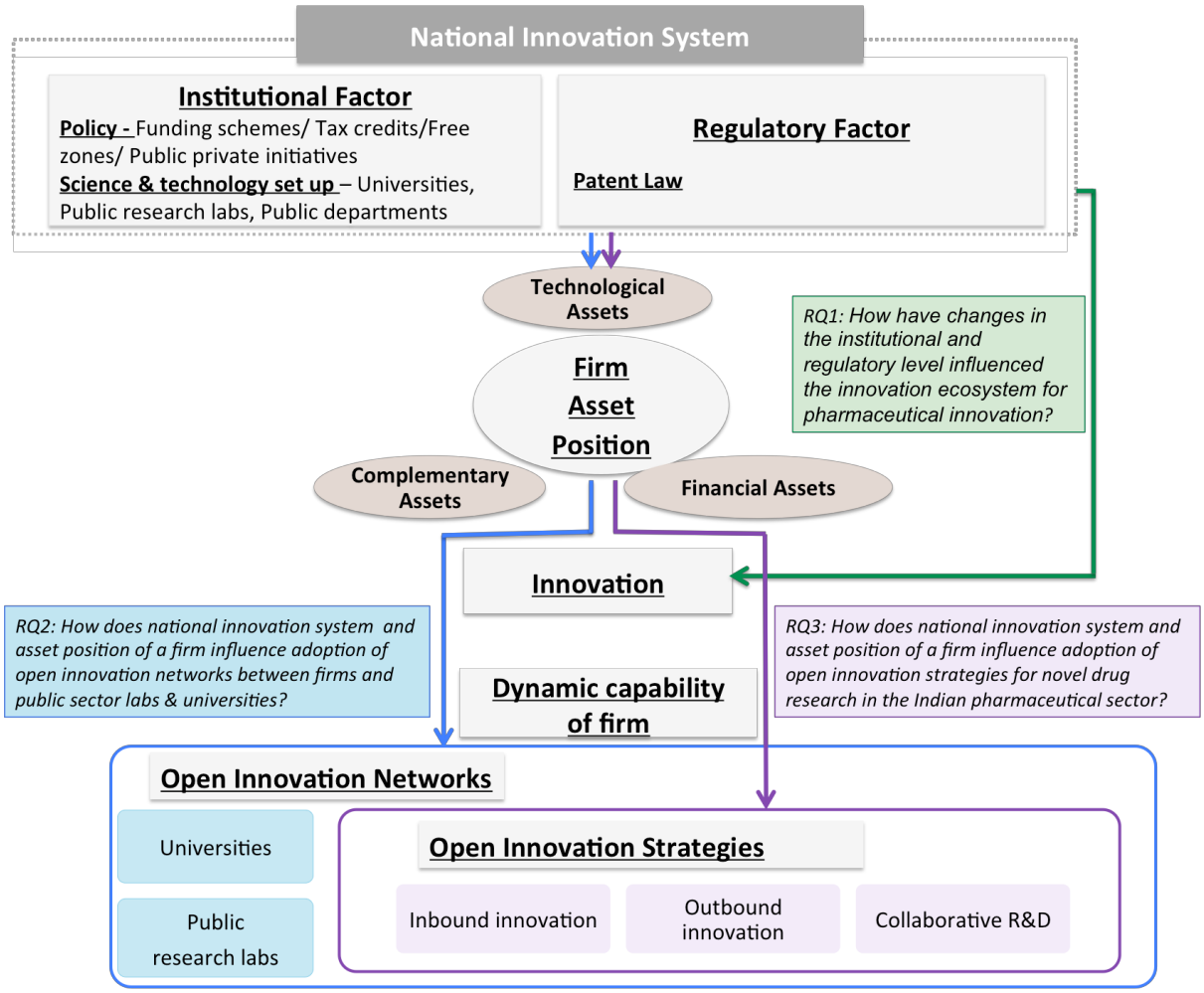


Figure 8: Conceptual framework used in the study

The purpose of this research is to explore how changes in the national context have influenced innovation and openness in Indian pharmaceutical firms engaged in the research for novel drugs. More specifically, the objective of the study is to look into the role of institutional framework, public policies and appropriability regimes at the national level in influencing formation of innovation networks with entities and the open innovation strategies pursued. Four sets of institutions are recognised as central feature of National Innovation system: business firms, universities and mixture of public and private institutions providing education, and training (Patel and Pavitt, 1994). In this study, the set of entities considered for this study are pharmaceutical firms, public research labs and universities.

The main research question of this dissertation is - **How does national innovation system and asset position of a firm influence open innovation pathways for new drug innovation in the Indian pharmaceutical sector?**

The primary research questions used to explore the main research question are:
RQ1: How have changes in the institutional and regulatory level influenced the innovation ecosystem for pharmaceutical innovation?
RQ2: How does national innovation system and asset position of a firm influence adoption of open innovation networks between firms and public sector labs & universities?
RQ3: How does national innovation system and asset position of a firm influence adoption of open innovation strategies for novel drug research in the Indian pharmaceutical sector?

In this dissertation, open innovation pathway is defined as a mix of local innovation networks and open innovation strategies pursued by firms at different stages of research. This research study uses cases of pharmaceutical firms of established and SMEs to study patterns of innovation through patent data and explores openness in the sector using primary and secondary data. Prior literature testifies that resource constrained small scale firms as more likely to form partnerships with external partners for complementary assets, funds, access to markets and key business functions (Koput and Powell, 2000; Rothaermel and Deeds, 2004). Large companies differ from small & medium sized firms in their strategic motives to form partnerships (Arora and Gambardella, 1990; Baum et al., 2000). This study explores this difference in strategies in relation to their asset position through cases of established and SMEs.

The research findings in this dissertation is presented under three central themes –

a) Role of national innovation system in shaping the ecosystem for innovation
b) Open innovation networks within the national innovation system
c) Open Innovation strategies used in new drug innovation process.

The conceptual framework used in the study is based on the theoretical and empirical work of others and the study aims to build on this by providing evidence-based insights from an emerging economy like India. The scope of the study is product innovation (new drug) in the pharmaceutical industry viewed through the lens of national innovation system (Lundvall, 1992; Nelson Richard, 1993), open innovation (HW Chesbrough, 2003) and dynamic capabilities (Teece and Pisano, 1994; Teece et al., 1997) to study the open innovation networks and strategies employed by firms with public research institutes/universities for new drug research. A nested outlook is used to view innovation networks formed within the local innovation system and open innovation strategies pursued by firms as both are intermeshed within each other. This study does not foray into the biotechnology industry and the innovation of biological drugs. Though there are some Indian companies in India that have forayed into the biological drugs, but the focus of business activities is more towards biosimilars than research for new biological drugs. The R&D activity for innovation in biological drugs is steadily increasing and this may form the basis for research in the future.

3.3 Research Opportunity

The national environment in India for the pharmaceutical sector has changed due to change in patent laws and the accompanying policy changes that have pushed the pharmaceutical industry to conduct new drug discovery research and triggered adaptive behaviour in firms. Based on National Innovation system perspective, the diversity in innovation patterns of a country can be attributed to three factors: differences in intra-firm organizations and strategy, inter firm relations, government polices and the role of public sector (Freeman, 1987; Hwang and Choung, 2014; Lundvall, 1992; Nelson Richard, 1993). It has been well established by now in academic research that the support of government and public research institutes are required in developing economies to support catch-up innovation. Literature provides examples of how firms in developing countries have gradually emerged to be successful to compete in international markets through technology assimilation, organizational learning and innovation processes (Hobday et al., 2004; Hwang and Choung, 2014).

The Indian pharmaceutical sector is in a state of transition. The industry was successful in adoption of process technology and manufacture of low cost generic drugs during the process patent regime. Post 2005, firms are under pressure to move to the next level of product innovation. Indian pharmaceutical firms with technological capabilities set in process research and incremental innovations are modifying their strategies to make use of new commercialization opportunities in the product patent regime. In this way, this research study presents an interesting research opportunity to understand how firms are making the transition from imitation drug research to new product innovation.

In developing countries, policies have played a critical role for sector development in a country (Mytelka, 2006). Historically, public sector has played an important role in shaping the Indian pharmaceutical industry. The institution and evolution of the Indian pharmaceutical companies can be traced back to the establishment of state led manufacturing facilities, Hindustan Antibiotics Limited (1954) & Indian Drugs and Pharmaceutical Company (1961) and public research centres. Of the many measures undertaken by the Indian Government in the 1970s, some of the important initiatives were The Patents Act 1970 and the New Drug Policy in 1978 which changed the landscape of the pharmaceutical sector in the decades to come. The New Drug Policy in 1978 structured the establishment of manufacturing capability and provided a thrust to the indigenous pharmaceutical to manufacture and supply quality drugs at low prices. However, the initiative that made the most impact was the introduction of the Patents Act 1970 that marked the beginning of the process patent regime (Srinivas, 2012).

Research by (Srinivas, 2004, 2012) examines the broad historical evidence to highlight the role of government policies in shaping the learning opportunities and pathways for Indian pharmaceutical companies. An investigative study by Dinar Kale (2005) on Indian pharmaceutical industry details the effect of the patent regime in transforming the knowledge structure and capability of the industry. These studies were relevant to understand the role of policy initiatives in enabling the genesis and growth of generics industry. However, there is a lack of literature to understand how the public sector is supporting the transition of the industry to the complex novel drug research.

The innovation policy is crucial in developing economies, as it should be context specific and modified as per the capabilities of innovator firms. The case of South Korea demonstrates that to be successful, government policy should nurture new entrants and support the

technological development of the SMEs (Choung et al., 2014). The Indian government has initiated many policy initiatives post 2005 to encourage research and development among various entities of the innovation system. This investigative research study provides an opportunity to understand the effectiveness of these policy initiatives and also provide useful implications for policy makers of other developing countries.

Companies tend to choose an imitation path that is easiest to implement and allows them to enter the global markets easily (Choung et al., 2014). With the generic drug research, Indian pharmaceutical firms were able to narrow the technological gap with the innovator firms by being able to reverse engineer drugs developed by innovator firms using process innovation and emerge as major exporters of generic drugs.

The new drug innovation is challenging and there is evidence to support that Indian firms are evolving and formulating new strategic pathways usually necessary in the process of catching up (Chowdhary, 2010). In this way the study of Indian pharmaceutical sector is useful to understand the barriers and enablers of innovation at firm level. Firms are also influenced by the resources available and the capability within the company to undertake innovation (Hobday, 2005). An insight into what factors are important and influence the path of a firm to undertake innovation is useful for academic research, strategy formulation in companies and practitioner training.

The period 1995-2005 was important for the Indian pharmaceutical industry for transitioning to the product patent regime under TRIPS. This witnessed a considerable increase in research papers pertaining to effect of amended patent law on the generic drugs dependent Indian industry (Chowdhary, 2010; Grace, 2004; D. Kale, 2005; Kamble et al., 2012; Kiran and Mishra, 2011; Mahajan, 2011; Sampath, 2005). Researchers have also debated on the need for a product patent regime in a developing country like India where affordability and access to medicines are key issues for poor people and a product patent regime would increase the price of drugs (Sampath, 2005). In the last decade, changes in the global landscape, declining prices, stringent regulations along with patent amendments led to mergers, acquisitions, diversification and employment of new business strategies to adapt to the new policy situation (Chowdhary, 2010; Deshmukh and Sahasrabudhe, 2012; Rai, 2008; Rao, 2008; Sampath, 2005). However there is a dearth of studies in the post TRIPS regime investigating the transition of the Indian sector to new drug innovation within the perspective of National Innovation System literature.

Studies on firm, university and public research interactions are relatively sparse and there are few studies that have focused specifically in this domain (Basant and Chandra, 2007; Joseph and Abraham, 2009). Various studies have verified that there is lack of inter-firm co-operation between different agents of the innovation system (Joseph and Abraham, 2009; Ramani, 2002; Srinivas, 2004) such as public research laboratories, pharmaceutical firms, universities and government for pharmaceutical research and there is a need for policy intervention to promote such networks (Ramani, 2002). Joseph and Abraham (2009) provide evidence of low university-firm interactions and mention that the types of interactions that take place are mainly for consultation, supervision or for participation and for industry related conferences/ seminars. These studies indicate the innovation networks between firms and national institutions have been weak especially in the process product regime. The role of innovation networks is crucial in technologically complex product innovation. In this way, the paucity of research studies in this area lends a research opportunity to investigate how firms are interacting with government and other public institutions for research.

This research study provides a useful research opportunity to understand how catch up innovation is taking place in a developing country setting of India. The path that each country takes is different and depends on the level of institutional infrastructure, and dynamic capabilities of firms (Hobday, 2005). The agility of the firms to adapt to the external environment and the path taken by the firms to overcome challenges is a useful lesson to learn for other developing countries embarking on this journey. This research also aims to fill the current gap in the literature and make a contribution to the national innovation system and open innovation literature. The changes in the national environment of a developing country are unique and offers an interesting research setting in the pharmaceutical industry to explore how open innovation is adopted by firms engaged in new drug research. In this way, this dissertation aims to contribute to both theory and praxis.

4 Methodological Considerations

This chapter discusses the research philosophy, research design, data collection and analysis methods that were employed to achieve the aim and objectives of this study. Research design refers to the approach that embody the research questions formulated and the methods used for data collection, analysis and reporting the research findings (Creswell et al., 2007). This section describes the case study research design, classification of cases and the philosophy underpinning this approach. The section further elaborates the three methods which have been employed for data analysis a) Gioia method (Corley and Gioia, 2004) to undertake systematic analysis of qualitative data, b) patent analysis to estimate patent counts and assess the innovative activity of Indian firms and c) analysis of other secondary data to compile events, timelines in a systematic manner to compile case profiles and categorise formal research partnerships on key parameters. The study relies on interview data as its main source. Secondary data such as patent data, company related information, formal research partnerships, government policies and initiatives were used as important supplementary sources for triangulation and validation.

4.1 Philosophical Foundations

The purpose of this section is to describe the underlying philosophical assumptions followed in this study. All research studies have ontological, epistemological and methodological assumptions that guide action within a paradigm (Norman, 1994). A paradigm is an implicit frame of reference that is used to organise observations and reasoning (Babbie, 1998). The word paradigm originated from Greek *paradeigma* and the Latin word *paradigma* meaning model, example or pattern (Stanage, 1987; Stierand, 2009). Kuhn (1962/1996) defines paradigm as a set of beliefs, values and techniques adopted to get answers to scientific problem specifically among a scientific community.

One important dimension of the paradigmatic approaches is subject–object distinction at ontological and epistemological levels, which provide the basis for methods used for knowledge and theory building. The objective view of reality used to establish the positivist science has been the predominant paradigm in science, mathematics and social sciences for

years. Objectivist assumptions are grounded on the notion that reality is concrete, external and that knowledge can be gained by measuring regularities, laws, and patterns by focusing on structures, actions, behaviours, systems, and/or processes (Cunliffe, 2010). This philosophical tradition gained prominence due to the need for science to be based on strict criteria for establishing the meaning and validity of the statements and this gave birth to logical positivism (Polanyi, 1967). The focus of positivist and post-positivist approaches have remained on a) objective view of reality b) eliminating bias during the process of data collection and c) providing solutions to scientific problems through verification with the purpose of prediction and control (Mottier, 2005).

On the other hand in the world of interpretivists, lived reality and situation-specific meanings constitute the general object of investigation (Schwandt, 1994). Proponents of subjectivist approach view reality as a figment of imagination of human mind and use research methods to understand the subjective experiences of the world (Cunliffe, 2010). It has been argued by critics and scholars of the positivist approach that an objective assessment of data is impossible and scientific data is continually interpreted as they are observed (Mottier, 2005).

Burrell and Morgan (1979) dichotomised the philosophies of social science prevalent in organisational analysis to either subjectivist or objectivist orientation. This typology drew great attention from researchers and scholars and has widely been used in the social science research. However in the past decades, there have been a multiplication of new perspectives such as hermeneutics, ethnomethodology, symbolic interactionism, dramaturgical analysis, post-structuralism, and discourse theory under the interpretivist approach (Mottier, 2005). In present day setting, the variety of studies in management research and availability of research methods that can be used lends many options for researchers to figure out their assumptions about reality (ontology), nature and purpose of knowledge (epistemology) and ways of knowing reality (research methods) (Cunliffe, 2010). The current state of research in organizational analysis illustrates the viewpoint of Kuhn (1962/1996) that the process of new theory development challenges the old paradigmatic assumptions and results in an overlap of philosophical assumptions, procedures and methods making way for new paradigms for scientific enquiry (Willmott, 1993).

A rough typology extended by (Morgan and Smircich, 1980) built on ideas of (Burrell and Morgan, 1979) provide a classification based on the objective-subjective scale and underlying ontology, epistemology and research methods commonly used in social sciences

as shown in Figure 9. The subjectivist assumptions view reality as socially constructed or as a projection of human mind based on how people interact with the world. Such an assumption endorses those research methods that allow exploring the subjective experiences and provide meaning to how people interact with the world. On the other hand, objectivist assumptions view reality as concrete and methods rely on measuring outcomes related to structures, actions, systems and processes (Cunliffe, 2010; Morgan and Smircich, 1980).

Table 1. Network of Basic Assumptions

	Subjectivist Approaches to Social Science ←					→ Objectivist Approaches to Social Science
Core Ontological assumptions	Reality as a projection of human imagination. *[Individual experience & consciousness. Transcendental phenomenology & solipsism.]*	Reality as a social construction. *[Individuals create meanings through language, routines, symbols etc.]*	Reality as a realm of symbolic discourse. *[Meanings sustained in human action & interaction. Subject to both rule-like activities & change.]*	Reality as a contextual field of information. *[Adapting & changing as information is exchanged.]*	Reality as a concrete process. *[Interacting, evolving, & contingent process.]*	Reality as a concrete structure. *[Comprised of constituent parts, observed in concrete behavior & activities.]*
Assumptions about human nature	Man as pure spirit, consciousness, being.	Man as social constructor, the symbol creator.	Man as an actor, the symbol user.	Man as information processor.	Man as an adaptor.	Man as a responder.
Basic epistemological stance	To obtain phenomenological insight, revelation.	To understand how social reality is created.	To understand the pattern of symbolic discourse.	To map contexts.	To study systems, process, change.	To construct a positivist science.
Some favored metaphors	Transcendental.	Language game, accomplishment, text.	Theatre, culture.	Cybernetic.	Organism.	Machine.
Research Methods	Exploration of pure subjectivity.	Hermeneutics.	Symbolic analysis. Social action theory.	Contextual analysis of Gestalten.	Historical analysis.	Lab experiments, surveys.

Note: Adapted from "The case for qualitative research," by G. Morgan & L. Smircich, 1980, *Academy of Management Review, 5*, 491-500.Adapted from the original with italics added from Table 2 (1980, pp. 494-495).

Figure 9: Typology showing range of ontological, epistemological and method assumptions along the subjectivist-objectivist continuum

This study, adopts the ontological position of 'reality as a concrete process' in line with Morgan and Smircich (1980) typology. The underlying assumption is that social world is evolving and is shaped by the interactions of constituent processes (Morgan and Smircich, 1980). This study uses a subjective approach to study the phenomenon of open innovation in the pharmaceutical innovation system. This subjective view allows to explore meanings through the subjective accounts of organisational members (Cunliffe, 2010) in the new drug research context. The interpretivist approach offers a contextualised understanding of the phenomenon at hand.

4.1.1 Underlying ontological assumptions

> *"The river flows continuously and appears to be the same from moment to moment, yet the waters are ever changing. So also fire. The flame keeps glowing and even maintains its shape and form, yet it is never the same flame and it changes every instant. So everything continually changes and life in all its forms is a stream of becoming. Reality is not something that is permanent and unchanging, but rather a kind of radiant energy, a thing of forces and movements, a succession of sequences. The idea of time is just 'a notion abstracted by mere usage, from this or that event." (Nehru, 1946: 120)*

The process philosophy in contemporary scholarly research has its roots in the writings of James (1907),Whitehead (1979) that embodies the flux of things as the ultimate generalisation for a philosophical system. Philosophers of 17th and 18th century have varied in what they see part of social world as static and what they view as changing. The writings of Whitehead (1979) have detailed and expanded the ideologies of Locke (1841) and labels the internal constitution of a particular existent, believed to be static, as *concrescence.* He also observes the existent to be continually in a state of *transition*.

The process philosophical thinking is based on this fundamental notion that individuals, organisations and other entities are in a process of constant flux (Nayak and Chia, 2011; Whitehead, 1979). Organisations change mostly in response to environmental events such as demographic, economic, social and political forces (March, 1981). The process philosophical thinking challenges the conventional way of viewing organisations as solid entities (Nayak and Chia, 2011). The basic premises of the process philosophical thinking rests on the assumption that individuals, organisations and social entities are "not things made but things in the making" (James, 1925: 263; Nayak and Chia, 2011). The nature of reality is addressed through the ontological assumptions of *becoming* rather than *being* a static solid entity (Nayak and Chia, 2011).

Organisational response to change has been the subject of academic interest for long and within this research study; special attention has been given to organisational change and innovation (March, 1981; Prahalad, 2006; Tidd and Bessant, 2011). The ontology of *becoming* rather than *being*, gives primacy to the strategies and course of action that shows how firms evolve in terms of adaptation and selection (Levinthal, 1991), learning and conflict

resolution (March, 1981), sense making (Weick, 1995), evolution of new organisational forms (Lewin et al., 1999) and effective selection of exploration or exploitation strategies (March, 1991). The process philosophy thinking proposes that reality can be viewed through an organisation's goals, cultures, strategies etc. (Chia, 1996).

The spread of literature in the area of organisation change is vast. In this context, (Van de Ven and Poole, 1995) has classified the theories of change into four types based on their event sequence and generative mechanism. These are the lifecycle theories, teleological theories, dialectical theory and evolutionary theory that differ on the unit of change and the outcome of change (Weick and Quinn, 1999). The research area in this dissertation partakes an evolutionary approach to growth of firms as firms compete for scarce resources and evolve through a natural selection and adaptation process (Chandler, 1990; Nelson and Winter, 1982; Simon, 1993). Firms undertake strategic decisions to deal with uncertainty and change constantly to adapt to the external environment through creativity and innovation (Baracskai et al., 2007; Simon, 1993). The amendment in patent law and policies triggered a host of changes in the Indian pharmaceutical sector. These changes at the environment level impelled Indian R&D firms to undertake strategic decisions to organise their innovation activities and develop new products with limited resources.

Process philosophical thinking does not particularly endorse tracing of synoptic events related to organisational change in distinct times to highlight change rather it supports capturing the flux of reality *from within* (Tsoukas and Chia, 2002). This study thus tries to represent reality through an interconnection of events, and activities, against a backdrop of changes in patent laws. In this way, *becoming of things* and events is given ontological primacy in this study.

4.1.2 Epistemological commitments

At the heart of organisational studies, change in organisations is assessed through an assessment of their strategy and outcomes. Process is used particularly in organisation theory to answer how things and events unfold over time (Nayak and Chia, 2011). Van de Ven (1992) classifies the process approach to strategy into three types: one that identifies a causal logic to explain between relationships, two, that categorises activities of individuals or organisations and three, that delves into the sequence of activities to describe change (Chia and MacKay, 2007). Based on this categorisation, this study uses a blend of category two and

three to understand the phenomenon of open innovation in the pharmaceutical sector by understanding their open innovation networks and strategies formed and classifying the strategic actions of firms into distinct open innovation pathways.

The realm of strategy literature has widened from the study of strategy making to include strategy as a practice. The strategy-as-practice research extends the process approach of strategy making to strategy practices and strategy practitioners to understand strategy in all its manifestations (Whittington, 2007). This dissertation uses a blend of process and practice strategy and combines development of events such as patenting activities, formal research partnerships and R&D activities of firms with qualitative inquiry to gain knowledge from within and perceive changes.

The epistemological stance of this study is to understand reality through a set of strategies, patenting activity, events, timeline and lived experience of people in a given set of organisations. This study does not rely only on stand-alone view of events and activities but also explores reality through the subjective accounts of the entities in the innovation system – universities, firms and public research labs. The accounts of practitioners allowed a broader understanding of the strategic practices and the challenges faced at the organisational level. In line with the praxis-practices-practitioners framework extended by Whittington (2007), this study traces the activities over time (patents, pipelines, research partnerships, events) linking them to strategic change in organizations (closed to open innovation) and strategic outcomes (open innovation pathways adopted).

4.2 Research Design

The different assumptions regarding ontology drives the epistemological stance and the choice of relevant methods (Morgan and Smircich, 1980). The choice of a qualitative research for this study is consistent with the philosophical assumptions (Patton, 1999). The research questions of this study required an intensive examination of the changes taking places in the national innovation system of India and its influence on the open innovation patterns in the pharmaceutical sector. Therefore, there is a need for an approach that is both reflexive and responsive. Qualitative inquiry is appropriate in this research to explore the subjective meanings of the phenomenon in their unique context and can generate highly informative data.

Case studies are particularly appropriate for studying a complex phenomenon that is difficult to find in archival data (Yin, 1994). Additionally, the array of options available to a researcher to conduct a qualitative study has increased in recent times (Creswell et al., 2007). Case study allows to synergistically combine qualitative and quantitative data and enables to keep in check conclusions drawn from one type of data alone (Eisenhardt, 1989; Yin, 1984).The research design of this study is a qualitative case study-based research. The definition of case study used in this research is congruent with the definitions of (Creswell et al., 2007; Evert Gummesson, 2007a; Stake, 2005). The approach used in this study is summed up by Creswell et al. (2007):

> *"Case study research is a qualitative approach in which the investigator explores a bounded system (a case) or multiple bounded systems (cases) over time through detailed, in-depth data collection involving multiple sources of information (e.g., observations, interviews, audio-visual material, and documents and reports) and reports a case description and case-based themes." (Creswell et al., 2007: 245).*

The Indian pharmaceutical industry dealing with contemporary issues such as patent amendments, policy changes, firm level adaptions entails posing of *what*, *how* or *why* questions that provides a rationale to pursue case study research than other methods (E. Gummesson, 2007). Flyvbjerg (2006) advocates that contextual knowledge in any research can be better achieved by proximity to the object of study and real life situations. Case study research enables to gain context based dependent knowledge and analyse the complexity through rich and thick descriptions to understand the given phenomenon (Geertz, 1973; Evert Gummesson, 2007b). A qualitative case study based research design also enables to gather a holistic view through detailed observations of different aspects, examination of these aspects in relation to each other and to view the process within its total environment (Gummesson, 2000; Valdelin, 1974). It was hence decided to focus on qualitative case studies that allow understanding the pertinent contextual conditions and gaining a better understanding of the phenomenon. Table 9 examines key studies and methods by various authors in the available literature. An examination of few studies based on Indian pharmaceutical industry reveals that a mix of qualitative and quantitative approaches has been used to study different aspects of the Indian pharmaceutical sector.

Table 9: Examples of studies and the methods used by various authors to study Indian pharmaceutical industry

Authors	Study objective	Research design/ Approach
(Srinivas, 2004)	This study examines the patterns of technological capabilities using sector-wide indicators and firm-level cases in synthetic and biological pharmaceuticals.	Case study research design using cases from pharmaceutical and bio-pharmaceutical firms
(Feinberg and Majumdar, 2001)	The study examined if knowledge spillovers from MNCs local R&D activities benefitted domestic firms in the Indian pharmaceutical industry in a restricted policy environment and weak intellectual property protection during the period 1980-1994	Quantitative method (Cobb Douglas production function) using firm level panel data
(Ramani, 2002)	This paper examines the impact of knowledge stocks and the nature of R&D strategies in Indian pharmaceutical firms that have integrated biotechnology in their marketing, production or research activities.	Quantitative method (using regression model)
(Rao, 2008)	The study examined the rise of pharmaceutical industry in India and strategic response of the emerging-country pharmaceutical firms to the new patent regime.	Extensive review of the relevant conceptual and empirical literature and secondary data
(Lanjouw, 1998)	The study explores the various implications of introducing products patents for pharmaceuticals in a developing country like India.	Qualitative personal interviews and published data
(Athreye et al., 2009)	The research study shows that radical regulatory changes can be tantamount to technological revolutions by studying Indian pharmaceutical firms. The winners and losers are selected as a function of the dynamic firm capabilities.	Case study research design using four cases from Indian pharmaceutical industry

Three salient features justify the use of case study research design in this study. Firstly, this study uses data from various sources such as interviews, patent documents, formal research agreements, government documents and other company related data. The case study research design is particularly useful as it enables the use of various methods and techniques to understand the phenomenon. Secondly, case study research design enables to combine a mix of qualitative approaches and quantitative approaches. In this study, the following methods are employed to interpret data from different sources: qualitative analysis of interview data using Gioia method, text analysis of patent claims to count product patent applications and analysis of formal research collaboration agreements. Thirdly, it allows focusing on multiple

subject areas such as national innovation system, dynamic capabilities and open innovation to investigate the phenomenon of pharmaceutical innovation in India.

4.2.1 Selection of cases

The research setting comprises of one country, *India* and one sector *pharmaceutical* for new drug research. The shift towards product patent regime has been marked with various measures by government to support innovation such as increased budgetary allocations for research, soft loans, grants, setting up of technology transfer offices, IP awareness programmes and programmes promoting public private partnerships (Department of Science and Technology, 2013). Of the many initiatives led by different public departments, four main public private partnership programmes have been selected to examine in detail. Table 10 lists the main government initiatives and the concerned agency responsible for its implementation.

Table 10: Government Initiatives to support New Drug Research

Initiation Year	Agency	Name of the programme
1994	Department of Science and Technology (DST)	Drugs and Pharmaceutical Research (DPRP)
2001	Council of Scientific & Industrial Research (CSIR)	New Millennium Indian Technology Leadership Initiative (NMITLI)
2005	Biotechnology Industry Research Assistance Council (BIRAC)	Small Business Innovation Research Initiative (SBIRI)
2008		Biotechnology Industry Partnership Programme (BIPP)

The change in patent regime coupled with policy measures has resulted in initiation of new drug research programmes by established firms (Chowdhary, 2010) and setup of research based small firms. The new patent regime also witnessed increased research efforts from universities and public research labs for new drug research along with public efforts to direct research towards innovation. Primarily, in the Indian new drug research landscape, there are 10-12 established firms involved in new drug research business (Chowdhary, 2010). The unit of analysis are nine Indian pharmaceutical firms involved in research of new drugs (small molecules). In this study, five established pharmaceutical companies and four SMEs are chosen to understand their unique contexts and experiences. The pharmaceutical companies form the cases to be investigated in detail. The research also captures the perspectives of scientists in universities and government research labs and officials in public departments to

get a holistic view of the sector. The four key government initiatives were used as instrumental case studies to understand the influence of institutional factor on open innovation. Figure 10 shows the research design used for this study.

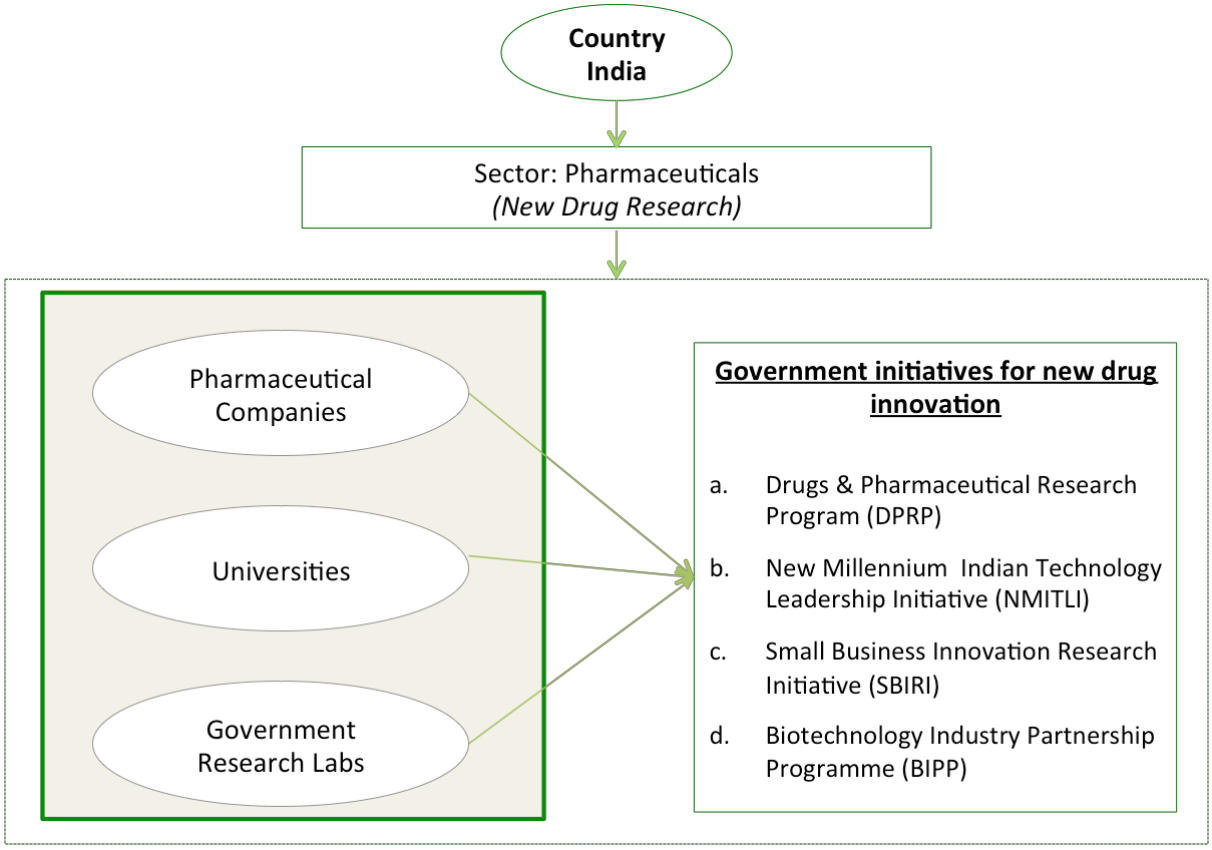


Figure 10: Research Design

The sampling strategy is purposive sampling and cases were selected on the basis of who would be eligible and willing to provide appropriate data. Purposive sampling involves selecting certain units or cases based on a specific purpose and this approach has been used during the course of fieldwork (Bryman, 2011; Creswell, 2009; Mark Easterby Smith, 2008).

At the initial stages of research, firms involved in new drug research in India were identified through pharmaceutical news, academic papers, talks with industry professionals & academics and desk research. Though the number of registered companies in India is more than 20,000, approximately 250 large units and 8000 Small Scale Units form the core of the pharmaceutical industry in India (including 5 Central Public Sector Units) (CCI, 2015). Of

these, there are less than 10 incumbent firms involved in new drug research business[9]. Most of the Indian pharmaceutical companies such as Dr. Reddy's Laboratories Ltd., Advinus Therapeutics Limited, Curadev Pharma Private Limited also have contract research business for new drug discovery services with internal drug discovery programmes. Preliminary interviews helped to gain an understanding of the drug discovery landscape in India and identify the companies primarily into new drug research of small molecules. There are few biopharmaceutical firms such as Biocon, Wockhardt limited, Bharat Serums and Vaccines Limited, Shantha Biotechnics that have predominant biotechnology programmes and these firms were not considered for the study. Thus, the boundaries of the case study were tentative and evolved during the field research. The preliminary interviews in Phase 1 of data collection enabled the finalization of the target group of case companies (E. Gummesson, 2007).

Most of the research studies in the Indian pharmaceutical industry have focused on large established pharmaceutical companies (Chowdhary, 2010; Dinar Kale, 2005; Sampath, 2008). However, researchers have ignored studies related to small research companies. The preliminary interviews conducted with pharmaceutical experts revealed that large companies, which are self-sufficient in resources, traditionally follow a closed approach with their in-house R&D programme as compared to young smaller companies with more open approaches towards innovation. The findings also exposed the challenges faced by small and medium sized companies to conduct new drug research in India. From a research standpoint, the perspective of SMEs seemed important to complete the picture of national innovation system in India. Within the pharmaceutical industry, case selection focused on two sample types:

Sample 1: Established firms

Sample 2: Small and Medium Enterprises (SMEs)

The selection of SMEs allowed maximum variation in cases and allowed to gain an understanding on the differences between cases (Flyvbjerg, 2006). SMEs comprise of companies that have initiated new drug research programmes in 2005 or after and have sales

[9] The exact number of companies involved in new drug research keeps changing at a rapid pace. Most of the pharmaceutical companies open a new drug research division. The companies either after some time change their focus from new drug research to offering contract research services or close their internal drug discovery programme. Mergers and acquisitions are also common hence the number of companies involved in new drug research is till the year 2016.

revenues less than $50 million. With the exception of Lifecare Innovations, which was started in 2000, the other SMEs have been set up post 2005. Table 11 classifies the case companies as established and SMEs based on their resource profile. Secondary data from company websites, annual reports and other sources have been used to compile the resource profile of case study firms.

Table 11: Resource profile of case study firms

Sample Type	Year of start of new drug research	Technological Assets (Compounds in pipeline)	Financial Assets (Sales Revenues)	Complementary Assets	Specific Assets
Established firms	Pre-2005	5-20 pipeline compounds in different stages of drug research	More than $ 500 million - $ 2 billion	• Manufacturing locations abroad • Well entrenched sales and distribution channels in India	• R&D centres in India and abroad • Equipped with sophisticated facilities
Small and Medium Enterprises (SMEs)	2005 and later	1- 15 mostly in early stages of new drug research	Less than $ 50 million	• Limited or No manufacturing/marketing capabilities	• R&D centres in India. • Limited instruments and lab facilities

The largest pharmaceutical companies of India – Dr. Reddy's Laboratories and Ranbaxy set up their new drug division in the early 1990s. Other pharmaceutical companies followed suit and by 2005, there were around 10 companies with their in-house drug discovery programmes and pipelines (Chowdhary, 2010). Each of these companies were hence critical cases, of strategic importance (Flyvbjerg, 2006) to understand how the new drug innovation works in India.

The cases of established firms used in this study are:

- Dr. Reddy's Laboratories Ltd.
- Ranbaxy Laboratories *(now Sun Pharma)*
- Torrent Pharmaceuticals Limited
- Piramal Life Sciences *(previously Nicholas Piramal)*
- Lupin Limited

During the course of my data collection phase, I got access to two established companies– Ranbaxy Laboratories and Piramal Life Sciences. Both companies are different in more ways than one; however due to unforeseen events, these two case examples changed from critical cases to extreme cases (Flyvbjerg, 2006)[10].

Example 1: Ranbaxy is one of the largest pharmaceutical companies in India with a global footprint in more than 43 countries and manufacturing facilities in 8 countries. It started its operations, as a small private company in 1961 and in 2011 was one of the first Indian pharmaceutical companies to have crossed the sales revenues mark of $2billion. The company is one of the few companies in India to have successfully developed and launched a new drug 'Synriam' for malaria. However, in recent years, patent litigations for generic drugs and regulatory problems with USFDA leading to drug recalls and sanctions led the company to strategically restructure itself. In 2008, Japanese based pharmaceutical major Daiichi Sankyo became a major shareholder in Ranbaxy and also bought out completely its new drug research business. In the year 2013, Daiichi Sankyo sold off its stake in Ranbaxy to pharmaceutical giant Sun Pharmaceutical Industries thus exiting the Indian market. Ranbaxy is an important case as it is one of the few companies in India to have launched an indigenously developed new chemical entity and had also forged various landmark drug discovery alliances with GlaxoSmithKline. At the time of data collection, the company was a part of Daiichi Sankyo. The company history through press releases, patent data and news archives has been traced till December 2014.

Example 2: The second case company, Piramal Enterprises, the flagship company is one of the reputed companies in India and in 2011 was ranked amongst the top 50 largest corporations across India by Fortune 500. The company has operations in over 30 countries and brand presence across 100 markets around the world. Piramal Life Sciences forayed into new drug research in late 1980s. The R&D unit in Mumbai possesses state of the art facilities and capabilities for progression in different stages of new drug research from target

[10]Critical case - A critical case can be defined as one having strategic importance in relation to the general problem Flyvbjerg B (2006) Five misunderstandings about case-study research. *Qualitative inquiry* 12(2): 219-245.
Extreme/deviant cases -To obtain information on unusual cases, which can be especially problematic or especially good in a more closely defined sense.
Maximum variation cases – To obtain information about the significance of various circumstances for case process and outcome (e.g. three to four cases that are very different on one dimension: size, form of organization, location, budget) ibid.

identification to clinical development. During the course of my data collection phase in 2014, the company abruptly closed down its new drug research operations. The company however intends to carry forward the research work of the molecules in pipeline and is looking for partners to out-license.

There is no published data on the number of small scale research companies in India. However extensive secondary research and interviews have revealed an estimate of six to eight SMEs involved in the research of small molecules in India. The cases of SMEs used in this study are:

- Advinus Therapeutics Limited
- Curadev Pharma Private Limited
- Invictus Oncology Private Limited
- Lifecare Innovations

Table 12 below summarises the nine cases of pharmaceutical firms used in the study using annual reports, company websites and press releases.

Table 12: Summary of Cases of pharmaceutical firms used in the study

Sl. No.	Company Names	Names used throughout dissertation	Business activities	Year of inception	Number of inter-views
1.	Dr. Reddy's Laboratories Limited	Dr. Reddy's	Generics and differentiated formulations /API Business Biosimilars/ Contract research services /New molecule research	1984	2
2.	Lupin Lim-ited	Lupin	Generics and differentiated formulations/API business Biotechnology/New molecule research	1968	2
3.	Piramal Life Sciences	Piramal	Generics and differentiated formulations/ API business Contract manufacturing/ New molecule research (Closed) Diagnostic imaging/ Phytomedicines (herbal)	1988	4
4.	Ranbaxy Laboratories (now Sun Pharma)	Ranbaxy	Generics and differentiated formulations/ API business New molecule research (sold to Daiichi)	1961	2
5.	Torrent Pharmaceuti-cals Limited	Torrent	Generics and differentiated formulations/API business New molecule research	1959	1
6.	Advinus Therapeutics Limited	Advinus	New molecule research/Contract Research services	2006	1
7.	Curadev Pharma Pri-vate Limited	Curadev	New molecule research/Contract Research services	2010	1

8.	Invictus Oncology Private Limited	Invictus Oncology	New molecule research	2011	1
9.	Lifecare Innovations	Lifecare Innovations	Differentiated formulations/ New molecule research	2000	1

4.2.2 Using the Case Study

> *"The advantage of a case study is that it can 'close in' on real life situations and test views directly in relation to phenomenon as they unfold in practice" (Flyvbjerg, 2006: 19).*

The researcher who is exposed to the cases and the vast information has the choice to summarize the findings or to focus in-depth on events or minutiae. The cases selected vary at different levels. Firstly, pharmaceutical firms, universities and public research labs vary significantly as an entity. Secondly within the pharmaceutical firms, the companies vary in size, age of new drug discovery programme and nature of business activities. Thirdly, as most of the new drug research programme in universities and public research labs are based on personal motivation, the empirical data vacillated between personal experiences vs. data related to the institution. Despite these differences, all the cases showed some similar characteristics and were a part of the Indian innovation system. The cases were actively involved in new drug research and were affected by the same institutional and regulatory environment at the national level. In order to analyse such a multi-layered empirical data, there was a need to classify the cases based on the objective of the study and analytical focus. The main research interest of the study is classified as *intrinsic case* while a supportive case, which aids in better understanding of the research issue, is referred to as *instrumental case* study. When researchers study a collection of cases to understand a given phenomenon they are referred to as *collective cases*. Figure 11 shows how the cases of this study have been segregated using the definitions provided by (Stake, 2005).

Figure 11: Classification of cases

The classification of cases enables to grasp the richness of the cases while allowing comparability. The intrinsic cases allow a holistic view of cases (Gummesson, 2000) while also allowing cross case analysis (Huberman and Miles, 2005; Stake, 2005). By combining the strategies of collective cases and intrinsic case study, the study aims to avoid comparison of few attributes; obscuring important knowledge gained with respect to the case and enable to gain a holistic view of the phenomenon (Gummesson, 2000; Stake, 2005).

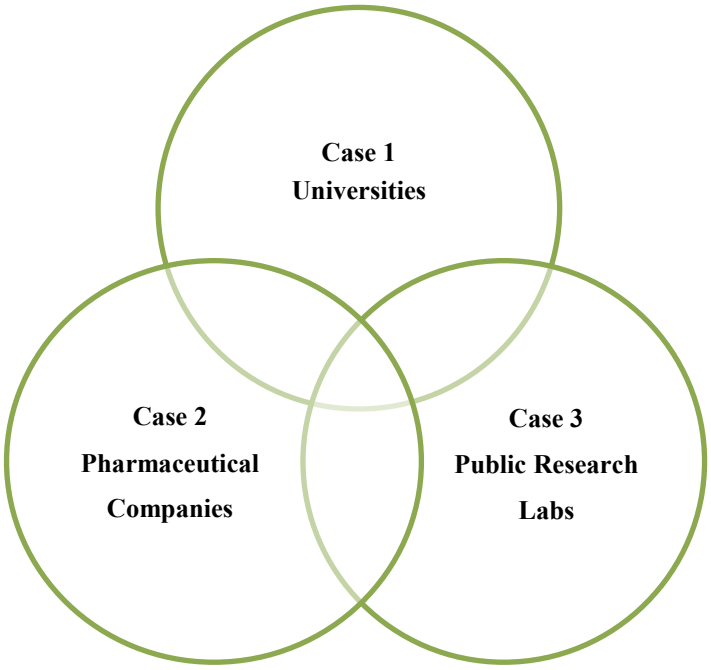


Figure 12: Cross Case Analysis

The cases of universities, public research labs and pharmaceutical companies were used as collective case study[11] (Stake, 2005) for cross case analysis (Huberman and Miles, 2005). This was done to gather multiplicity of perspectives and analyse a series of themes (Creswell et al., 2007; Piekkari et al., 2009; Stake, 2005) related to connectedness, issues in collaboration, and the role of institutional and regulatory environment in influencing the formation of innovation networks.

Of the several government initiatives, four national level programmes are prominent to foster industry academia partnerships and support innovation for new drug research - a) Drugs & Pharmaceutical Research Programme (DPRP), b) New Millennium Indian Technology Leadership Initiative (NMITLI), c) Small Business Innovation Research Initiative (SBIRI) and d) Biotechnology Industry Partnership Programme (BIPP). These instrumental case studies[12] (Stake, 2005) aim to provide further insights into the types of innovation networks formed between industry and academia under policy support. Within the stated aim, the instrumental cases are intended to provide clarity to the above given issue and enable understanding of the underlying meanings within a triangular configuration of universities, firms and public research labs.

The intrinsic cases of pharmaceutical firms were chosen to understand in depth, their unique contexts and experiences with respect to open strategies pursued and the innovation networks formed. The cases were examined closely for their history and the insights gathered during the interview, replete with events and minutiae, were used for case oriented explanations. This enabled to obtain a holistic view (Gummesson, 2000) of the specific cases by detailing specific issues, contexts and interpretations (Stake, 2005).

[11] Collective Case Study: 'Researchers may study a number of cases jointly in order to inquire into the phenomenon, population or general condition' Stake R (2005) Qualitative Case Studies. Denzin, NK & YS Lincoln. The Sage Handbook of Qualitative Research. Thousand Oaks, California.

[12] Instrumental Case Study: 'a particular case is examined to provide insight into an issue or refinement of theory. The case is of secondary interest; it plays a supportive role facilitating our understanding of something else…..the choice of the case is made because it is expected to advance our understanding of that other interest' ibid.

4.3 Data Collection

This study uses several data sources 1) qualitative data from semi – structured interviews 2) additional data through follow up interviews 3) available data from company websites, annual reports, government websites, patent office websites, business publications and materials provided by informants. Data collection hence involved multiple layers of data to provide insights into the research issue.

The vastness of the science and technology set up in India and the wide geographical spread of public research institutions, universities and firms across the country posed locational difficulties. There are umpteen pharmacy colleges affiliated to reputed universities across the country. Apart from geographical challenges, it is also difficult to identify academic scholars and public research scientists who are engaged in new drug research work. In spite of the vast infrastructure, very few universities engage in a new drug research programme at a large scale. Most of the work in India in new drug research is carried out of personal research interests and motivation. Low number of research publications and lack of a database of researchers made things even more difficult.

This constraint was overcome by using drug discovery conferences as the research setting. Two drug discovery conferences -5th International Conference on Drug Discovery and Therapy, 2013, Dubai, UAE and SELECTBIO - Drug Discovery India 2014, Mumbai, India constituted as suitable venues to get in touch with most of the academics and scientists. Key speakers at the conference, academics at professor level and scientists at the level of Principal Scientist in Indian public research labs were contacted. The setting of two drug discovery conferences ensured homogeneity of the respondents and enabled snowball effect.

The setting of the conference also put me in touch with scientists based abroad and professionals working in leading multinational companies in India. Their regular interactions with industry and academics allowed me to get first hand account of the challenges they encounter in undertaking research collaboration in the Indian setting. The conference also ensured maximum variation in sampling and enabled to take advantage of new leads generated through snowball effect (Mark Easterby Smith, 2008). Almost all the respondents agreed to be contacted again for clarification or additional information.

Table 13: Number of interviews by respondent type

Respondent type	Number of interviews
Pharmaceutical Firm - Case company	16
University	13
Pharmaceutical experts*	10
Public Research Institute	6
Public Department	5
Total	50

*Experts comprised of experienced professionals with wide experience in Indian pharmaceutical industry currently associated with drug discovery in contract research, herbal, biotechnology and spinoff companies. It also included scientists who have now moved abroad but are closely connected to the Indian industry.

The qualitative inquiry process in this research study was more iterative than linear. The interview process was undertaken in two phases and 50 interviews were conducted over a period of two years. The phase 1 interviews were preliminary interviews undertaken at early stage of research to gain an understanding of the current innovation system in India for new drug research, identify main issues and provide a research direction for literature review. Stage 2 was undertaken after the formulation of conceptual framework and research questions.

Table 14: Phases of Data Collection

Interview phase	Time period	Number of Interviews	Research Setting
Stage 1	Feb 2013 – Apr 2013	12	• 5th International Conference on Drug Discovery and Therapy, 2013, in Dubai, UAE • Company visits in New Delhi, India
Stage 2	Sep 2014 – Feb 2015	38	• SELECTBIO - Drug Discovery India 2014, Mumbai, India • Company visits in Mumbai, India • Public Departments and universities in New Delhi India

Semi structured interviews were used as the primary method of inquiry to a) gain an in-depth understanding of the institution and regulatory effects in enabling innovation networks for new drug research b) investigate *why* and *how* firm resource and competence influence formation of innovation networks and the strategies pursued. The interviews for the field study were conducted at different points of time and universities, pharmaceutical companies, public research labs were contacted for empirical enquiry. The use of interviews provided a

rich opportunity to gain in depth understanding of social context and allowed to explore large number of issues (Reed and Payton, 1997).

Semi structured interviews constituted the main source of data and was supplemented with secondary research sources and patent analysis serving as important triangulation and supplementary sources to get answers to the main research question under study.

Table 15: Types of secondary data used in the study

Type of data	Purpose	Source
Patent data	Tracking of patent documents for the period: Jan 1995-Dec 2014	Patent database of India, US and WIPO
Research partnerships*	Tracking of alliances formed by case companies for new drug research.	Annual reports, company web-sites, press releases in online magazines – *Pharmabiz*, *Express Pharma* and project list of four public initiatives − DPRP, BIPP, SBIRI and NMITLI
Case profiles	Tracked and compiled company history for events, timelines, nature of business activities, research partnerships by stage of new drug research and open innovation strategies adopted.	Annual reports, company websites, other available published data
Asset position of case companies	Quantitative data related to sales revenues, R&D intensity, number of R&D labs and manufacturing plants, strength of marketing force were compiled.	Annual reports, company websites
Government documents	Tracking government policies, key public private partnership initiatives, their project list and measures taken for promoting R&D in India.	Government department websites, Five year plans by Planning Commission, Government of India

**Compilation was undertaken till August 2015*

4.3.1 Interview process

The interviews were set up using three different modes a) personal referrals b) formal mode and c) networking at conference.

a) Personal referrals – My work experience in Indian pharmaceutical industry gave me an opportunity to work with people at different job levels. I used these contacts to get in touch with experienced professionals in senior management positions working in pharmaceutical firms in the area of new drug research. I also had the opportunity to interview three ex-colleagues in pharmaceutical companies for my research study.

b) Formal mode – The personal referral networks mode was not sufficient to garner sufficient participants for the research study. In spite of personal referrals, many respondents declined for an interview. As the number of companies involved in new drug research is limited, it was important to reach out to all the companies in order to gather sufficient data. Pharmaceutical executives holding senior management positions were formally contacted through emails. Since email addresses are not readily available, the initial contact was established through phone calls, subsequent to which introduction emails were sent out. It was crucial to convince the admin staff who effectively played the role of gatekeepers due to high level of confidentiality maintained at R&D sites. Interviews with company professionals were conducted at the company offices or over the telephone if the interviews could not be fixed during the time I was in India. Most of the senior management professionals provided research interviews on conditions of anonymity.

c) Networking at conference - The interviews with academics and scientists were mainly scheduled and conducted at the conference venue. The mailing list given at the conferences and networking apps provided a suitable platform to interact with the participants before the conference and schedule meetings. Interviews were also conducted impromptu during the conference.

The interviews were semi structured and questions were not posed in any pre-established order. For most of the interviews, only the topic was introduced and it was observed that the informants themselves engaged in a free flowing discussion of the topic with minimal intervention. Not all questions were used in every interview, as some of the questions were not relevant for firms/universities/public research labs. A separate short discussion guide was prepared for the public research departments. I received an overwhelming response from the public departments officials handling the initiatives, who were very keen and enthusiastic to share information about their various initiatives. As a result, the conversation flowed easily in the manner of an unstructured interview.

The discussion guide first provided the background of the researcher, the purpose of the research and the sections to be covered. The flow of the interview was introduced and the first set of questions touched upon the role and responsibility of the interviewee, company history and R&D activities of the company. The initial conversation before the start of the interview was not recorded to preserve the anonymity of the informant. A typical recorded

interview lasted for about 35-40 minutes and generated 700-1,000 lines. With the exception of three interviews, 47 interviews were audio recorded.

List of Questions used for Firms/Universities/Public Research Labs

1. How does funding for new drug development take place?
2. Does the financial market support procurement of funds from venture capitalists, financial markets?
3. Has the public funding for R&D increased for your organization in recent years?
4. After India signed the TRIPS agreement in 1995, Government announced various policy initiatives to encourage new drug research in India. Has your organisation benefitted from any government initiatives/ policies for new drug research? Which one did you find particularly beneficial? Please give examples. If not, why?
5. What are the different ways in which your organisation has partnered with industry/universities/public research labs for new drug research in the past five years? Did the patent regime have an effect on networking opportunities?
6. Is your organisation involved in any of the public private partnerships or research consortiums initiated by the government? If yes, please elaborate on the partnership and your firm's role in that.
7. Do you feel that the government initiatives have helped in creating a positive environment for collaboration? What are the key challenges? What are the areas where you think Government needs to take action to further collaboration for new drug research?
8. Indian companies are engaging in out-licensing, in-licensing and/or collaborative R&D strategies for new drug research. Which strategies are adopted by your organisation? What factors govern these choices?
9. Universities typically engage in out-licensing, in-licensing and/or collaborative R&D strategies for new drug research. Which strategies are adopted by your organization? What factors govern these choices?
10. Is there an effect of patent regime in adoption of strategies like out-licensing, in licensing and joint R&D? If yes, why do you think so?

List of Questions for Public Research Departments

1. What are the major public initiatives taken by your department to encourage new drug research? b) What are the major goals of these initiatives (funding, promoting collaboration, capacity building and transfer of research output)?
2. How do these programmes work – (stage of drug development, IP related issues, length of projects)? What approaches are used to monitor and review progress of key implementation deliverables?
3. How have these initiatives helped to foster academia-research-industry partnerships? What is the role of each of the partners in the various drug development stages? Do you have examples of major projects?
4. What are the key challenges in executing this model?
5. Have changes in patent regime (post 2005) helped to form innovation networks among the institutions involved in new drug research?
6. What are the key challenges the government faces in fostering academia-research-industry partnerships? What are the areas, where you think Government needs to take action to further the new drug innovation agenda?

4.4 Methods for Data Analysis

The following section attempts to elaborate on the methods employed to arrive at the research results. The methods of analysis used in the present research study follow the general outline sketched by (Corley and Gioia, 2004) to analyze qualitative interview data. This method is particularly useful as it allows following a systematic approach to analyze the qualitative interview data.

The qualitative data was supplemented with quantitative data of case studies to understand how organisations used open innovation to further their new drug through different stages. The data came from a combination of primary and secondary sources including company annual reports for ten years, field interviews, press releases, online pharmaceutical magazines and patent data.

This study uses the patent data to undertake count of unique, active, priority patent applications by different patent types (basic patents, secondary patents and method patents) using 20-year data from PCT, Indian and US patent offices. This dissertation also presents a

unique patent analysis method, which involves two steps a) workable adjustments to the patent dataset and b) text analysis of claims to segregate process-based patents from product patents. The method detailed in this study is not new per se but the uniqueness of the approach lies in solving data related issues to extract a meaningful dataset and using text analysis to identify different patent types.

In addition, case profiles of nine case companies were built by synthesizing interview data, archival data such as important milestones in the history of the company, prior history of research partnerships, details of the collaborations undertaken for new drug research and asset position of the company. The case histories of the companies have been used to provide insights to the three central themes that emerged from the qualitative interview data. The case histories were shared with the interviewees to validate the information synthesized from multiple sources. Of these, the interviewees verified case profiles for six of the nine companies. However, three case profiles could not be verified as the respondents failed to respond to emails and reminders.

4.4.1 Analysing Interview data using Gioia method

The Gioia method was used to perform a fine-grained analysis on the interview data. This method provides a systematic analysis of data through hierarchical categorisation into informant terms, themes and dimensions (Gioia et al., 2013). Organizational studies require the use of theoretical concepts to describe or explain a phenomenon of theoretical interest (Gioia et al., 2013). In this way, the use of a method to analyse the qualitative data provides a credible approach to make connections between data and theory.

The literature review in the initial stages of research allowed identifying relevant literature and important theoretical concepts related to the study. However, no predetermined concepts used in existing theory such as ‘open innovation’, ‘dynamic capabilities’, ‘asset position’ were used in designing the interview questions. The purpose was to allow the data to be captured by the participants’ in their own terminology. All the interviews except three were audio recorded and subsequently transcribed verbatim. Detailed notes were taken during the interview process for the three interviews that were not recorded.

The interview transcripts were reviewed many times to get a broader understanding of the phenomenon of pharmaceutical innovation and the important issues. The process of going back and forth between transcripts and recurring topics allowed to capture the informant

terms and codes and to identify patterns in the descriptive findings. The codes were then synthesized into broader categories for themes and aggregated dimensions to emerge. The analysis using the framework served multiple purposes – a) facilitated data interpretation through identification of patterns in data b) allowed concepts and relationships in data to evolve and enable interpretation and c) enabled the emergence of new concepts.

The approach adopted to code the interview data using Gioia framework can be segregated into two steps: 1st order analysis (using informant centric terms and codes) and 2nd order analysis (using researcher centric concepts, themes and dimensions).

a) 1st order analysis (Discrimination of informant centric themes and codes) - The analysis of interview data started with segregation of data into initial list of terms and codes using in vivo-terms and phrases used by the respondents. In a further round of coding, these terms were further collapsed into higher first-order codes by searching for relationships between and among the list of codes. This enabled the formation of more meaningful categories.

b) 2nd order analysis (using researcher centric concepts, themes and dimensions) - Additionally, the codes were further collapsed into 2nd order codes by associating with theory and the research questions that guided the data collection. During this stage, conceptual links started emerging between the theoretically relevant 2nd order codes. Adhering closely to the guidelines provided in (Corley and Gioia, 2004), the codes were further combined into fewer and more theoretically relevant themes and aggregate dimensions. The preliminary data collection and analysis followed by the second round of more detailed data collection led to the validation of the emergent themes and dimensions. This iterative process led to answering the research questions that formed the basis of this investigation. Figure 13 provides the data structure where the first and second order codes are assembled to form themes and overarching dimensions.

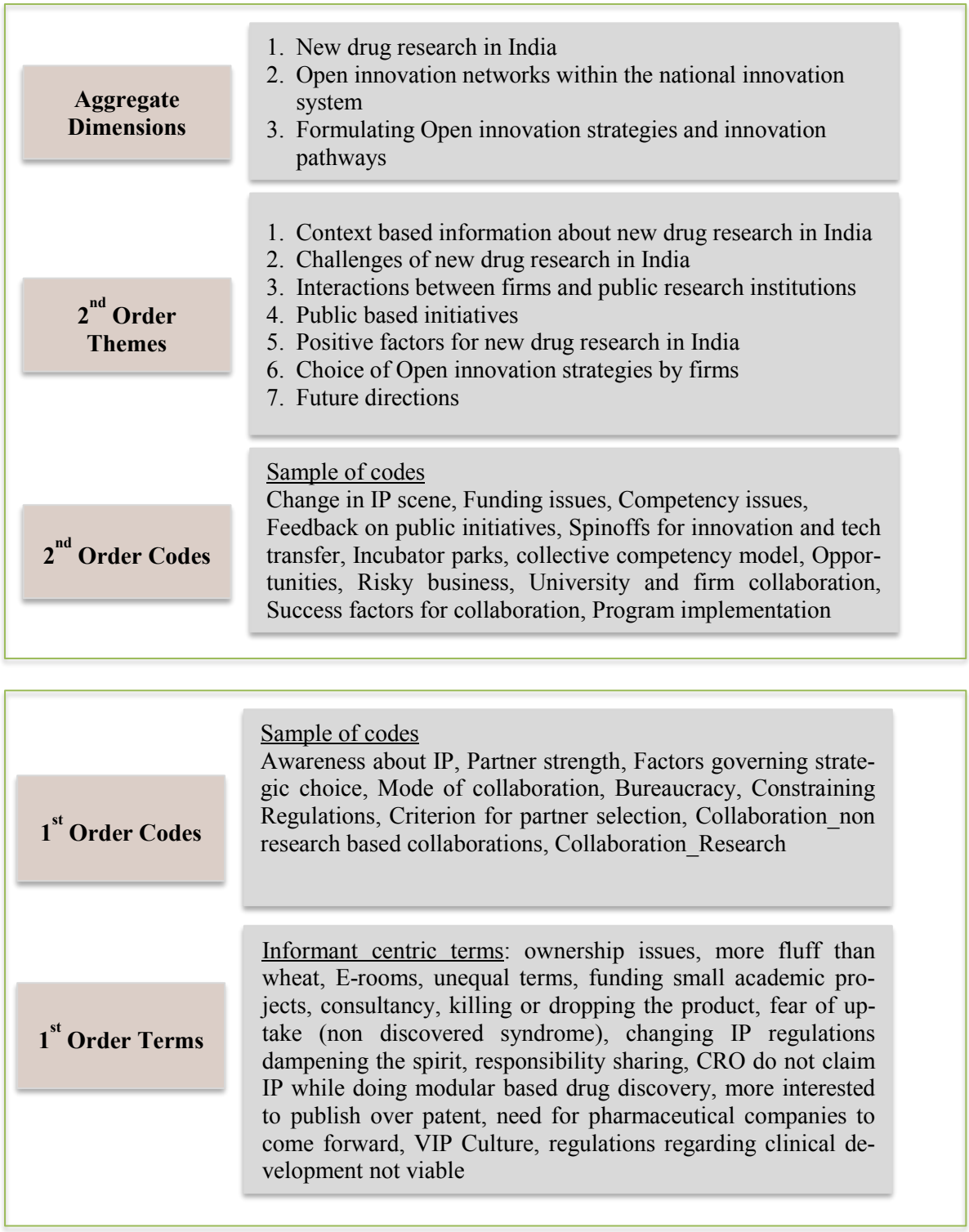


Figure 13: Emergent terms, codes, themes and aggregate dimensions

The process used can be illustrated further by showing an example of how the theme 'Interactions between firms and public research institutions' emerged from the analysis of interview data. The frequent and explicit use of informant terms in the interview text such as 'access to facilities', 'consultancy work', 'new drug research collaborations' led to the first

order terms. In a further round of coding, these terms were categorised into first order codes – 'Collaboration_Non research based collaborations' and 'Collaboration Research'. These codes were then associated with the theory on innovation networks and the corresponding research question to group the codes into a second order code 'Univ and Firms collaboration'. This second order code became a part of the theme 'Interactions between firms and public research institutions' that formed a subset of the aggregate dimension 'Open innovation networks within the national innovation system.' Figure 14 illustrates the example further.

Figure 14: Coding example

Several steps were undertaken to ensure trustworthiness of the process. First, all the data was meticulously managed using the qualitative software NVivo. Second, the analysis of data was an evolving process and not confined to a stand-alone step. The preliminary interview data analysis provided an opportunity to come up with the initial set of terms and codes. The subsequent interviews allowed verifying the initial list and led to another round of coding and categorization. Data from the interview transcripts were repetitively reviewed, coded, categorized and studied for content and meaning until patterns emerged. As illustrated in Figure **13**, three aggregate dimensions 'patenting and innovation' New Drug Research in India, 'innovation networks' and 'open innovation strategies' emerged which began to serve as guides for further analysis.

These three main aggregate dimensions along with their constitutive themes formed the narrative of the research findings in this dissertation. The narrative describes in detail the types of networks formed between industry and public institutions for research and the factors that emerged to be barriers to undertake open innovation. The details of the challenges faced by firms and the open innovation strategies adopted to mitigate some of these challenges have helped to relate the emerging interpretations to the national innovation system of the setting.

4.4.2 Patent Analysis

The study analyses patent applications filed by nine case companies to undertake a patent count by different patent types – product patents (basic and secondary) and method (process) patents. The unit of analysis is patent applications and a twenty-year period from 1995 to 2014 is the measurement period to analyse the patterns in patent data. The results of patent analysis indicates three things: a) innovativeness of the firm (Comanor and Scherer, 1969), b) nature of innovation (substantial vs. incremental) and c) patenting strategy of a firm in different patenting regimes (Lanjouw et al., 1998). While patent counts indicate firm innovativeness, the type of patents filed indicates the nature of innovation. Patent data also provides useful information to assess globalization of technological activities (WIPO, 2007).The patent analysis approach presented in this study is used to undertake patent counts at firm level and is more valid for developing countries that have witnessed recent changes in patent laws.

The compilation of patent dataset is not straightforward and requires the use of appropriate filters and suitable data adjustments to arrive at conclusive number free of bias and errors (Zuniga et al., 2009). The implementation of the method requires consideration of several key issues and follows guidelines mentioned in the OECD manual (Zuniga et al., 2009). Various patent counting methods used in different studies were also assessed before finalizing the approach (De Rassenfosse et al., 2013; Grupp and Schmoch, 1999). The text analysis method used by Scherer (1984) to technologically characterize patents based on their specifications has been used. Further, a certified patent professional with extensive experience in pharmaceutical industry has validated this approach.

The patent analysis approach has two important steps:

1. Patent dataset preparation
2. Text analysis of patent claims.

The outcome is a unique count of active patent applications based on priority dates categorized by patent type. The key issues considered for the implementation of the approach includes: a) choice of patent office b) using priority dates c) removal of duplicate patents by identification of patent families and using priority dates d) use of single source to extract patent data and e) weeding out inactive or dormant patent applications.

Patent dataset preparation: The first step involves the *choice of patent office*. There are three major patent offices in the world - the European Patent Office (EPO), the Japan Patent Office (JPO), the United States and Patent and Trademark Office (USPTO). Recently, World Intellectual Property Organisation (WIPO), an agency affiliated to the United Nations is gaining prominence as important entity in the global arena for intellectual property. WIPO plays an overbearing role as it enables harmonization of intellectual property (IP) system and its membership constitutes 188 member states (WIPO, 2016). The Patent Cooperation Treaty (PCT) is an international patent law treaty that provides a unified procedure for filing patent applications to protect inventions in each of its contracting states. A patent application filed under the PCT is called an international application, or PCT application (Danguy et al., 2014). World Intellectual Property Organization (WIPO) administers the Patent Cooperation Treaty and a PCT application has the same effect as national applications filed in designated countries (Zuniga et al., 2009).

Patenting trends suggest that until the mid-1990s, the US Patent Office (USPTO) was the preferred office for filing patent applications by Indian companies (Bhattacharya et al., 2007). India ratified the Patent Co-operation Treaty (PCT) in 1998, which opened another convenient route for patent filing. PCT applications started gaining prominence in India and the number of patents filed by Indian organizations through the PCT increased from 7 in 1999 to 216 in 2002 (Bhattacharya et al., 2007; Mueller, 2007). In 2005, India was ranked third highest after China and Republic of Korea in filing of PCT applications by Indians (Mueller, 2007). Prior studies related to Indian pharmaceutical industry have used patent counts in US and Indian patent offices as an indicator to measure the innovative output of these firms (Abrol et al., 2010; Simonetti et al., 2007). In current times, inclusion of patent documents from USPTO and Indian office alone may not suffice to provide a complete picture of the patenting activity of the firms. Hence, this study considers patent application filed in Indian, US and PCT patent offices.

A second important aspect while dealing with patent data is to know the meaning of each of the dates used in the patent application and *choose a relevant date* for data extraction as shown in Table 16.

Table 16: Important dates in a patent application

Date	Definition	Time lag from the invention date
Priority date	First date for filing a patent application	Earliest date, closest to the invention date
Application date	Date for filing a patent at a specific patent office	In case of PCT procedures, the lag is 12 months for PCT filing and 30 months for transfer to national phase
Publication date	Date on which information about the invention is disclosed to public	18 month delay from the priority date except for USPTO
Grant date	Date for conferring patent rights to the applicant by the authorized body	3 years on an average at USPTO 5 years at EPO, 10 years in some cases

Source: Adapted from (Zuniga et al., 2009)

The different dates, reflect the patenting process and choice of dates as a filter criterion affect the patent counts. As new drug research is recent in India, the use of publication/grant date as a retrieval date significantly reduces the patent data and is less informative in understanding the inventive activity of the firms. Additionally, the time lag associated with the filing of patent application and patent acceptance also leads to counting of patents in different years together (calendar effect). With different pendency times in different patent offices to process the patent applications (on an average 44 months in EPO office, 31.8 months at the JPO office and 31.3 at the USPTO office in 2005-06), the OECD manual suggests the use of *priority date* to compile patent statistics (Zuniga et al., 2009).

A third issue faced is that patent applications extracted from different patent databases generate *duplicate* patent applications. The spread of business activities and filing of a single patent in different countries, country specific laws, different functioning of patent offices and treatment of data in different databases adds to the complexity. A company may file a single patent application in different countries that are traced through patent family identification. A patent family is defined as a "set of patents (or applications) filed in several countries, related to each other by one, or several common priority filings (Zuniga et al., 2009: 71). The first patent filing to protect the invention is termed as priority filing and subsequent filings are

referred as external patents, equivalents, duplicated patents, secondary filings, or patent family members (Martinez 2010).

For patent counts, it is important that patent families are identified and only priority patents are counted (Martinez, 2010). Additionally, different patent offices, based on their national patent systems and procedures, use different definitions of patent families, and follow different rules to assign patents to a family (Zuniga et al., 2009). This leads to differences in patent counts using different databases in spite of using appropriate filters to retrieve data. In order to avoid duplicate counting of same inventions, firstly, priority date is used to extract patent applications. Secondly, Espacenet database is used to trace and match patent applications to their patent families, so only one patent application per patent family is considered for analysis. To illustrate this further, the example in Figure 15 shows two patent applications with similar names and similar inventor name that suggests of belonging to the same patent family

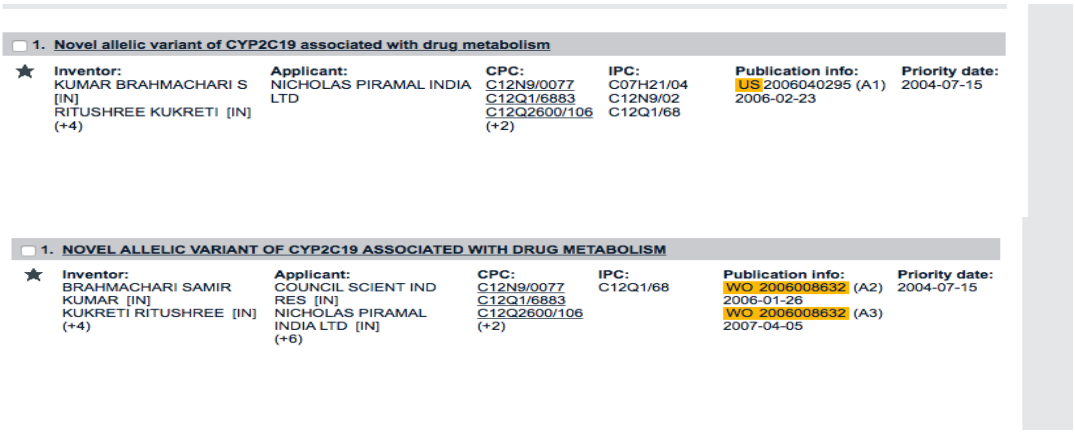


Figure 15: Identification of duplicate patent applications with similar titles and inventor names

Such patent applications were checked for their patent families in Espacenet[13] as shown in Figure 16. Once confirmed that both the applications belonged to the same patent same family, such applications were then tagged as one to avoid double counting and only one patent application was retained in the dataset.

[13] Espacenet is a database of European patent office that offers free access to more than 90 million patent documents from around the world. It includes links to the patent registers of many of the EPO member states and also shows the status of European patents Espacenet (2016) Available at: http://www.epo.org/searching-for-patents/technical/espacenet.html#tab1.

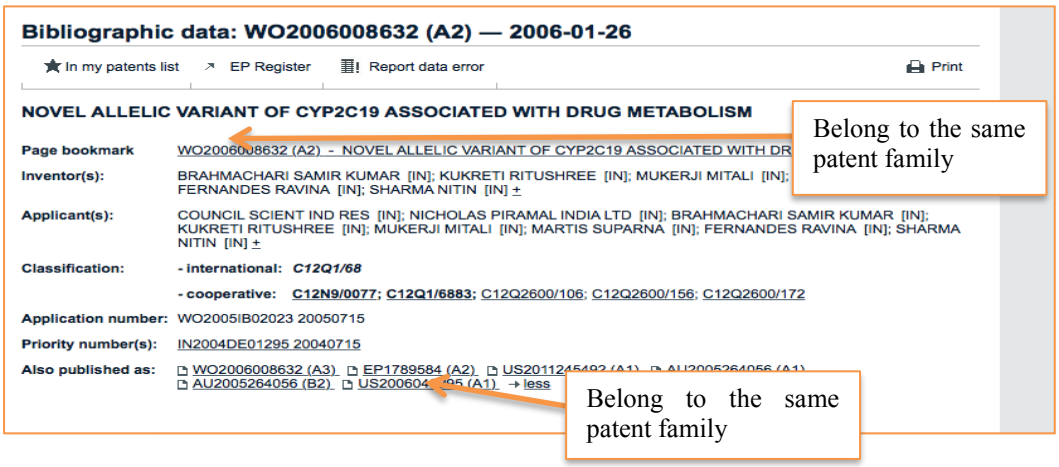


Figure 16: Checking patent family information using Espacenet

The differences in patent offices and their corresponding databases make it preferable to extract data from a *single source*. In this study, WIPO that publishes comprehensive patent data on US and PCT patent applications through its database 'Patentscope' is used to extract patent applications. The Indian patent applications were extracted from Intellectual Property Indian Office (IPAIRS) patent database for the period 1995 to 2014.

Last steps to cleanse the data involved are checking the current status of patent applications and removal of patents with inactive, withdrawn or revoked status. The flexibility in the Indian patent law allows to challenge a patent application through pre-grant and post-grant opposition (Correa, 2007). A patent may be challenged and subject to patent controller's decision and based on the decision, patent applications were either retained or removed from the dataset.

Using this logic, the final dataset comprising of 785 unique utility patent applications was analyzed for patent claims.

Text analysis of patent claims: The claims in each patent document were analyzed and coded using a text analysis approach and classified as device, method or product innovation. A patent may include multiple claims; the first independent claim is the one, which provides the broadest scope of the claimed invention. The specification is the written description of the invention and claims are the scope of the invention based on which exclusive rights are granted to the inventor. A patent may include multiple claims; the first independent claim is the one which provides the broadest scope of the claimed invention (Roehrs, 2003).

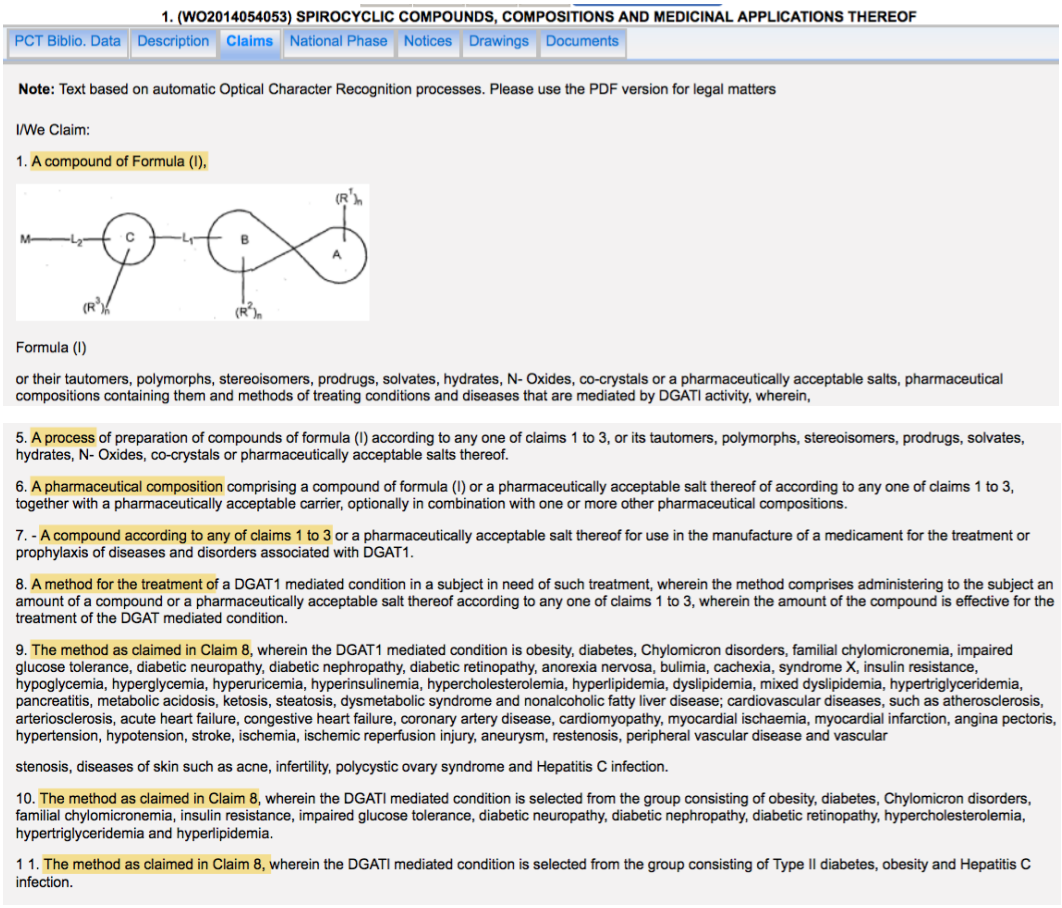
The text analysis approach used by Scherer (1984) that sorts patent documents based on specifications listed in the patent documents, has been adopted in this study for systematic assessment of patent documents. Patent claims were examined and keywords such as 'compound having the formula', 'pharmaceutical composition', 'method', 'process' along with definitions outlined in Table 17 were used to sort patent documents. Each patent document was technologically characterized as product, method or device patents. The product patents were further segregated as basic and secondary patents.

Table 17: Major types of claims and their link to patent types

Major Claim types	Definition	Types of Patents
Apparatus or Device Claims	A claim that covers the embodiments of an invention – the device and its essential elements.	Device Patent
Method or Process Claims	Claims that elaborate series of steps to complete a task.	Method Patent
Product by Process Claims	Claims for a product, which can be manufactured by a given process.	Product Patent
Composition Claims	Claims related to compositions where the invention to be claimed is of chemical nature and/or claims an active ingredient which is novel and not previously disclosed in prior art.	Product Patent
Biotechnology Claims	A claim that involves an invention related to biological matter.	Product Patent
Use Claims	Claims related to new uses of known substances specifically to subsequent medical uses or indicators of known substances and compositions.	Method Patent

Source: (WIPO, 2007)

An example of a patent document analysed using this approach is provided in Figure 17. In the patent document number WO2014054053, the main claim is for the compound that is the inventive subject matter and the dependent claims define process, composition and method of treatment. The claim type is considered to be 'product by process' and the patent document is classified as basic product patent.



1. (WO2014054053) SPIROCYCLIC COMPOUNDS, COMPOSITIONS AND MEDICINAL APPLICATIONS THEREOF

PCT Biblio. Data | Description | Claims | National Phase | Notices | Drawings | Documents

Note: Text based on automatic Optical Character Recognition processes. Please use the PDF version for legal matters

I/We Claim:

1. A compound of Formula (I),

Formula (I)

or their tautomers, polymorphs, stereoisomers, prodrugs, solvates, hydrates, N- Oxides, co-crystals or a pharmaceutically acceptable salts, pharmaceutical compositions containing them and methods of treating conditions and diseases that are mediated by DGATI activity, wherein,

5. A process of preparation of compounds of formula (I) according to any one of claims 1 to 3, or its tautomers, polymorphs, stereoisomers, prodrugs, solvates, hydrates, N- Oxides, co-crystals or pharmaceutically acceptable salts thereof.

6. A pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof of according to any one of claims 1 to 3, together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

7. - A compound according to any of claims 1 to 3 or a pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for the treatment or prophylaxis of diseases and disorders associated with DGAT1.

8. A method for the treatment of a DGAT1 mediated condition in a subject in need of such treatment, wherein the method comprises administering to the subject an amount of a compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein the amount of the compound is effective for the treatment of the DGAT mediated condition.

9. The method as claimed in Claim 8, wherein the DGAT1 mediated condition is obesity, diabetes, Chylomicron disorders, familial chylomicronemia, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, anorexia nervosa, bulimia, cachexia, syndrome X, insulin resistance, hypoglycemia, hyperglycemia, hyperuricemia, hyperinsulinemia, hypercholesterolemia, hyperlipidemia, dyslipidemia, mixed dyslipidemia, hypertriglyceridemia, pancreatitis, metabolic acidosis, ketosis, steatosis, dysmetabolic syndrome and nonalcoholic fatty liver disease; cardiovascular diseases, such as atherosclerosis, arteriosclerosis, acute heart failure, congestive heart failure, coronary artery disease, cardiomyopathy, myocardial ischaemia, myocardial infarction, angina pectoris, hypertension, hypotension, stroke, ischemia, ischemic reperfusion injury, aneurysm, restenosis, peripheral vascular disease and vascular

stenosis, diseases of skin such as acne, infertility, polycystic ovary syndrome and Hepatitis C infection.

10. The method as claimed in Claim 8, wherein the DGATI mediated condition is selected from the group consisting of obesity, diabetes, Chylomicron disorders, familial chylomicronemia, insulin resistance, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, hypercholesterolemia, hypertriglyceridemia and hyperlipidemia.

1 1. The method as claimed in Claim 8, wherein the DGATI mediated condition is selected from the group consisting of Type II diabetes, obesity and Hepatitis C infection.

Figure 17:Example of coding of claims to identify type of patent

Figure 18 provides the mapping used to analyze the claim information to identify claim types and further categorize them as method, product and device patents. Product patents are further categorized as basic patents and secondary patents.

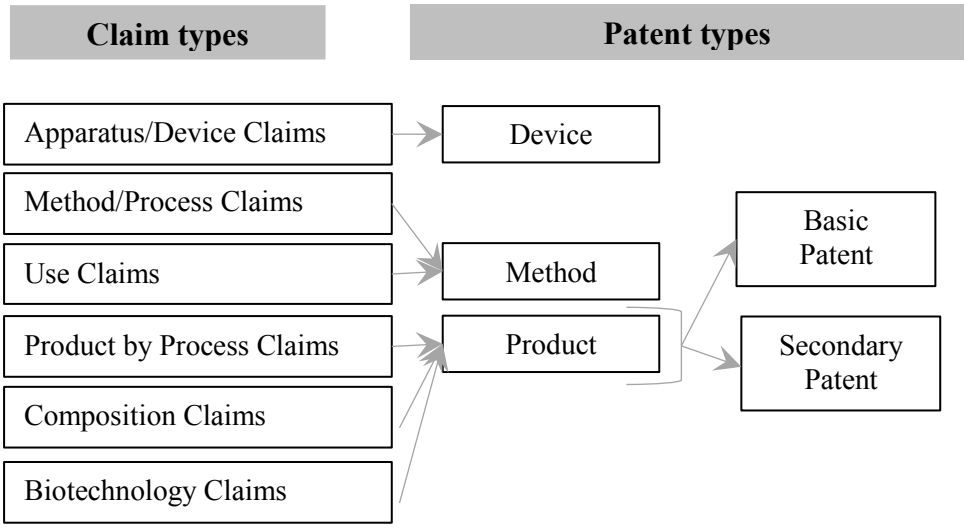


Figure 18: Mapping of claims to patent types

4.4.3 Analysis of other secondary data

This study employs the use of secondary data from multiple sources. A systematic data collection was undertaken to compile *case profiles* using annual reports from the period 1995-2014 and company websites. The archival data was synthesised with interview data to build case histories focusing on nature of innovative activities, important event timelines, research partnerships and open innovation strategies adopted by these companies. These write-ups about the case companies were one of the first steps used to synthesise the enormous volume of data (Eisenhardt, 1989). Six out of nine case profiles have been confirmed for correctness by the interviewees. The company profiles of three companies could not be verified, as the respondents did not reply back despite repeated reminders and calls. In case of Ranbaxy, a Senior Vice President who was previously interviewed had retired and could not be contacted. The present Senior Vice President refused to verify the information due to sensitive nature of R&D information.

The *asset position* of each of the case companies was compiled using data from annual reports and company websites.

Table 18: Data sources used to measure asset position of case firms

Types of assets	**Measures identified**	**Secondary sources**
Technological assets	Patent data Pipeline	Patent data from US, Indian and PCT offices Pipeline information from latest annual report (AY 2014-2015)
Financial assets	Sales revenues R&D intensity	Annual report (AY 2014-2015)
Specific assets	Number of R&D labs	Annual report (AY 2014-2015)
Complementary assets	Number of Manufacturing plants Strength of sales force	Annual report (AY 2014-2015)

In addition, data regarding the institutional set up, key policies and public private partnership initiatives were sourced and compiled from archival sources such as government reports, academic journals, government five-year plans and government websites. The data compiled has been segregated and reported by two time periods: 1970 – 2005 and 2005-2014.

This study also used publicly available formal *research partnerships* to understand the embeddedness of the Indian companies engaged in new drug innovation within the local innovation system and the open innovation strategies. Data for the research partnerships was compiled using company websites, annual reports (2005-2015) and project list of four public private initiatives DPRP, NMITLI, BIPP and SBIRI. The project list for DPRP and BIRAC initiatives – BIPP and SBIRI was made available by the programme heads at the time of interview. The project list for NMITLI was sourced from secondary research. NMITLI also caters to many other sectors apart from pharmaceutical sector hence the projects sponsored by the programme for pharmaceutical sector is not elaborate.

Two online pharmaceutical magazines - *Express Pharma* and *Pharmabiz* were screened for the period 2005 to 2015 to complete and validate the data for the research partnerships after TRIPS agreement in 2005. The research partnerships data used in this study is based on publicly available data. This implies that research projects that have taken place informally between case companies and public sector has not been included in the study.

As gathered from the research findings, the level of interaction and innovation networks between companies and public sector is low. Therefore, it is less likely that any major collaborative research project has been missed out. It was also witnessed during the primary research interviews that respondents were most likely to mention about the research partnerships that were already reported in the media. By gaining multiple perspectives from the primary interview data, media reports in addition to the company annual reports, the likelihood of inaccuracy and incompleteness is low. The approach of combining various different sources and focussing on secondary sources for historical information enabled to remove retrospective bias.

The research partnerships once compiled followed a categorisation approach. The research partnerships were first categorised by the collaborative partner. If the collaborative partner was local university or public research institute within the local innovation system then such partnerships were labelled as *Public Private Partnerships* (PPP). Partnerships with foreign companies and institutes were categorised as *Other Research Partnerships.*

PPPs that originated from policy initiative schemes - DPRP, NMITLI, and BIRAC were categorised as *policy initiated public private partnerships* while public private research partnerships sponsored by companies or through other government funds have been

categorised as *non-policy initiated partnerships*. Most of these public initiatives sponsored projects either as a) stand-alone projects or b) with a collaborative academic partner. Policy initiated PPPs were further classified as stand alone R&D projects and collaborative R&D projects to identify the number of collaborative projects undertaken under these initiatives. Unlike the policy initiated partnerships, non-policy initiated partnerships fell under the category of collaborative R&D only. Based on empirical findings, there are no projects between industry and public sector that can be categorised inbound or outbound innovation. Hence, all PPP projects are categorised as collaborative R&D.

The 'Other research partnerships' formed by firms were further classified by research phase (drug discovery and development) and by open innovation strategies: inbound, outbound and collaborative R&D. Figure 19 shows the categorisation of research partnerships collated from different secondary sources.

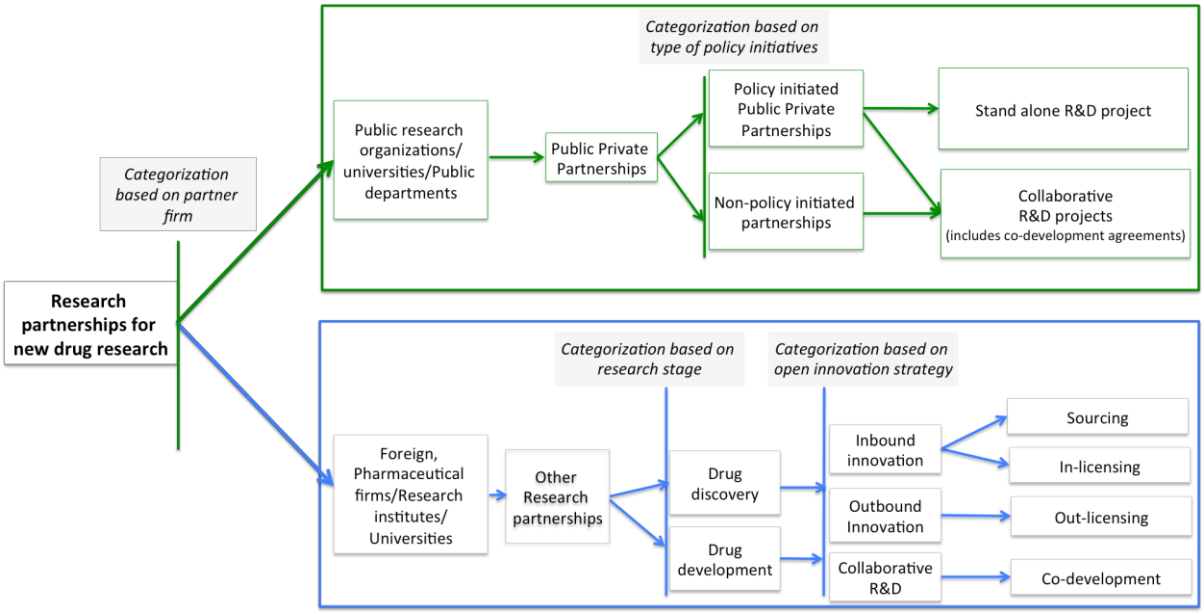


Figure 19: Categorization of formally reported research partnerships

Within the local innovation system, the bulk of interactions that take place are of the nature of informal research projects mostly that fall under the ambit of contract research services and consulting. Such projects are usually unreported. However, interview data mentions that the level and frequency of interactions within the local innovation system is generally low.

4.5 Rigor in method employed

The value and appropriateness of a qualitative research has been the centre of a long standing debate with issues focussing on the methods employed and the validity of the same (Creswell et al., 2007). Despite a long history and tradition of the use of qualitative methods in management and business research, qualitative methods are still viewed as a prelude to quantitative designs (Cassell et al., 2006: 301). In this research study, the research problem in hand and the context to be studied (Creswell et al., 2007; Flyvbjerg, 2006) guided the choice of the method to be employed.

All forms of enquiry have strengths and weaknesses. Qualitative research has been criticized to be subjective, difficult to replicate, and suffers from problems of generalizability and lack of transparency in approach (Bryman, 2011). It is also considered less credible because it does not adopt the traditional indicators of credibility, such as quantification, statistical analysis, rigor and systematization (Cassell et al., 2006). External validity or the degree to which findings can be generalized across social settings is also a major issue with qualitative studies (Bryman, 2011) and is also a limitation of this study. The case study research is considered inferior as a scientific method for reasons of generalizing from a limited number of cases as compared to statistical methods based on large number of observations (Gummesson, 2000). The qualitative case research design also suffers from the criticisms of subjectivity, validity and reliability (Flyvbjerg, 2006; Gummesson, 2000).

The weaknesses pointed out in the preceding paragraphs cannot be singled out as major limitations of this study as reliability, validity and generalizability are not suitable criteria to judge a qualitative study (Bryman, 2011; Lincoln and Guba, 1985; Tobin and Begley, 2004). The value of a qualitative research study lies not in the generalizability of findings but in the description of themes developed in the context of a specific site (Creswell, 2009). Gummesson (2000) reasons that an in-depth study to identify a phenomenon based on detailed investigations and analysis makes it possible to generalize from a few cases or even one single case (Gummesson, 2000). He advocates that ‘particularization’ is more meaningful to understand social phenomenon in a specific situation. Particularization means to understand the particulars of a social phenomenon embedded in specific situation and this makes generalization less meaningful (Gummesson, 2000; Patton, 1980). For this reason, this study partakes Gummesson (2000) viewpoint that a search for new knowledge should not

succumb to the traditional demands of generalization, which blocks the understanding of a phenomenon in a given context (Gummesson, 2000).

Lincoln and Guba (1985) have suggested two criteria to assess a qualitative research study: trustworthiness and authenticity. Additionally, Yardley (2000) has proposed the following measures for assessment of a qualitative study i) sensitivity to context ii) commitment & rigor iii) transparency & coherence and iv) significant impact on theory (Bryman, 2011). Gummesson (2000) proposes that validity in a case study research can be enhanced by integrating the research process with theory which allows the researcher to assess assumptions, constantly revise the results, retest theories, model and review limitations of the study (Gummesson, 2000). However, the problem faced by qualitative researchers is that reliability and validity are not as readily codified as is the case in a quantitative research (Seale and Silverman, 1997).

In this study, the quality issues have been addressed through member validation and data triangulation.

a) Member validation (Bryman, 2011; Miles and Huberman, 1994): The findings of the research analysis were shared with select participants to seek validation of researcher findings. Additionally, feedback was gathered from the respondents throughout the data collection stage.
b) Data triangulation: In this research study, a combination of strategies have been used to enhance validity and trustworthiness of study (Bryman, 2011; Tobin and Begley, 2004). Triangulation was used to reduce the likelihood of misinterpretation and verify findings (Bryman, 2011; Patton, 1999). Triangulation within a qualitative inquiry strategy can be achieved by four ways i) checking the consistency of findings generated by different data collection methods - methods triangulation ii) examining the consistency of different data sources within the same method- triangulation of sources; iii) using multiple analysts to review findings - analyst triangulation and iv) using multiple perspectives or theories to interpret the data - theory/perspective triangulation (Patton, 1999: 1193).

   In this study, triangulation of sources and perspective triangulation (Patton, 1999) have been used in the following ways. Firstly, multiple sources of evidence (Huberman and Miles, 2005; Patton, 1999) like annual reports, company websites, government publications, third party reports allowed to confirm data from multiple accounts.

Secondly, by gathering interview data from academics, pharmaceutical firms and public research scientists, this research study employed a lens of triadic research foci. The findings from multiple sources were useful in getting a multidimensional perspective of the phenomenon, enabled corroboration of findings and enhanced the trustworthiness of the study (Creswell, 2009; Miles and Huberman, 1994). Thirdly, in addition four public private partnership programmes were used as instrumental case studies to observe the phenomenon in depth and get more evidence to arrive at logical conclusion (Stake, 2005).

The quality in this case study research was also ascertained through a two stage sampling process where the initial fieldwork guided the selection of cases for the empirical inquiry. Data collected from initial preliminary interviews in Stage 1 allowed an initial appraisal and conceptualization of the research issue in hand that was further probed during Stage 2 interviews. The initial understanding gained during these preliminary interviews enabled to collect additional focused data based on the emergent themes and enhanced the internal validity of the study (Huberman and Miles, 2005).

In the end, the value of a case study depends on the validity claims of the researcher and how these are tied to other validity claims related to the study (Flyvbjerg, 2006). As stated, the aim of the research study would be to enhance learning through these cases and to gain an understanding of the phenomenon of open innovation in the Indian setting. Although there are limits to generalizations that can be made from the data obtained, the methods are satisfactory for an exploratory study. In the end, the following quote summarises the crux of this study.

> *"According to Vedic philosophy all knowledge is a symbiosis between the knower (the one who knows something, here referring to the researcher), the process of knowing (the implementation of the research project) and the known (what we already know plus the results of the research project)."* (Evert Gummesson, 2007a: 90)

4.6 Summary

This chapter portrayed the data collection and analysis procedures that were employed to get answers to the research questions and meet the desired objectives of the study. The literature review led to the formulation of conceptual framework and research questions. The methodological considerations thus entailed using appropriate methods of data collection, organisation and use of quantitative and qualitative analytical procedures to understand open innovation practices in a specific setting. The analysis of data from primary and secondary data sources formed the crux of the research results that led to three central themes and open innovation framework.

In this way, this research used a combination of a) theoretical perspectives b) a set of case studies, and c) use of different data and methods to suitably gather meaningful empirical evidence. There was hence a need to formulate a way to blend the results into a common research framework. The following Figure 20 illustrates how this has been achieved in this study.

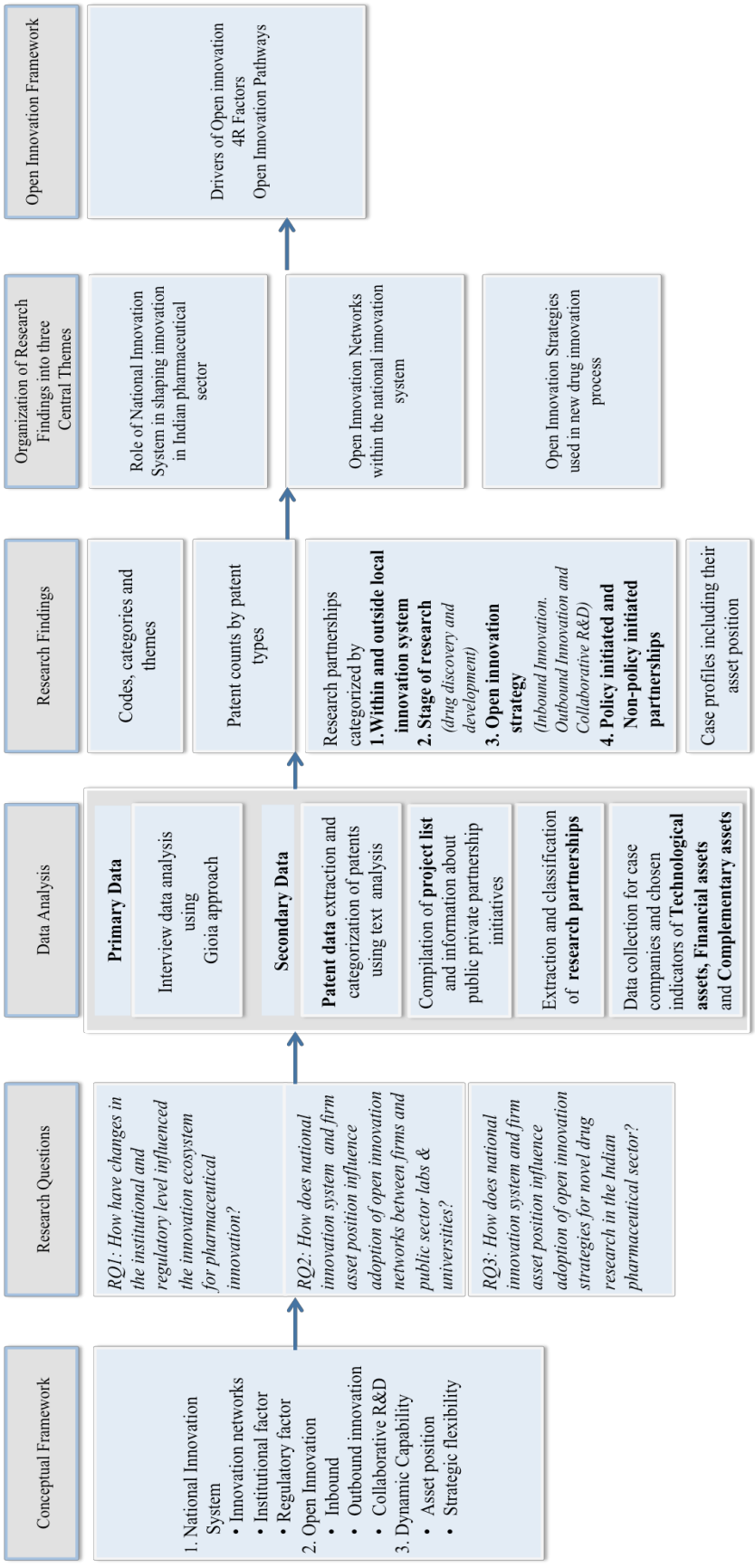


Figure 20: Process flow illustrating the progression of research study

5 Progression of Indian Pharmaceutical Industry in Two Distinct Regimes

"A potent combination of constraints and ambitions has ignited a new genre of innovation." (Prahalad and Mashelkar, 2010: 3)

The objective of this chapter is to highlight the importance of national innovation systems in shaping the selection environment and playing a critical role in the evolution and progression of an industry. The theory of national innovation systems enables to sketch the evolution of the Indian pharmaceutical sector against a backdrop of institutional and regulatory forces. The evidence gathered from historical tracing of institutional policies and empirical examination of the patent data describes the shift from incremental innovation to more substantial innovation in the pharmaceutical industry. The case firms serve as examples to provide evidence as to how regulatory and institutional initiatives have intertwined to scale up the nature of innovation in different patent environments. The Indian pharmaceutical industry is examined as a case study to illustrate how a change in patent regime had an impacting role in alternating competencies in pharmaceutical firms.

This chapter provides answers to the research question: How have changes in the institutional and regulatory level influenced the innovation ecosystem for pharmaceutical innovation? The objective of the chapter is twofold. On one hand, it provides a background of the Indian pharmaceutical sector and describes how the changes at the institutional and regulatory level geared the local innovation system to exploit new research opportunities at different periods. On the other hand, it focuses on how the changes witnessed at the macro level allowed technological progression at firm level. Section 5.1 of this chapter details how the pharmaceutical sector evolved under the two appropriability regimes by providing a snapshot of institutional setup, key policies and business activities of firms. Section 5.2 highlights the positive aspects of TRIPS patent regime such as public private partnership initiatives that has propelled innovation in India. The section also presents the findings of patent data analysis and secondary data for cases of five established and four SMEs that shows the advancement in pharmaceutical research in different appropriability regimes. This section also underlines the challenges inherent in the institutional setup that hinders new drug innovation in India.

The Indian pharmaceutical sector is an important case to study for many reasons. India is one of the largest producers and supplier of low priced generic medicines in the world (Iyer, 2012). The industry accounts for 8% of the global generics production and accounts for 20% of global generic medicines supply. The industry ranks third largest in volume and thirteen largest in terms of value (IndiaPharmaSummit, 2015). Exports form a major revenue for the industry and continues to be the key focus for Indian domestic companies (KPMG). India is among the top 20 pharmaceutical exporting countries of the world with exports touching at INR 690.23 billion in 2013-2014 ($10.39 billion) (IndiaPharmaSummit, 2015). Some of the large Indian firms derive 50% of their revenues from international business (DoP, 2015b). As an example, in 2014-2015, 85% of turnover of Dr. Reddy's was from export business (Dr.Reddy, 2015). In terms of value, the US is the largest market for exports with 30.7% followed by other countries (KPMG, 2014).

The Indian pharmaceutical market is estimated to be INR 1584 billion (USD 34.5 billion) as of 2014 and is estimated to grow at 12-15% (KPMG). The growth is driven by increasing population leading to high demand, rising personal income, improved healthcare spending, changing disease profile, increase in penetration of health insurance and increase in number of specialised clinics, hospitals and treatment centres (KPMG, 2014; Sampath, 2008). Government initiatives to boost growth and investment and enabling of 100 per cent FDI through the automatic route has facilitated significant growth in this sector (KPMG, 2014).

The Indian pharmaceutical sector is a diverse mixture of many large, medium sized and small sized companies. The large pharmaceutical firms comprise of domestic Indian firms as well as subsidiaries of multinational companies in India (Sampath, 2005). Indian pharmaceutical industry has strong manufacturing capacity. There are more than 10,000 manufacturing units in India with 44% of the units confined in western parts of India. Manufacturing costs in India are 35-40% lower than the costs in any developed country (KPMG, 2014). Additionally, many Indian manufacturing units have got approvals from international regulatory agencies of US, UK, Australia and South Africa. The strength of India's manufacturing capacity is evidenced from the fact that outside USA, India has the largest number of USFDA approved plants for generic drugs manufacture (DoP, 2015b).

The R&D intensity among the Indian pharmaceutical firms is quite low as compared to developed countries (Joseph, 2011). The initiation of drug discovery programmes saw an increase in the R&D investments by firms. In the early 2000s, large Indian firms invested

approximately around 10% of their total sales into R&D (Sampath, 2008). In the year 2014-2015, the R&D intensity for Dr. Reddy's, Lupin and Piramal was in the range of 9% - 14% (Case profiles). A large share of this R&D expenditures is used in the development of novel delivery systems, non-infringing processes, and research activities for generics business (Sampath, 2008). Indian pharma companies are involved in a wide spectrum of business activities such as development of pharmaceuticals, new drugs and biotechnology related products. Indian firms are also leveraging their presence across different manufacturing segments and have a huge capacity base to enter new business segments such as contract research and development, biopharmaceuticals, clinical trials and bio-generics (KPMG, 2014).

5.1 Two distinct periods of appropriability regimes in India

Over the past forty years, the Indian pharmaceutical sector has participated in the changes in regulatory regime, from a process patent environment in 1970 to a product patent environment in 2005. India witnessed a change in patent law with the implementation of Indian Patents (Amendment) Act, 2005 and saw a shift from process patent regime to the more stringent product patent regime (Chowdhary, 2010). The TRIPS initiated amendment brought about changes such as extension of patent rights to new subject matter such as pharmaceutical substance and granting of patents for 20 years (Basheer, 2005). It allows firms to patent new products developed after 1995 and restricts firms to manufacture products under patents (Simonetti et al., 2007).

In contrast to this, the 1970 patent law recognised only process patents, which implies that firms could develop non-infringing process to produce drugs at a lower cost. The Indian pharmaceutical industry achieved considerable success under the old patent law (Simonetti et al., 2007). It allowed the industry to entrench themselves as leaders in the generics industry and facilitated their diversification into value added generics, bio generics and biotechnology (Chowdhary, 2010). The change in patent regime meant that domestic development and manufacturing opportunities are lost for drugs still protected by patents. However, the Indian firms have found new opportunities to develop generic drugs whose patents have expired recently and from international outsourcing opportunities for contract research and manufacturing services (CRAMS) from developed countries (Simonetti et al., 2007). The

shift in appropriability regime also witnessed a scale up from a process based R&D alone to develop modifications of existing chemical entities such as new formulations, compositions and combinations and advanced innovative R&D for new drug research (Chaudhuri, 2007; Kale and Little, 2007). Post 2005, the nature of business activities includes a) formulation and manufacture of patent expired drugs b) R&D for new formulations, drug delivery systems to manufacture differentiated generic drugs c) R&D for development of new drugs and d) contract research and manufacturing for innovator companies (Chowdhary, 2010).

The table below dichotomises the pharmaceutical industry environment into two appropriability regimes during two different time periods. Teece (1986)'s theory defines the two important constituents of appropriability regime as *nature of technology* and *patent regime*. The change in patent laws accompanied by changes in the research activities of the firms allows distinguishing the Indian pharmaceutical industry environment into strong and weak appropriability regimes.

Table 19: Dichotomy of Indian pharmaceutical industry environment

Time Period	**Patent Regime**	**Nature of Technology**	**Appropriability Regime**
Pre-2005 (1970 – 2004)	Process Patent Regime - Patents Act, 1970	Process and incremental product innovation	Weak
Post-2005 (2005-Present)	Product Patent Regime - Patents (Amendment) Act, 2005	New product innovation	Strong

Source: Classified using Teece (1986)'s definition of appropriability regime

5.1.1 Process patent regime, 1970 – 2005: Humble beginnings

At the time of independence of India in 1947, the 1911 Indian Patents and Designs Act enacted by the British was functional. The 1911 Patent Act permitted patenting of pharmaceutical products however the lack of a domestic pharmaceutical industry favoured imports and business of multinational companies. The British rule saw the emergence of textile, food processing and metal sector but the growth of indigenous pharmaceutical sector remained largely stunted. In order to promote the development of Indian pharmaceutical sector and curb the presence of multinational companies, the Indian government abolished the Patent Act 1911 paving way for The Patent Act 1970 (Mueller, 2007).

The Patent Act 1970, based on the recommendation of the Ayyangar committee report prohibited patents on products for food and drugs and expanded the scope of compulsory licensing (Basheer, 2005). Under this law, patenting of processes for developing pharmaceutical substance was allowed and patent was granted a term of five years from sealing or seven years from date of filing of complete specification whichever period is shorter. A further implication of this law was that pharmaceutical products patented elsewhere could be developed if produced through a non-infringing process. This resulted in two important developments a) foreign firms started to cut back on patent filings in India b) it gave birth to private pharmaceutical firms that started developing competencies to reverse engineer patent drugs using different processes (Mueller, 2007).

Institutional setup and policies

Science and Technology setup

Under the British rule, the foundation of scientific research was laid by setting up of two authoritative bodies: Board of Scientific and Industrial Research in 1940 and Council of Scientific and Industrial Research was formed in 1942 (GOI, 1951). Post independence, in the 1950s, the government of India focused on heavy investments to build scientific infrastructure and educational institutions. A chain of national laboratories and research institutes were set up in different parts of the country to stimulate industrial research. It is during this period that institutes such as National Chemical Laboratory, Poona and Central Drug Research Institute, Lucknow, which have gained much prominence in the field of pharmaceutical research, were set up. The government realised the need for trained personnel to manage the research institutions and industries and set up educational institutions across the country (GOI, 1951). It was during this period that government set up manufacturing facilities to make available indigenously manufactured drugs. The government established state controlled pharmaceutical companies, Hindustan Antibiotics Limited (HAL) and Indian Drugs and Pharmaceuticals Limited (IDPL) (Ramani, 2002). For most part of the post independence, these state led pharmaceutical companies were mainly engaged in the substitution of imported materials with indigenous materials, formulation activities and manufacture of bulk drugs from intermediates (GOI, 1961).

During the 1960's, government encouraged carrying out basic research, training of scientific personnel and co-ordination of research work amongst different units of government departments. The scope of operations for Council of Scientific and Industrial Research

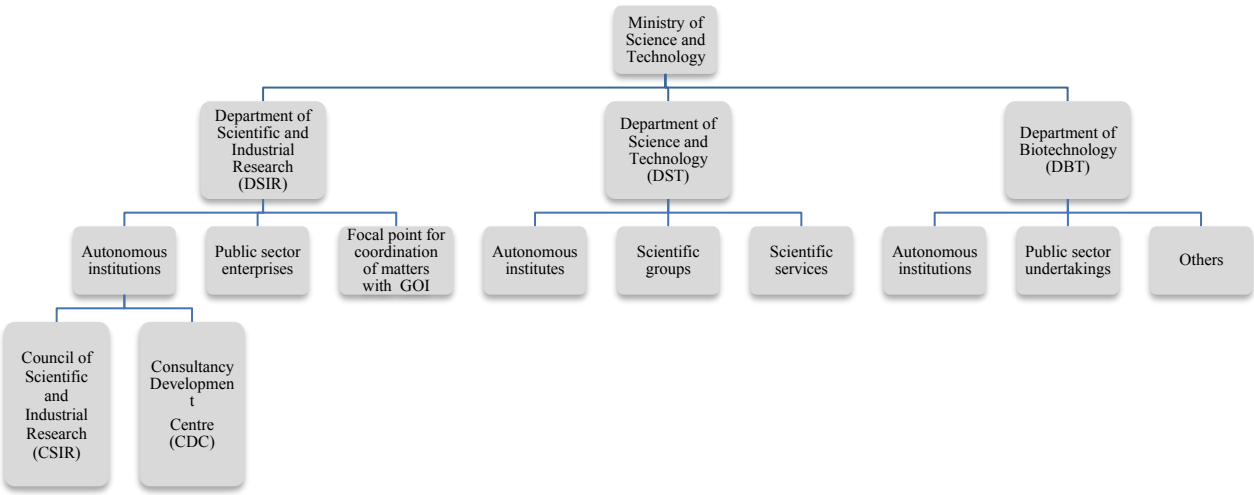
greatly increased after 1947. CSIR initiated new research schemes, scientific study for problems afflicting industries and set up new laboratories (GOI, 1974). The state led initiatives provided a strong foundation in terms of capacity development for research and development to move in the right direction.

To orchestrate science and technology in the country, the Department of Science and Technology was established in May 1971, which played a pivotal role in establishing the infrastructure and providing a thrust to basic research technology development and scientific service (GOI, 2005). By 1980-85, India had established about 119 universities, affiliating about 1050 colleges, 5 institutes of technology, 150 engineering colleges, about 100 medical colleges producing 150,000 qualified scientific technical personnel every year. The total manpower of scientific and technically qualified personnel was estimated at 2.5 million, ranking India as the third largest country of such manpower in the world. The 130 specialised laboratories established by government and 600 odd in-house R&D established by public and private sector, completed the science and technology infrastructure picture (GOI, 1980).

In India, basic and long-term research is primarily carried out by publicly funded research organizations (universities and public laboratories) and industry. The Indian government has supported basic and mission oriented science and technology programmes through various policy measures. India has a massive infrastructure of national labs, academic institutes and private R&D labs. The public research system in India is believed to have contributed effectively to scientific training and development of science and technological capability in a crucial sector such as pharmaceuticals (Feinberg and Majumdar, 2001; Iyer, 2012).

The formulation of policies for pharmaceutical sector is split between the Ministry of Chemicals and Fertilizers, Ministry of Commerce and Industry, Ministry of Health and Family Welfare and Ministry of Science and Technology (Sampath, 2008). In the public sector, the bulk of R&D expenditure for pharmaceuticals is carried out chiefly by scientific agencies such as Department of Science & Technology (DST), and Department of Biotechnology (DBT), Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha & Homoeopathy (AYUSH), Council of Scientific & Industrial Research (CSIR), Indian Council of Medical Research (ICMR), Department of Ocean Development etc. (Secretariat, 2006). These entities have autonomous institutions, schemes, and public sector undertakings, which cumulatively form the scientific base of the country. The Ministry of Science and Technology is the nodal agency that plays a key role in funding of research and development

in the country and houses key departments DST, DBT and DSIR under its umbrella responsible for the development of pharmaceutical research in India. Figure 21 shows the current organisational structure of Ministry of Science and technology with key departments that support pharmaceutical research.



Source: (DST, 2016a)

Figure 21: Organisational set up of Ministry of Science and technology

Department of Science and Technology (DST) - The Department of Science and Technology was set up in 1971 for promoting new areas of science and technology and to play the role of a nodal department for organizing and coordinating science and technology activities in the country. The department set up several streams of research which in due course of time evolved into separate departments with focused goal (DST, 2016b).

Department of Scientific and Industrial Research (DSIR) - The DSIR was set up under this Ministry of Science and Technology in 1985 with a mandate to support industry for indigenous technology promotion, development, utilization and transfer. It is the nodal department for granting recognition to commercial and non-commercial R&D organizations in the country. CSIR is an autonomous R&D organization under DSIR that was established in 1942. It has 38 laboratories, 39 outreach centres, 3 innovation complexes and 5 units engaged in physical, chemical, earth, engineering and biological, scientific and industrial research activities (DSIR, 2015). Prominent research institutes under CSIR which engage in discovery research in new drug areas are – Central Drug Research Institute (CDRI), Centre for Cellular Molecular Biology (CCMB), Indian Institute of Chemical Technology (IICT), National

Chemical Laboratory (Hasenclever and Paranhos), Indian Institute of Chemical Biology (IICB) and the CSIR-UNIT: Open Source Drug Discovery (OSDD) (DSIR, 2015).

Department of Biotechnology (DBT) - was set up to support research in all areas of sciences that uses modern biotechnology. The department supports setting up world-class facilities, and provides access to specialized equipment to a networked community of researchers and students. It also plays a role in technology transfer and commercialization of technologies to industry by setting up technology transfer offices in research institutes and universities. One of the prominent initiatives of the department was the setting up of Biotechnology Industry Research Assistance Council (BIRAC), a public sector undertaking to work on public private partnership programmes (DBT, 2015).

Other prominent departments - There are other departments in the science technology systems of India that do not fall under DST but provide support to the research and development of pharmaceutical drugs. The Ministry of AYUSH was set up to preserve and nurture the traditional systems of medicine prevalent in India. It primarily provides research support to Ayurveda, Siddha, Unani & Homoeopathy systems of medicine to leverage the ancient knowledge of India in the alternative systems of medicines. One of the important objectives of this department is standardization and quality control of herbal drugs (Secretariat, 2006).

The Indian Council of Medical Research, ICMR has been setup with the objective of sponsoring and coordinating medical research in the country. The ICMR is funded through the Department of Health Research, Ministry of Health & Family Welfare. The Council promotes research through intramural as well as extramural research. Intramural research is carried out in research of specific areas such as tuberculosis, leprosy, cholera and diarrhoeal diseases, viral diseases including AIDS, malaria, kala-azar, oncology etc. and to address regional health problems. The extramural research sets up advanced research centres and promotes research in non-ICMR institutes through grant in aids (ICMR, 2016).

In June 2008, a new Department of Pharmaceuticals was created under the Ministry of Chemicals and Fertilizers to focus more on the growth and development of the pharmaceutical industry (Sampath, 2008). The department has played an important role in capacity building of pharmaceutical industry, establishment of educational institutions like National Institutes of Pharmaceutical Education and Research (NIPER), providing access to quality drugs at reasonable prices and facilitating exports (DoP, 2015a). Apart from these prominent departments

which are engaged in the science based R&D projects for new drug research, the Ministry of Ocean Development has also initiated a research programme to harness the marine flora and fauna for extraction of drugs for medicinal purposes. The project has yielded 10,000 compounds isolated from marine organisms. A number of compounds have been identified that are in various phases of clinical trials (Secretariat, 2006).

Another notable public initiative is the establishment of Biotech Consortium India Limited (BCIL) a public sector financing company promoted by Department of Biotechnology, Ministry of Science and Technology and All India Financial Institutions. BCIL has been actively involved in assisting the public research institutions and corporate with technology transfer, project consultancy, funding and manpower training & placement related to biotechnology (BCIL, 2016).

Policies

A prominent feature in the shaping of the industrial sector has been the Industrial Policy resolution, which in the initial years offered protectionism to the young industries. From the 1960s till the liberalization policy adopted in 1991, India adopted the policy of self-reliance and import substitution (Feinberg and Majumdar, 2001). The Industries Development and Regulation Act of 1951 sought increased state control on industrial activities. The second Industrial Policy Resolution in 1956 shaped the industrial landscape in such a manner so as to favor the state sector and reduce the dominance of multinational companies. The role of foreign firms was further restricted by the introduction of Foreign Exchange Regulation Act (FERA), which limited foreign ownership in companies to 40% (Majumdar, 2009). The Monopolies and Restrictive Trade Practices (MRTP) Act 1969 was introduced to oversee legislation on prices, monopoly and ensure fair trade. The Monopolies and Restrictive Trade Practices aimed to prevent concentration of economic power, prohibit monopolistic trade practices and ensure a fair competitive environment (Srinivas, 2012).

Two policies that played an important role during this regime in influencing the pharmaceutical sector are the New Drug Policy, 1978 and the Drug Price Control Order (DPCO), 1970. The New Drug Policy 1978 categorized drugs into three categories and allocated licenses accordingly. The essential drugs were restricted to public sector manufacturing, 27 drug items were allocated for private sector manufacturing while 64 items were open to all applicants. The New Drug Policy aimed to improve self reliance in local production of drugs,

ensuring availability of essential drugs, strengthening quality control and restrict participation of foreign firms (Srinivas, 2012). The Drug Prices Control Order formally instituted in 1970 was promulgated to bring drugs under price control by setting a limit of 15% on pretax profits from sales of pharmaceuticals. The subsequent revisions in 1979, 1987, 1995 and 2002 aimed to remove drugs from price controls. The DPCO gradually decreased the number of drugs it monitored and the controls in due course of time. However, the policy had an important effect in meeting shortfall of essential drugs, keeping MNCs away and enabling domestic private firms to make sizeable profits (Srinivas, 2012). Currently, National Pharmaceutical Pricing Policy, 2012 and the Drugs Prices Control Order (DPCO), 2013 have been implemented with the aim of ensuring adequate availability of essential and lifesaving drugs at affordable prices (NPPA, 2016).

The 1981 industrial policy shifted the focus away from protectionism. Foreign exchange restrictions were removed for export oriented firms and regulations were eased for technology acquisitions and foreign ownership. However, it was the liberalization in 1991 that promoted international diversification of firm activities. Industrial licensing rules were relaxed in most sectors and limits on foreign ownership were raised so that firms could possess majority control (Feinberg and Majumdar, 2001). The New Economic Policy of 1991 had a significant impact in opening up the economy leading to the liberalization reforms. These changes brought about massive restructuring in the economy, did away with the complex system of licensing, gave a greater role to the private sector and provided a big boost to the globalization activities of all economic sectors (Srinivas, 2012).

Business activities of firms

In 1947 at the time of India's independence, western multinational companies dominated India's pharmaceutical market and controlled 99 per cent of all pharmaceutical products. Reliance was mainly on imported drugs and domestic Indian drug prices were among the highest in the world (Kamble et al., 2012). The foreign multinational companies imported bulk drugs from their home countries and formulated the drugs in India, which led to high prices. The government tried to control the prices of bulk drugs and select formulations through Drug Price Control Order of 1970 but the low margins only suppressed the R&D investments by foreign firms and did not help the fledgling domestic industry (Ramani, 2002).

The genesis of the pharmaceutical sector took place in 1970 with the entry of private sector, and the change in patent regime and government policies, which aided the growth of the budding industry. The Patents Act 1970, which abolished the product patent protection (Chowdhary, 2010) enabled firms to reverse engineer drugs that were product patented in other countries (Chittoor et al., 2009). During the years 1974-1978, Indian government eased licensing regulations for R&D based industries to stimulate indigenous research (GOI, 1974). This was an important step to introduce private sector investment in the pharmaceutical industry.

These important developments resulted in a change in the foreign versus local firm ratio. Statistics from Organisation of Pharmaceutical Producers of India reveal the ratio of Indian to foreign firms in 1970 grew from 15:85 to 50:50 by 1982 and further improved to 61: 37 by year 1999 (Sampath, 2005). The domestic industry flourished under the aegis of government policies. Multinationals were barred them from manufacturing de-licensed category of drugs during the 1980s (Iyer, 2012). The policy environment restricted FDI and the weak-patenting regime enabled the domestic firms to hone their capabilities of reverse engineering and to learn and adapt technology in a protected environment (Feinberg and Majumdar, 2001; Iyer, 2012).

During the period 1995-2006, multinational firms did not have any productivity hampering effect on the domestic industry, which continued to grow unabated during this period (Iyer, 2012; Mani, 2006). Before the TRIPs agreement, the Indian pharmaceutical market was largely generics based. The activities of the Indian pharmaceutical industry involved were a) production of active pharmaceutical ingredients and b) production of formulation drugs (Chowdhary, 2010). The emphasis was on research to adapt foreign technology, reverse engineer of existing drugs and research for technology substitutes (Krishna, 2007). The attainment of expertise in reverse engineering of processes for bulk drugs allowed the Indian firms to use locally manufactured bulk drugs instead of imported ones and keep prices of finished drugs amongst the lowest in the world market (Sampath, 2008). While generics remain the mainstay of the Indian market, firms have diversified their portfolios to include more complex formulations (KPMG, 2014). The pharmaceutical sector reached its pinnacle during the 1990s with growth of domestic formulation sales increasing at CAGR of 17% for the period 1995-1996 to 2007-2008 for the top 15 pharmaceutical companies of India (S. Chaudhuri,

2005). The table below shows the sales and growth rate of retail formulations of top Indian companies.

Table 20: Growth of Retail Formulations Sales of Top Indian Companies

Company	Retail Sales 1995/96 share (INR mn)	Market Share 1995/96 (percent)	Retail sales 2007/08 (INR mn)	Market Share 2007/08 (percent)	CAGR (1995/96 to 2007/08)
Cipla Ltd.	2863	4.18	16831	5.24	15.91
Ranbaxy Laboratories Ltd.	2686	3.92	15995	4.98	16.0
Alembic Ltd.	1664	2.43	6075	1.89	11.40
Torrent Pharmaceuticals Ltd.	1540	2.25	6584	2.05	12.87
Lupin Ltd.	1536	2.24	8513	2.65	15.34
Piramal Healthcare Ltd.	1363	1.99	11592	3.61	19.53
Cadila Healthcare Ltd.	1323	1.93	11902	3.71	20.09
Wockhardt Ltd.	998	1.46	6361	1.98	16.69
Unichem Laboratories Ltd.	931	1.36	5002	1.56	15.04
Ipca Laboratories Ltd.	796	1.16	4015	1.25	14.44
Sun Pharmaceutical Inds. Ltd.	722	1.05	10684	3.33	25.17
USV Ltd.	599	0.87	4579	1.43	18.47
Dr. Reddy's Laboratories Ltd.	557	0.81	7490	2.33	24.18
J B chemicals & Pharmaceuticals Ltd.	495	0.72	2058	0.64	12.61
Glenmark Pharmaceuticals Ltd.	460	0.57	4369	1.36	20.63
Elder Pharmaceuticals Ltd.	417	0.61	2912	0.91	17.58
Total (15 companies)	18950	27.55	124962	38.93	17.02

Source: (Nwaka and Ridley, 2003)

The pharmaceutical sector's strength lies in its ability to leverage strong chemistry skills, large human capital base and lower manufacturing costs to develop drugs at competitive prices. The capability to innovate processes for manufacturing enabled India to gain an international presence and emerge as a global source of drugs (S. Chaudhuri, 2005).

However, during this period, international R&D activities were at an ebb. A weak appropriability regime also inhibits licensing activities. Empirical research by Lee and Mansfield (1996) with US firms revealed that 81% of MNCs were hesitant to license out technology to India, which was regarded to have the weakest protection. The regulatory environment also influences the volume and composition of foreign direct investment (Lee and Mansfield, 1996). As the 1990s saw the liberalisation regime and growth in exports, import of foreign technology and R&D activities by foreign firms in India remained low (Iyer, 2012).

5.1.2 Product Patent Regime, 2005-2014: The journey 2005 onwards

India became a signatory to TRIPS agreement effective 1 January 1995 (Mueller, 2007). India received a ten year transition period to amend its patent laws and fully implement TRIPS based laws by January 1, 2005 (Mueller, 2007). The amended patent law allowed patent rights to new subject matter and grant of patents for 20 years (Basheer, 2005). The new patent law retains the pre-grant opposition mechanism endowed in the Patents Act 1970, which allows a patent to be opposed on several grounds. The 2005 Act also has introduced a post-grant opposition mechanism to allow opposition on similar grounds within a year of the patent being granted (Basheer, 2005).

The implication of the new law is that Indian firms will not be able to manufacture drugs under patents unless a voluntary or compulsory license is granted (Chowdhary, 2010). This is significant for the generics dominated pharmaceutical industry in India as it prevents reverse engineering of patented drugs and makes it imperative for the Indian companies to undertake new drug research. The shift in patent regime generated widespread concerns among the academic scholars on the effect of TRIPS on drug prices and access to essential medicines (Lanjouw, 1998).

The TRIPS agreement provides the flexibility of compulsory licensing whereby member states can grant licenses for the supply of patented medicines to ensure access to healthcare. Despite these flexibilities, the TRIPS agreement was threatening for developing countries without sufficient manufacturing capacity to eventually become dependent on patented medicines for their healthcare needs (Correa, 2002). In that respect, the case of India is different. It has a well-developed pharmaceutical industry and is a global supplier of affordable medicines especially in the supply of low priced generic anti-retroviral medicines

to global pharmaceutical market. With strengths in developing non infringing cost effective processes and significant manufacturing capacity, the new patent amendment act hoped to increase R&D investments for development of new drugs and prove beneficial to the industry at large (Chowdhary, 2010).

Institutional initiatives for new drug research

The implementation of Trade Related Intellectual Property Rights (TRIPS) agreement and the ensuing Patent Amendments Act in 2005, engendered new policy initiatives, increased funds for research and development (R&D) and efforts to boost state-industry-academic relationship. Government introduced various measures such as increased budgetary allocations for research, soft loans, grants, setting up of technology transfer offices, IP awareness programmes and promoting public private partnerships (Department of Science and Technology, 2013).

The government has given special attention to the promotion and support of industrial research in the country through tax incentives, financially attractive schemes. DSIR has a scheme for granting recognition to in-house R&D units in industry. This recognition not only allows such R&D units to avail of various fiscal incentives but also become eligible to receive R&D grants from other departments (DSIR, 2015). Another major thrust of government initiatives have been to steer research for new drug for neglected diseases such as malaria, tuberculosis, leishmaniasis through the setting up of open source drug discovery initiative (OSDD). The Council for Scientific and Industrial Research (CSIR) initiated OSDD is a research consortium, which has leveraged the virtual lab concept to encourage collaboration among Indian researchers to discover drugs for neglected diseases (Årdal and Røttingen, 2012). Currently, the OSDD is focused on discovering drugs for tuberculosis. (DSIR, 2011).

The key public funded institutions – DST, DBT and CSIR support research for pharmaceutical research through various schemes such as The Drugs and Pharmaceuticals Research programme (DPRP), Biotechnology Industry Research Assistance Council (BIRAC) initiatives and New Millennium Indian Technology Leadership Initiative (NMITLI). The government has initiated these public initiatives to mobilise pharmaceutical innovation in four ways:

a) Promote R&D initiatives for new and incremental scientific and technological inventions
b) Strengthen R&D infrastructure
c) Facilitate collaboration between industry and academia and increase opportunities for translational research
d) Build human capital

DST initiated the DPRP initiative in 1995 to support research in pharmaceutical drugs, however the programme failed to pick up momentum during the first ten years of its inception and was nearly dormant. It was only in 2005 that this programme gained considerable attention when it was restructured and re-introduced. Even the NMITLI programme that was introduced in 2000 facilitated most of the new drug research projects after 2005. These programmes though initiated before 2005 gained considerable momentum after 2005 and have thus been included in this study as post TRIPs initiative.

The Drugs and Pharmaceuticals Research programme (DPRP)

The programme established by DST in 1994-1995 was the first among the new wave of government programmes to support R&D for pharmaceutical research. The specific objectives of the scheme are to promote industry – institutional collaboration, create infrastructure and mechanisms to facilitate new drug development, stimulate skill development of human resources in R&D and enhance self reliance in drugs and pharmaceuticals in areas critical to national health requirements. The beneficiaries of the scheme are industry, academic institutions and laboratories. The programme supports research in three ways a) by providing financial assistance for *collaborative R&D projects* b) *soft loans* to industry and c) *funds* for creating or revamping facilities in universities (Department of Science and Technology, 2015; Secretariat, 2006).

a) Collaborative R&D projects – Under these types of projects, firms need to seek partnership either with a national laboratory or academic institution or any public funded R&D institution to avail funding opportunities. Funds are shared on 50:50 basis between industry and public institution and sharing of intellectual property is subject to the agreement between collaborating partners (Department of Science and Technology, 2015). The advantage of such a programme is that the industry is able to reduce its R&D expenditure and also able to leverage the expertise of the collaborative partner.

b) Loan projects - Under this project type, firms can receive funding from 50% to 70% of the total project cost. Grants are also provided for clinical trials in Phase I, II and II, for neglected diseases like tuberculosis, malaria, kala-azar, filariasis, etc. (Department of Science and Technology, 2015). The firm retains intellectual property rights to its innovation. Such incentives induce firms to seek funding for projects in clinical development stages that are cost intensive and prone to high failure rates.

c) National facility projects - This programme also extends funding support to creation or revamping of infrastructure projects such as cold rooms, animal house, and purchase of specialised equipment. This benefit can be availed by academic institutions, national laboratories and other public research institutes involved in pharmaceutical research - (Advisor, Department of Science and Technology [20]).

The programme was revamped in 2004-2005 and thereafter expanded rapidly. DPRP realigned its focus to support industry relevant projects and in this way differs from other policy initiatives, which emphasise on basic research.

> *"The major goal of the programme is to promote indigenous development of the drugs in India. The focus is to support the Indian pharmaceutical sector encompassing their research activities, their development activities, clinical trials, the basic infrastructure, manpower and all sorts of things." (Advisor, Department of Science and Technology [20])*

The DPRP initiative encourages commercialization of late stage research projects. From a policy funding perspective, the advisor feels that the more advanced stages of the drug research project, the closer it is to the commercialization stage. However, this is not to imply that the programme does not support early stage projects. DPRP has a wide scope, funds drug research projects in all stages of research and provides equal support to incremental and novel drug research projects.

The programme has an advisory committee comprising of members of eminent scientists, members from Drug Controller of India, Department of Biotechnology, Ministry of Health and Welfare and AYUSH. The advisory committee uses a competitive review process to make funding decision on project proposals. In some complex projects, a subcommittee is also formed for project review. The advisory committee through review meetings and site visits undertakes periodic monitoring of the project.

A significant achievement of the programme has been to fund many clinical trials projects. The highlight of the DPRP programme initiative has been to support clinical development of Ranbaxy's new anti-malarial drug 'Synriam' (Arterolane maleate 150mg + Piperaquine phosphate 750 mg). This was the first new chemical entity to have been launched in India. The support from the programme was in the form of grant in aid and the clinical development of the drug was 100% sponsored by Department of Science and Technology - (Advisor, Department of Science and Technology [20]).

New Millennium Indian Technology Leadership Initiative (NMITLI)

NMITLI was initiated by CSIR in 2000 with the mandate to encourage public private partnership between industry and public research institutions in select sectors of science. NMITLI supports mainly two types of projects – a) nationally evolved projects initiated by the NMITLI programme b) and industry originated projects (CSIR, 2016).

a) Nationally evolved projects: These are projects, which are selected by the NMITLI committee to be sponsored by this programme. The NMITLI committee brainstorms to identify and select project proposals based on unmet research need and national priorities. Example, a domain of medicinal implants was identified as a potential research project to be developed through this programme.

b) Industry originated projects: Like DPRP, firms submit proposals to seek grants for research projects. One of the mandatory requirements of the project proposal is the inclusion of a collaborative partner in the research project from public research labs or universities. In this way, NMITLI programme encourages firms to network with public sector scientists and thus funds many research collaborations (CSIR, 2016).

NMITLI has also funded projects, which originated in CSIR labs and has been transferred to the industry. If the project has potential for commercialization, the programme allocates funds to the industry for further development. Lysostaphin is an example where the whole research was done in a CSIR laboratory called Institute of Genomics & Integrative Biology (IGIB, New Delhi). It was transferred to Bharat Biotech International Limited, a biotech firm and sponsored by NMITLI for further advanced stages of development (Head, NMITLI [23]).

Firms retain all intellectual property rights from any innovation. In case of collaborative partnerships programmes, IP may be shared based on the contribution and agreement among

the partners. CSIR laboratories may assist in technology transfer of IP and research assets so that the ownership of IP lies with the firms (Head, NMITLI [23]).

There are two committees, the advisory and monitoring committee, which form the backbone of the programme. At the inception of the project, the advisory committee scrutinizes the project and suggests partners from academic institutions/public research labs depending on project requirement and the level of expertise required. The review committee holds regular meetings in order to evaluate the progress of the project properly (Head, NMITLI [23]).

A constraint of the NMITLI programme is the capacity to provide funding for public private partnerships only. DPRP on the other hand has more flexibility and provides funds for stand-alone projects too. However, an advantage with the NMITLI programme is that the committee reviews the proposal even if the firm has not finalized a collaborative partner at the proposal stage. Based on merit of the case, the NMITLI committee may suggest collaborative partners for furthering the project. This is not the case with DPRP that mandatorily requires a joint collaborative academic partner at the time of proposal submission.

NMITLI programme is credited with initiating drug discovery projects for discovery and development of new molecules for tuberculosis and psoriasis (CSIR, 2006). Under the NMITLI programme, the expertise of 12 institutional partners and an industry were synergized for the discovery of new drug LL 3858/4858 (Sudoterb) for tuberculosis (Head, NMITLI [23]).

Biotechnology Industry Research Assistance Council (BIRAC) initiatives

BIRAC is a not for profit company, set up by the Department of Biotechnology established in the year 2012. BIRAC is one of the newest of government initiative intended to support industrial R&D and encourage commercialisation of innovation by small firms. BIRAC has initiated many important schemes to stimulate bio-innovations available to scientists from research institutes, academia and start-ups. It supports all major areas of biotechnology sector i.e. healthcare, agriculture and industrial biotechnology (BIRAC, 2014).

BIRAC has many initiatives to support pharmaceutical research that can be segregated by different stages of research and development:

a) Discovery to proof of concept stage

Biotechnology Ignition Grant (BIG) - This scheme has been designed to support early stage discoveries and is available to research institutes, academia and start-ups. The five important centres which provide mentoring and networking are: C-Camp Bangalore, IKP Hyderabad, FITT, IIT Delhi, NCL Venture Centre, Pune and KIIT-TBI, Bhubaneshwar (BIRAC, 2014).

b) Early and late stage research

Small Business Innovation Research Initiative (SBIRI) - This is a public private partnership initiative to support early stage innovation by SMEs (BIRAC, 2014). Research projects from the proof of concept to validation stages are supported under this scheme (Advisor, BIRAC [21]).

c) High risk discovery led innovation

Biotechnology Industry Partnership Programme (BIPP) - This scheme provides support from early to late stage research to the industry in a partnership scheme. It works on a 50:50 cost-sharing model.

d) Validation of academic POC/research leads

Contract Research and Services Scheme (CRSS) - This scheme supports academic institutes to enable validation of research work by industry. Funding is provided for the contractual work done by the industry. The intellectual property rights are retained with the academic partner.

Other schemes of BIRAC include the Research Alliance for Product Innovation and Development (RAPID) and Social Innovation Programme for Products Affordable and Relevant to Social Health (SPARSH) and support system provided to start-ups through the Bioincubator Support scheme (BISS) (BIRAC, 2014). In addition to this, BIRAC provides ecosystem support by setting up incubators, mentoring, training on regulatory requirements and hands on training workshops on various areas throughout the country (Advisor, BIRAC [21]). The span of projects sponsored under these schemes depends on the type of project. Projects under the BIG scheme, which are in initial discovery stages range from 18 months to 24 months. The new drug research projects supported by BIPP and SBIRI have longer project duration and are therefore executed in phases. The firm retains commercialisation and intellectual property rights to its innovation. In cases, where the company fails to commercialise, the government can intervene to facilitate the transfer to other organisation for commercialisation (Advisor, BIRAC [21]).

Table 21: Summary of Public private partnership programmes

Name of the initiative	Initiation year	Agency	Type of projects supported	Target	Need for collaborative partner	Scope of programme	Stage of drug research	IP sharing strategy	Project length
Drugs & Pharmaceutical Research (DPRP)	1995	Department of Science and Technology (DST)	• Loan projects • Collaborative R&D projects • Facility projects	Industry National laboratories Academic institutions	No	Pharmaceutical research All systems of medicine Priority for neglected diseases like malaria, TB, Kala-azar, Filariasis, etc.	Drug discovery Drug development	Ownership of IP as per agreed terms	3-5 years
New Millennium Indian Technology Leadership Initiative (NMITLI)	2000	Council of Scientific & Industrial Research (CSIR)	• Collaborative R&D projects	Industry National laboratories Academic institutions	Yes	R&D projects with unmet needs	Drug discovery Drug development	Company initiated projects - IP with company Joint research projects - IP transferred to the company for subsequent development	3- 5 years. In some cases seven years.
BIRAC Initiatives - SBIRI	2005	Department of Biotechnology	• Loan projects • Collaborative R&D projects	Small Biotech enterprises	No	Biotechnology Pharmaceuticals Devices	Early stage (Pre-Proof of concept) Late stage development	IP is with companies or entrepreneur.	Long term projects
BIRAC Initiatives - BIPP	2009	Department of Biotechnology	• Loan projects • Collaborative R&D projects	Biotech	No	Product development needs of national importance	Early stage (Pre-Proof of concept) Late stage development	IP is with companies or entrepreneur. In case of collaborative partner, its on mutually agreed terms among the partners.	Long term projects

Business activities of firms

The previous section showed how the Indian pharmaceutical industry evolved from a nascent stage in 1970 to emerge as a leading supplier of generics in global world market. By 2005, when the TRIPs implementation took place, the Indian pharmaceutical firms were engaged in generics production for patent expired drugs, R&D for proprietary research and contract research & manufacturing businesses (Sampath, 2008).

With the change in patent regime in 2005, there were two key developments in the Indian pharmaceutical sector. Firstly, the sector witnessed R&D investments in research for new medicines through established firms and a handful of start-ups. Established firms substantially increased their R&D intensity and increased their patenting activity (Chowdhary, 2010; Gehl Sampath, 2006). In 2012, Ranbaxy launched India's first domestically developed new chemical entity, Synriam, indicated for malaria. In 2013, another Indian firm Zydus Cadila launched a new drug Saroglitazar (Lipaglyn), approved for the treatment of dyslipidaemia or hypertriglyceridemia in patients with type 2 diabetes (Balganesh et al., 2014). A study conducted in 2014 reported that the Indian pharmaceutical firms have developed an impressive pipeline of more than 120 new chemical entities (NCEs) with some molecules in Phase II and III of the approval process (Differding, 2014). The table below shows the sales revenues of top ten leading firms of India collated from various secondary sources.

Table 22: Top ten Indian pharmaceutical firms by sales revenues (Financial year 2015)

Company Name	Sales revenues (USD billion)*	Sales revenues (INR crores)
Sun Pharmaceutical Industries Ltd.	4.5	30,105.00
Dr. Reddy's Labs	2.38	15,297.40
Lupin	1.88	12,599.70
Cipla	1.73	11,620.00
Cadila Healthcare	1.29	8,656.00
Aurobindo Pharma	1.09	7,271.62
Glenmark Pharmaceuticals	0.99	6,650.22
GlaxoSmithKline Pharmaceuticals	0.52	3,486.25
Divi's Laboratories	0.47	3126.85
Abbot India Ltd	0.35	2,336.00

**Exchange rate using 1 USD=66.9 INR*

The second important development has been the extraordinary growth of the contract research and manufacturing business in India. Globally, leading pharmaceutical firms are witnessing a decrease in product approvals for new drugs by regulatory authorities, decline in research productivity, increase in R&D costs and significant profit erosion due to patent expiry of blockbuster drugs. The entry of cheap generics in the market has put immense pressure on globally large pharmaceutical firms to reduce costs and led to increase in outsourcing of research activities to cheaper destinations such as India and China. The need to cut down costs specifically in clinical development stage and explore various cost cutting initiatives has made offshoring and outsourcing a lucrative option (Antani and Gokhale, 2012; Sampath, 2008). With outsourcing now an important part of strategic model of large pharmaceutical firms such as Merck, Pfizer, GSK, AstraZeneca, Mayne, Wyeth the contract research organisation space in India has seen a big boom in the past few years (Sampath, 2008).

Indian firms have been quick to make use of these opportunities and develop capabilities in various stages of drug discovery and development. Local Indian firms conduct manufacturing, clinical trials and customised chemistry services for foreign firms and are entering into long term agreements with foreign firms (Sampath, 2008). The Indian CRO business can be broken down into key areas based on the drug development value chain in which they operate – a) outsourcing (including clinical trials) and b) contract manufacturing outsourcing. (Antani and Gokhale, 2012).

Contract research outsourcing: Companies engaged in contract research business can be segregated into two types based on the drug development value chain in which they operate: a) contract research organisations and b) clinical research organisations.

a) Contract research organisations (Chesbrough and Crowther)– These organisations are involved in providing research services during the drug discovery and preclinical stage. Some of the contract research organisations that provide integrated services from drug discovery process to preclinical stages are Syngene, GVK Biosciences (KPMG, 2014). The key services provided are disease study/target discovery, target validation, lead discovery, lead testing, lead optimization and in vivo, in vitro animal studies (KPMG, 2014). India leveraged its strong process chemistry skills acquired during the generics era to enter into the contract research business. Few companies like Dabur which had a drug discovery programme even

before the TRIPS, benefitted considerably from these developments and restructured its business to contract research organisation.

> *"We benefitted a lot because of our background and genesis, which was being a research arm of a drug discovery company. I think that has helped us differentiate ourselves from other CROs. We are more of a discovery partner to a lot of these companies than just pure CRO. [ ] In terms of business model, we are not just fee for service company. [ ] We are driving the clients' projects from discovery until IND enabling studies and there are milestone based payments." (Vice President, Dabur Research Foundation [44])*

The drug discovery and pre-clinical contract market alone is estimated at about USD 2 billion in the financial year 2014 with the industry reporting a CAGR of 31% in the period 2010-2014 (KPMG, 2014). In the clinical research market, there are large numbers of players, which operate as clinical research organisations and specialise in conducting clinical research from Phase I to Phase IV studies (Sampath, 2008). Facilitating factors for clinical trial industry include India's large population, huge infrastructure of hospitals, familiarity with regulatory process and an increasing population with lifestyle diseases (Antani and Gokhale, 2012).

b) Contract manufacturing outsourcing – This involves custom manufacturing of pharmaceutical ingredients and requires capital investments in facilities and long term assured supply contracts. Custom manufacturing activities include manufacture of bulk drugs, fine chemicals, custom chemicals, intermediates and protein based biopharmaceutical products. The factors which have played an important role in the development of the industry include existence of high number of USFDA and UK MHRA approved plants in India, low labour cost, and availability of skilled human resource (Antani and Gokhale, 2012).

5.2 Changes in the Indian ecosystem – Post TRIPS

The TRIPS brought about important changes in the system with changes at the macro and micro level. In the aftermath of implementation of product patent law, India put in place various policies to encourage innovation in universities and public research institutions and support R&D in private sector. The shift to a product patent regime posed a challenge for the Indian industry heavily dependent on generic drugs business. Moreover, the existence of process patent regime combined with underinvestment in R&D had also weakened innovation and research in the system for many decades. The amendment in patent law enthused the system and government put in more emphasis on science based research. Many types of initiatives have been implemented in the last decade. Preliminary evidences on the effectiveness of these programmes are mixed. Though many of these public initiatives have potential, they must overcome many challenges in order to be successful. This section draws on a combination of insights from primary research, patent data analysis and reinterpretation of secondary data available for the case companies to examine the effects of TRIPS regime on the research and innovative activities of the firms.

The section begins with brief description of the positive changes in the research environment in India post 2005. The second section uses count of patent applications filed by Indian companies to understand patent and innovative activities of Indian pharmaceutical firms in the background of a shift in appropriability regime. The third section provides available evidence on the significant hurdles in the system, which makes drug discovery and development a challenging exercise for firm.

5.2.1 TRIPS led changes – positive for innovation

The patent regime brought with it other enabling changes such as increased budgetary allocations for research, IP awareness programmes, and policies to link science with industry and other scientific community (Department of Science and Technology, 2013). The entities in the innovation system realise that the shift towards product patent regime is important to propel research and innovation. This coupled with laws to curtail incremental innovation such as Section 3D in Patents Amendment Act, shows the emphasis placed by government for enabling breakthrough innovations and reducing the scope for incremental innovations. The R&D sops offered to firms, introduction of new public initiatives and restructuring of old ones to suit current needs, endorses government's commitment towards steering innovation

in the right direction. The government policies aim to enhance funding for basic research, make available money for infrastructural work and encourage collaboration between key entities in the innovation. The policy initiatives are aimed not only to fund basic research but also nurture the near dormant innovation system.

On the positive side, the government has made sizeable investments in skills, competencies and capabilities to enable discovery of new drugs. Historically, the government has supported efforts to bring science and technology together and build national innovation system through the Science and Technology Policy 2003. The public focus is now in emphasising on innovation as reflected in the Science and Technology and Innovation Policy of 2013. One of the main aims of the policy is to create an environment for private sector participation in R&D and create a robust national innovation system (Science and Technology policy, 2013).

The important changes that took place in the Indian innovation system include increase in funding for research, increased efforts by the government agencies to improve IP awareness and infrastructure in universities and set up of different platforms for dissemination of research through various channels. Table 23 shows the summary of three most frequently mentioned categories in the interview data that represent the important changes that have taken place in the ecosystem.

Table 23: Top three frequently mentioned categories in the interview data

Important Issues	Representative 1st order informant centric terms and codes	Frequency
Increase in funding for research	"Various policy initiatives", " Increase in research grants", "Government funds has increased",	38%
Increase in IP awareness	"Establishment of IP cell and policies", "Facilitation of IP for universities", "Awareness about IP",	26%
Diffusion of research through various platforms	"Spinoffs", "incubators", "technology transfer board", "technology park", "biopark", "science park", "public private research institute"	36%

Increase in funding for research

India's R&D funding is currently under 1% of the GDP and is predominantly undertaken by the public sector (STI policy, 2013). In recent years, government has increased funding and state funded research institutes have been the biggest beneficiaries of the budgetary

allocations in research. Ostensibly for universities, funding has increased significantly for research grants and capacity building.

Public universities on the other hand are not funded directly for research by the government. Academic researchers seek grants for research from funding agencies such as Department of Biotechnology and Department of Science and Technology. There are also various scholarships and fellowships available for young scholars. Funds for conferences have increased and also the approval rate for the grants is also high (Professor, Jamia Hamdard [8]). Academics agree that the environment is now much more conducive for research.

Saurashtra University, which is funded by the state and the central government through University Grant Commission, has seen a considerable increase in R&D funding from 2001 onwards. The university has received funding from University Grant Commission as well as from Fund for Improvement of S&T Infrastructure (FIST) scheme of DST. As per the UGC rules, a university can avail different funding schemes in different stages based on the research output and milestone achieved at each stage. Saurashtra University has been able to utilise these opportunities to procure around INR 1.8 crores ($0.3 million) in the fourth stage. In addition, the university also received a grant of approximately INR 80 lakhs ($0.12 million) for investment in infrastructure (Professor, Saurashtra University [5]).

Despite the available money for research, the system faces considerable variations in research budgets and potential reduction whenever there is a change in government. There is also considerable discontent among the academics in the flow of funds across the academic institutions. Academics complain that funds are easily allocated to elite institutions while the other state universities feel the crunch in funds. Premier academic institutions like IITs are funded liberally for research and feel *lucky* in that aspect (Dean, IIT Delhi [11]). Other state universities feel left out in fund distribution and desire for a revised mechanism for distribution of government funds towards academic research.

> *"Finances are now available liberally and there is lot of money pumped in for research in India. […] But I personally feel that grants are not allocated fairly. We feel that universities in north get a better share and universities in south do not get a share of cake." (Professor, University of Mysore [1]).*

In addition, the government also extends R&D grants to firms through various policy initiatives that support university-corporate R&D spending projects, lab to industry

conversion, soft loans, and indigenous innovation. Such facilities have been availed by private sector R&D firms through various public initiative schemes.

> *"In terms of financial incentives, we have got new grants from the government to help us develop novel chemical entities; either we take them during the discovery, pre-clinical development or clinical development." (Chief Scientific Officer, Advinus [35])*

The increase in public research funding has also been accompanied by increase in R&D investments by the private sector. Thirty-seven Indian pharmaceutical firms have increased their R&D expenditure as a percentage of sales from an average of 1.39 per cent in 1992-1993 to 7.04 per cent in 2007-2008. The R&D expenditure for NCE research by 11 firms has increased from 3.14 % in 1996-1997 to 8.18% in 2007-2008 (Chowdhary, 2010). The use of internal funds constitutes the main source for research. Large pharmaceutical firms rely mainly on their generics businesses to fund new drug research programme. Small and medium sized firms explore the venture capital funding option to seek funds. In India, venture capital funds market is in nascent stages and SMEs face difficulties to attract funds for the next growth stages.

In addition, to focus on the sectoral development, Government had created National Institute of Pharmaceutical Education and Research (NIPER), an institute for pharmaceutical sciences, to impart quality education in pharmaceuticals and promote innovative and translational research (NIPER, 2014). In the recent 2015 budget, government has proposed setting up of new NIPERs in Maharashtra, Rajasthan and Chhattisgarh.

> *"NIPER is completely government funded. It comes under the Ministry of Chemicals and Fertilizers. In fact our maintenance, salaries for faculty and staff come primarily from central government." (Professor and Head, NIPER [6]).*

Additionally, an Institute of Science Education and Research (IISER) is proposed to be set up in the states of Nagaland and Orissa (KPMG, 2015).

Increase in IP awareness

An important issue plaguing the system is the lack of awareness of patenting and the benefits associated with it. Public research institutions particularly state led universities have floundered in their efforts to commercialise discoveries. The government has initiated key policy changes to enable public research institutes and universities to patent during the pursuit of research and development.

NRDC is an organisation set up by the Government of India to facilitate technology transfer. The organisation facilitates the commercialisation of technology or knowhow from public R&D institutions to the industry through formal arrangements. It also provides technical and financial assistance for filing of patent applications from universities, public research institutions and individual researchers (NRDC, 2016). These services are especially useful for universities where the academics need support in getting their inventions patented (Professor, University of Mysore [1]).

In the past few years, the role of NRDC has seen a shift in its role from being a mediator in technology transfer agreements to a facilitator for setting up IP policy framework in public universities and research institutes. It also conducts patent awareness programmes periodically among research scientists and faculty members on effective management of intellectual property and technology transfer.

> *"Each year, we conduct more than 10 or 12 workshops in various institutes to make the scientists aware of different laws and regulations. Usually in 90% of cases, patents are not filed by Indian academic researchers." (Manager, NRDC [25]).*

The lack of patent awareness is a big gap increasingly felt across by the policy managers of the government policies particularly in universities that lack the necessary set up. One of the objectives that BIRAC has is to increase patent awareness among public scientists to facilitate technology transfer of academic research.

> *"Most of our major public research institutes like CSIR have business with different companies which guide their scientists in one way or the other. However, in universities where a lot of innovation happens there is no awareness of IP. Scientists who are proactive in their research don't know*

what to do after that and where to go to seek help. [ ]. BIRAC has come forward now to help them to a great extent, but I think we really have to set up these technology transfer officers and IP officers across the country to help them." (Advisor, BIRAC [21])

The Ministry of Micro, Small & Medium Enterprises (MSME) is mandated with the task of facilitating infrastructural set up of IP cells in universities (Manager, NRDC [25]. There is an increased awareness among the universities regarding the importance of patenting and putting in place an IP cell. Despite the awareness campaigns, the setting up of a functional IP department is very much dependant on initiatives of the universities. IIT Delhi, one of the premier institutes of the country has a fully functional Foundation for Innovation and Technology Transfer (FITT) department, which manages all the intellectual property rights issue for the institute. FITT enables liasioning with the industry and facilitating technology transfer to the industry. Recently the policies of intellectual property rights were amended to reflect the changes taking place in the pharmaceutical sector (Dean, IIT Delhi [11]).

"In India, we were the first to have our own IPR policy this was somewhere in 1994- 95. After about 20 years in 2014, we have revised the policy. [….]. Even in the IIT system, we have not been patenting so much. It is a new phenomenon. We never looked at patenting seriously…mostly there have been research publications. So this transition is taking place." (Dean, IIT [11])

On the other hand, small size universities are increasing their efforts to raise awareness about patents. A professor in University of Pune states that one of the benefits of the TRIPS agreement has been the setting up of a patent department in the university.

'We got funds from CSIR for setting up an IP department in our university. However, it took a long time to get a suitable person to chair that position. I feel even now there are not many universities who have a formal IP policy' – (Professor, University of Pune [3])

The findings suggest that public initiatives are underway to set up technology transfer offices, enact patent and technology transfer policies in university set up and most importantly convince faculty on the benefits of patenting. The transition towards more patent awareness has started taking place in India however there is still a long way to go.

Diffusion of research through various platforms

Against this backdrop of changes, government has set up various channels to increase collaboration between science and industry and facilitate transfer of basic science into industry for commercial development. Within the pharmaceutical research domain, uptake of research in the technology transfer has been very low in the Indian setup. The government is enabling active interaction between academics, R&D institutions and industry by setting up science parks, technology incubation centres and public private research institutes.

The government is setting up biotech parks in different parts of the country to foster an environment for innovation, promote entrepreneurship and facilitate networking between industry and academia. Government has supported the setting up of these parks through various programmes such as the Science & Technology Entrepreneurship Park of DST. Table 24 lists a sample of few biotech parks recently set up or planned by the government for supporting pharmaceutical and biotech research. The list is a compilation of examples from primary research data and supplemented with other secondary sources such as press releases and website of Department of Biotechnology.

Table 24: List of operational and approved biotech parks in India

Fully operational	**Proposed**
Biotech park, Lucknow, Uttar Pradesh	Guwahati Biotech Park, Assam
Hyderabad BT Park, Hyderabad, Andhra Pradesh	Bangalore Biotech Park, Karnataka:
TICEL Bio Park, Chennai	KINFRA Biotech Park, Kerala
The Golden Jubilee Biotech Park for Women, Siruseri, Kanchipuram District, Tamilnadu	Bio Pharma-IT Park, Andharua, Bhubaneswar, Orissa
ICICI Knowledge Park, Hyderabad	Bhiwadi Biotech Park, Rajasthan.
Life Science Park, Visakhapatnam	Manesar Biotech Park, Gurgaon, Haryana.
Shapoorji Pallonji Biotech Park, Secunderabad	Pantnagar Biotech Park, Haldi, Uttaranchal.
Bio 360 , Life Science Park, Kerala	Peninsula Biotech Park, Goa.
International Biotech Park, Pune	Pharma Park, Vizag, Andhra Pradesh.
Genome Valley, Hyderabad	Sitapura Biotech Park, Jaipur, Rajasthan.
Mini life science parks at Kakinada, Anantapur and Guntur or Chittoor.	Solan Biotech Park, Himachal Pradesh.

Academics feel that biotech parks are an important way to stimulate innovation and facilitate academic industrial collaborations. A project for setting up a 50 acre science park in Haryana has been initiated by IIT Delhi. The park will focus on biotechnology and life science research and has research institutes like All India Institute of Medical Sciences in the vicinity. Research based companies are also setting up operations in this park. A proposed campus in Jhajjar is also being set up for research-based activities.

> *"The new campus is not going to be a teaching hub like IIT Delhi old campus. It will be more of an extension of IIT for research, development, skill development, industrial interface." (Dean, IIT Delhi [11])*

A biotech park set up in Noida in UP has good infrastructure, well equipped laboratories, instruments and common facilities such as animal house, green house and allows the firms in the park to use these facilities (Vice President, Piramal [33]). Some of the universities like University of Pune have set up a science and technology park to facilitate industrial collaborations with faculty. MOUs are signed between the park, university and industry (Professor, University of Pune [3]).

In order to increase outreach with the industry, few academic institutions such as NIPER and IIT Delhi have setup technology transfer offices to facilitate commercialisation of research and gain revenues (Professor, NIPER [7]). These offices commercialise academic research through a) technology transfer and licensing and b) spinoff companies (FITT, IIT Delhi [10]). Spinoffs are an effective way to capitalise on the expertise, research and entrepreneur spirit professors in the West. The seed funding, infrastructural support and facilitation from a technology transfer office promotes innovation (Senior Director, SRI International [49]). In similar lines, NIPER has set up an incubation centre to facilitate to promote entrepreneurship and insulate start-ups at early stages (Professor and Head, NIPER [6]). IIT Delhi has a technology business incubator unit active since 2000 that has already incubated two drug discovery companies– Lead Invent and Novo Informatics (FITT, IIT Delhi [10]). The company Novo Informatics was set up by IIT students as a spinoff from the SCFBio (Super Computing Facility for Bioinformatics & Computational Biology) of IIT Delhi (Director, Novo Informatics [43]). Novo Informatics uses a suite of bioinformatics tool for predictive genomics and the technology was transferred from IIT Delhi (FITT, IIT Delhi [10]). The company provides services to pharmaceutical companies and also has an in-house drug discovery programme.

"The experience has been quite nice. Being a part of IIT Delhi we got so much support in the form of facilities such as space, electricity, internet, access to labs, faculty support. Apart from the direct benefits, the indirect benefit is that when you introduce your company to clients the reputation of IIT Delhi helps in getting their attention." (Director, Novo Informatics [43])

In a similar manner, Saurashtra University has set up a Facility for Preservation of Molecular Diversity. Under this project, professors have contributed their molecules under study to make a repository. The facility employs postgraduate student to use various bioinformatics and tools available in the university to screen these compounds for potential pharmacological activity (Professor, Saurashtra University [5]).

Another notable venture worth mentioning is the Institute of Life Sciences, a public private partnership set up in 2007 to serve as a centre for research in the life sciences. The institute is a result of collaborative effort by Government of Andhra Pradesh, University of Hyderabad and Dr. Reddy's Laboratories Limited in 2004. Besides providing research services to the industry, the institute also participates in research projects for cancer, cardiovascular, metabolic and infectious diseases. The institute has recently been renamed as Dr. Reddy's Institute of Life Sciences also referred as DRILS (Professor, DRILS [17]).

5.2.2 Patterns of innovation through patent data analysis

The TRIPS led changes in the institutional environment have strengthened the patent protection and encouraged innovation in the pharmaceutical sector. The setting up of the new drug discovery programmes and increase in R&D intensity of firms shows the changes in the system were effective to spur innovation in the pharmaceutical sector. This section traces the innovative performance of the Indian pharmaceutical industry through trends in patent data of case companies and using data from company reports to demonstrate how Indian pharmaceutical firms have shown technological progression in different appropriability regimes.

The use of patent counts as a measure of innovative output has been used in various studies and has been upheld to be a relevant indicator of the technological activities undertaken by a firm (Acs et al., 2002; Griliches, 1990; Pavitt, 1985). Intellectual property rights (IPR) especially patents are the most evident and formal means of protection among all the other prevalent forms of appropriability (Hurmelinna and Puumalainen, 2005) specifically in the

pharmaceutical and biotech industry (Khilji et al., 2006; Mansfield, 1986). The objective of patent analysis in this dissertation is to undertake a count of unique, active, priority patent applications by different patent types.

New patent applications filed by the nine pharmaceutical case companies climbed from nearly 176 during the period (1995-2004) to 609 during the period (2005-2014). Figure 22 shows the patenting trend of nine pharmaceutical companies for the time period 1995 to 2014.

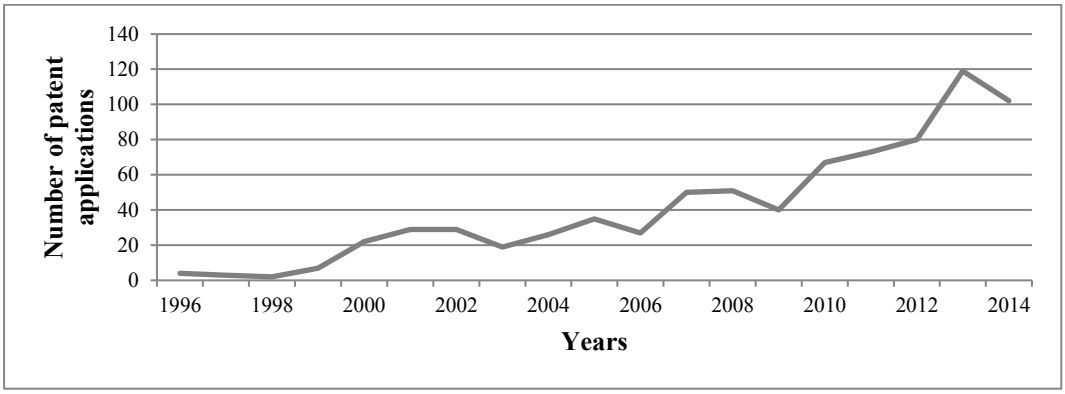


Figure 22: Growth of patent applications filed by year of application date 1995-2014

During the late 1990s, the number of active patent applications remained at a very low level less than 10 each year. From 2000 to 2005, the number of patent applications filed ranged between 22 and 35. Post 2006 to 2010, onwards there is a gradual increase in the patent applications from a couple of dozens in the early years of that decade to about seventy applications in 2010. This phenomenon appears to have moved to a next level at the turn of the decade during the years 2012-2014. These years mark a steep increase from about 80 annual patent applications to over 100 new patent applications. Overall, if one looks at the historical data since 1994, there is a steady pattern of growth in patenting with an acceleration post 2005. The positive pattern in growth as seen in patent data can be related to the change in patent regime, increased R&D spending by pharmaceutical companies and increased complexity of scientific and technological development (Chaudhuri, 2007). Post 2005, most of the established companies increased their R&D spending and expanded their R&D activities to begin new drug research unit.

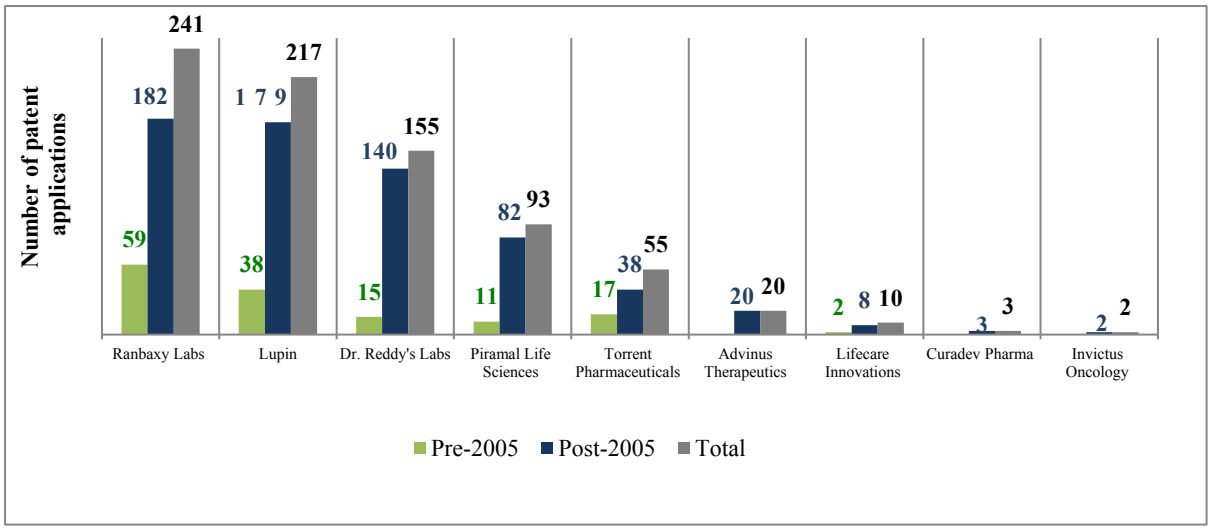


Figure 23: Number of patent applications filed by firms in two time periods

Figure 23 shows the total number of patent applications filed by the nine case companies in pre and post-2005 period. The figure shows that established companies such as Ranbaxy, Lupin, Dr. Reddy's and Piramal largely contributed to the first surge in patents post 2005. Though Torrent initiated its new drug research program in 1998, the patenting activity developed gradually and is substantially lower than other case companies. The change in patent system has also encouraged innovation through new small-scale research based companies. The number of patent applications from SMEs is lesser in number and may increase in the coming years.

Ranbaxy, Dr. Reddy's and Piramal were the forerunners to initiate new drug research in the Indian pharmaceutical sector. Until the 1990s, the Indian pharmaceutical companies had focused their research efforts on developing commercially viable processes for formulation of active pharmaceutical ingredients and generic drugs. The signing of TRIPS agreement in 1995 and implementation of product patent system from January 1, 2005 (Sudip Chaudhuri, 2005) implied that companies needed to take strategic action to realign their research efforts in the wake of impending product patent regime. The strong generics business provided the capital required for research and development of novel drugs. The established firms geared up to advance their technological capabilities and leverage the core technology strengths in chemistry to initiate research for discovery and development of new medicines. In parallel to this, Indian government initiated new drug research programs and increased budget for R&D to make available grants for new drug research.

The patent and company data indicate three major developments: (a) established companies are realigning their strategy and initiating research for novel drugs, (b) there is emergence of research based small companies for pharmaceutical research, and (c) companies are increasing use of patents to protect their innovation and capture returns on investment in R&D. These changes are examined through the firm characteristics of established and SMEs.

Firm characteristics and influence of appropriability regime

The progression in the technological capability of the firms is reflected in the decreasing share of method patents over time and increase in the number of secondary and basic product patent applications.

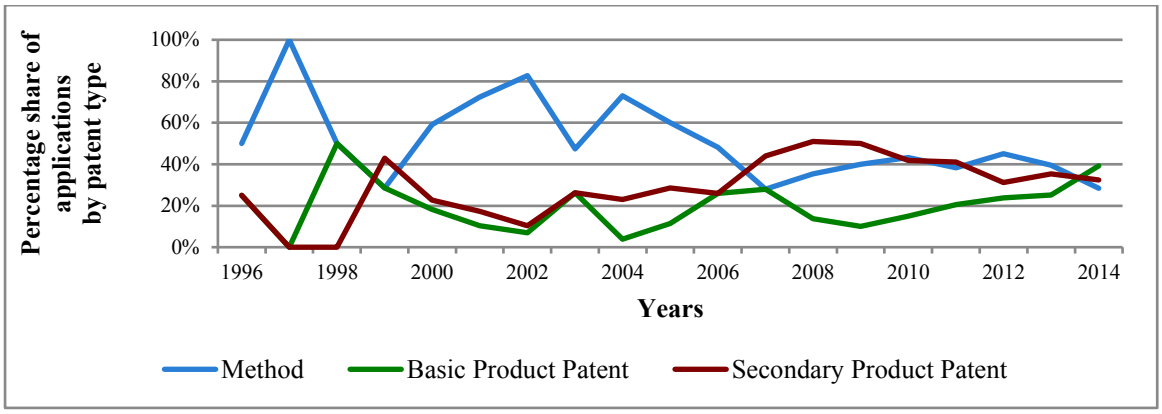


Figure 24: Type of patent filed by established companies during the period 1995-2014

The period 1995 to 2004 marked the dominance of generic drugs business, which led to increased R&D efforts by pharmaceutical companies to develop non-infringing processes. This is visible from the number of method patents filed during this period. Method patents dominated from 1995 to 2004 with an average share of 50.0% in 1995 but showed a considerable decline during the product patent regime and accounted for only 28.4% of patents applications in 2014. On the other hand, the share of product patents, which includes both basic and secondary patent applications, rose from 50.0% in 1995 to 71.6% in 2014. Secondary patents gained a prominent share of 26.3% in 2003 and peaked to around 50.0% in 2008-09. It then oscillated in the range of 42%-32.4% between 2010 and 2014. Basic patent applications for new drugs increased from almost 11.4% in 2005 to 39.2% in 2014 with a slight downward trend experienced in 2008-2009. In spite of the increase in basic patent applications, the share of basic patents is lesser than method patents and secondary patents.

The pattern observed in the decline of process patents and rise of product patents over time reflects where the inventions have been vivid in the past years. It also indicates the increasing technological capabilities of the Indian pharmaceutical firms over a period. In the initial years, process patents dominated the research efforts of the companies. The increase in capabilities of the firms resulted in secondary patents applications for new combinations, new formulations, and uses of already patented drugs. With the stepping up of R&D efforts to discover and develop novel drugs, basic patent applications started surfacing from 1997 onwards.

The two major points highlighted are- a) the technological capability of firms have increased over time, b) there is evidence in the patent data to link patent regime with the nature of innovation taking place in Indian pharmaceutical companies. In this way, patent data is a good reflector of research and innovation activities of firms. In order to further understand the happenings during these years, the below section analyses patenting data of established and SMEs.

Innovative behaviour of established firms

Figure *25* shows the changing focus of established firms in the two appropriability regimes.

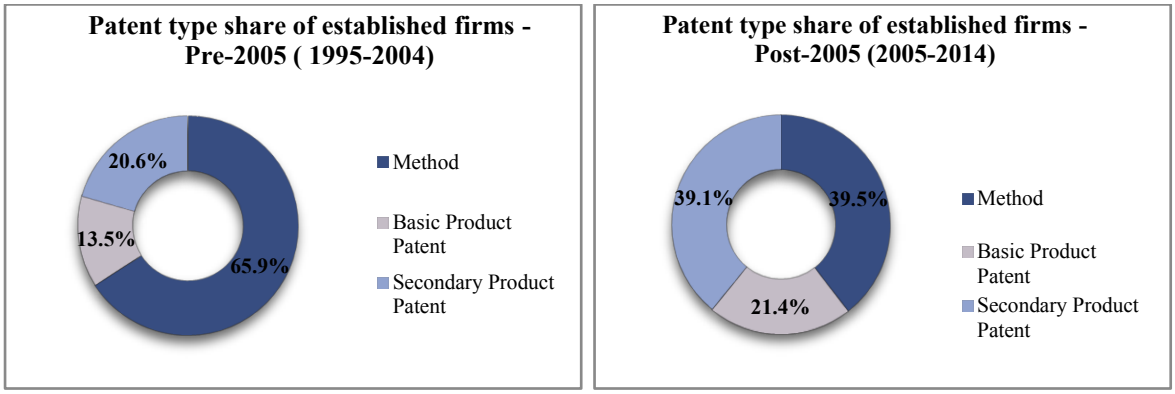


Figure 25: Patent share filed by established companies in two time periods

If one looks at the patterns of the established firms, method patents, which constituted ~66% of the patent applications in pre-2005 period, declined to 39.1% post 2005. Product patents, which include both basic and secondary patents, increased from a share of 34.1% (Basic – 20.6% and Secondary patents – 13.5%) in 1995-2004 to 60.5% (Basic – 21.4% and Secondary patents – 39.1%) during the period 2005 to 2014. During the period 1995-2014, the share of secondary patents nearly doubled while the share of basic patents increased by

1.6 times that shows the increase in R&D efforts of firms for product innovation. It is important to understand these patenting trends against the technological developments that took place in these companies. The analyses of firm profiles of established firms show that India's leading firms have capabilities to develop alternative forms, new combinations or formulations based on new drug delivery systems of an existing drug. These incremental product innovations allowed the firms to extend their product lines, gain a quicker entry into the market through the 505b regulatory route and enabled three years of exclusive market access if proved to be an entirely new version of drug or new use of a drug (Hunt, 2002). The established companies subsequently entered into new drug research business. Figure 26 shows the number of patent applications filed by established firms by patent type during the two time periods.

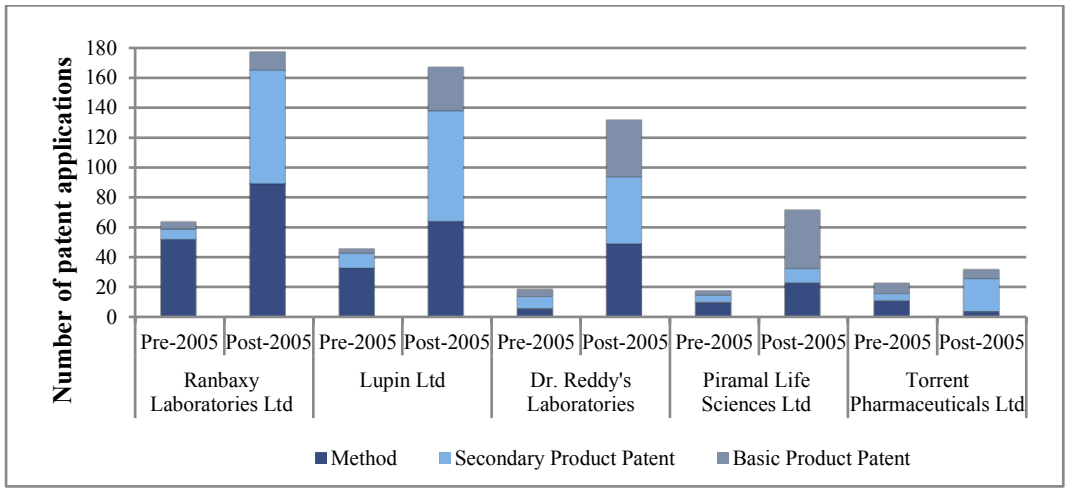


Figure 26: Number of patents filed by established companies in different time periods

Of the established case companies, Ranbaxy with 83 patents and Lupin with 84 patents have filed the highest number of secondary patents from 1995-2014. The biggest contributions to the basic patents are from established firms such as Dr. Reddy's, Lupin and Piramal. Post 2005, Lupin has filed 74 secondary patents and 29 basic patents. The high number of secondary patents can be attributed to the strong capabilities, which Lupin has in advanced drug delivery systems and more complex formulations. Lupin started research in new drugs in 2001 and focused its new drug research efforts in the areas of tuberculosis, psoriasis and migraine. The company has six NCEs in pipeline and has successfully discovered new molecules for tuberculosis and psoriasis.

Ranbaxy has filed 76 secondary patents and 12 basic patents in the period 2005 to 2014, which demonstrates its technical strengths in value added generics through differentiated

formulations. Ranbaxy was one of the pioneer companies to start new drug research in the early 1990s. Interestingly, though the number of patents filed for basic patents is relatively less but Ranbaxy is the first Indian company to develop and launch a NCE for malaria in 2012. The research and development efforts of the company however took a back seat when Ranbaxy started facing serious quality problems with the US regulatory authority Food and Drug Administration (USFDA). In 2008, Ranbaxy sold its majority stake to Japanese based pharmaceutical company Daiichi, which continued the new drug research work, initiated in Ranbaxy. In April 2015, Indian pharmaceutical company Sun Pharmaceutical Industries completely acquired Ranbaxy from Daicchi.

Post 2005, Dr. Reddy's has filed 49 method patents, 45 secondary patents and 38 product patents. The patenting patterns of Dr. Reddy's reflect the wider technology capabilities and strengths in all areas of innovation. The company started its new drug research in the early 1990s and is one of the first Indian companies to develop and out-license its NCEs to a foreign firm at clinical development stage. However, Dr. Reddy's witnessed setbacks with its new drug discovery program with many molecules failing at the clinical trial stage. In 2009, as part of strategic restructuring initiative, Dr. Reddy's transferred all of its discovery-related assets to Aurigene and has strengthened its infrastructure and technical capabilities. Some of the recent out-licensing deals of Aurigene (subsidiary of Dr. Reddy's Laboratories) are with Curis, Orion Pharma and Pierre Fabre for the clinical development of its new drug molecules. The resilience of the company to sustain its drug discovery efforts is reflected in the high number of secondary and basic patents it has filed and the number of collaborative deals it has struck with foreign firms for its NCE molecules in 2015.

Torrent filed 22 secondary patents and 6 basic patents in the period 2005-2014. Torrent, an established generics player, has developed proprietary technologies in drug delivery systems, which allowed the company to create new dosage forms and formulations of existing drugs and value added generics. The company is a leading generics player in the cardiovascular segment and undertakes new drug research in the area of cardio metabolic risks. Piramal started its new drug program in early 2000 and is one of the remarkable companies that have demonstrated successful capabilities in new product innovations. Post 2005, Piramal has filed 39 product patents and 10 secondary patents. Piramal is credited with building a strong pipeline of new drugs reflected in the high number basic patent applications. In spite of its

ability to build a strong pipeline of new drugs in a short period, Piramal took the decision to exit from new drug research in September 2014.

The examination of patenting patterns in this way tells the story of enhancement of technological capabilities in established Indian pharmaceutical companies. The setbacks faced by Dr. Reddy's and the closure of Piramal and Ranbaxy reflect the difficult nature of technology involved in discovering and developing new drugs. Dr. Reddy's faced initial losses when its initial pipeline of NCE compounds failed to progress through the clinical development stages. The long gestation period required to sustain drug discovery business and high risk of the business led the company to scale back its operations and move towards contract research business. The company now operates its drug discovery business through Aurigene, a subsidiary company that is primarily a contract research firm but also carries out proprietary drug discovery projects. Piramal also found it difficult to sustain drug discovery efforts due to escalating R&D costs, constraining clinical trial regulations that made the company shifts its clinical trials to offshore locations such as Singapore resulting in further increase of R&D costs. The unwillingness of the management to keep huge capital invested in a high-risk project led to shutting down of the drug discovery unit. Ranbaxy had to sell its business as it got embroiled in USFDA related controversies and hence exited the pharmaceutical space in 2014. Despite the challenges, the established companies have shown successful commercialization potential in each of the appropriability regimes. Companies initiated the generic drugs business in the early 1970s and forayed into the high price low risk business of differentiated products during the 1990s that enabled them to gain higher market share in advanced markets (Hunt, 2002). The shift to product patent regime propelled firms to venture into new drug research.

Innovative behaviour of small and medium enterprises (SMEs)

While the established firms were busy etching out strategies to cope up with the changes in the appropriability environment, the pharmaceutical sector also saw the emergence of research-based small companies for new drug research. Curadev, which started research operations in 2010, has five molecules in pipeline. The therapeutic focus of the company is in cancer and inflammation. The company has filed two basic product patents and one secondary product patent till now. Another start-up venture, Invictus Oncology established in 2011 by Dr. Shiladitya Sengupta, who along with his team, is credited with developing a technology to help in cancer treatment at Harvard-MIT division of the Health Sciences and

Technology in Boston. Invictus Oncology has in-licensed the technology to formulate a modified Cisplatin, an effective but toxic drug. The novel platinum-based supramolecular therapeutic IO-125 of the company is in late stages of pre-clinical development for treatment of triple-negative breast cancer. The company has filed two secondary patent applications. Advinus Therapeutics, a drug discovery company started in 2005 focuses in the areas of metabolic diseases, inflammatory diseases, pain/degenerative diseases, leishmaniasis and malaria for the discovery of novel therapies. The company has a pipeline of two Phase II compounds and other compounds at different stages of drug discovery. Advinus has filed 20 basic product patents during the period 2005-2014. Lifecare Innovations is a noteworthy SME specialized in development and manufacture of new formulations of existing drugs using array of novel drug delivery systems (NDDS) and involved in the research of novel drugs. The company has commercialized five liposomal drugs and a number of other drugs are at different stages of development and clinical trials. The company has filed in all four method patents and six secondary patents till 2014.

These are important takeaways as they reflect the technological progress made by the Indian pharmaceutical firms to innovate. Established firms have successfully made the shift from process-based innovation and incremental innovations to the radical new drug innovation. SMEs, most of which were founded by scientists with drug discovery experience in foreign firms, are exploring new technological pathways to discover new therapies for chronic diseases. Indian firms are pursuing a mix of strategies between these options to innovate. The change in appropriability regime in the Indian pharmaceutical sector reinforces the notion that a change in appropriability regime not only stimulates innovation but also affects the nature of the innovation process.

Patenting strategy trends: The rise of international applications

The number of international patent application signifies the strategic intention of companies to go global with their drug discovery. It is hence important to look at the trend of patents filed at different offices. Figure 27 shows that over the years, there has been a steady decline in the filing of patent applications in Indian patent office and increasing preference for filing international applications more predominantly through the PCT route. The patent filing trend in the three patent offices reveals that till 2010, Indian patent office was the preferred patent office followed by filings in PCT and US patent offices. Post 2010, the number of patent applications filed through PCT applications rose significantly from 43 to around 100 in 2014.

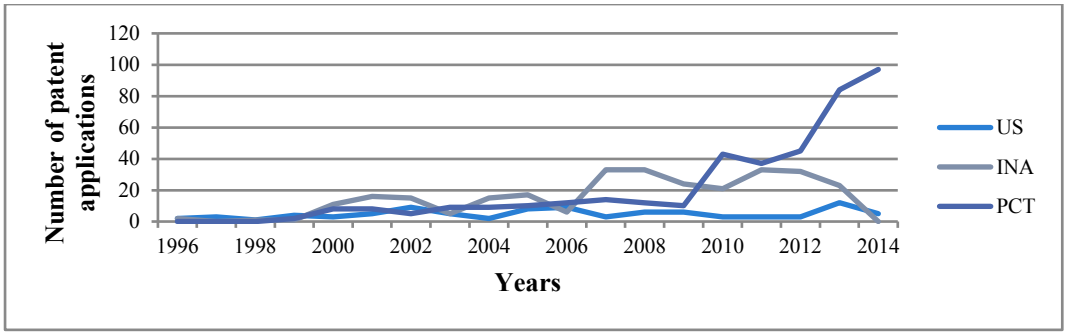


Figure 27: Total patents filed in key patent offices by year of filing

India became a signatory to the Patent Cooperation Treaty (PCT) as of December 7, 1998 which offers the convenience of filing international patent applications (Mueller, 2007). The advantages offered by PCT applications are the benefits of uniform formality requirements, optional value added international search report and written opinion provided by the PCT leading to cost and time savings (WIPO, 2013). Interestingly, in spite of the multifold advantages and ability to file patents through the PCT route, the preference for PCT office became apparent only after 2009. This merits a detailed look at the data and further research about the type of patent applications and patent offices used to file these patent applications.

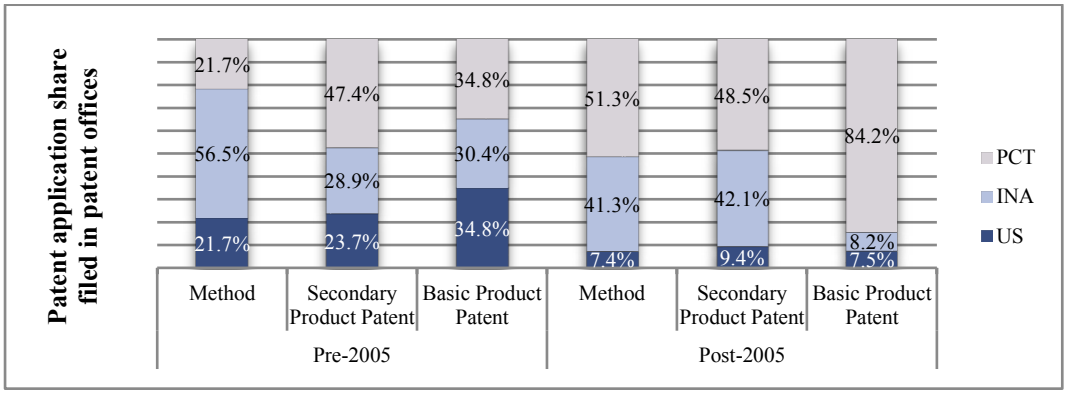


Figure 28: Share of patent type filed by established companies in different patent offices

A closer examination of Figure 28 reveals that in the pre-2005 era (1995-2004), 57% of method patents were filed in the Indian patent office. Post-2005, the share decreased to around 41%. Figure 28 indicates that the share of secondary patents increased considerably in the two time periods. Indian companies have advanced their research from the manufacture of simple generic formulations to undertake research for generics with new drug delivery systems and more complex formulations. The increase in the number of secondary patents reflects the upscale of innovative activity among the established firms to move from process-based research to incremental innovations, however, it had minimal effect on the preference

of patent office used. The number of basic patents filed was very less from the period 1995-2004 which is no surprise, as new drug research did not take off in most of the companies until early 2000s. Of the 23 basic patents filed during this period the share of the patent offices was somehow equal. However, post 2005, 84% of the basic patents were filed using the PCT route.

The current period (2005-2014) shows approximately 50% of the method and secondary patents and nearly 84% of the basic patents were PCT applications. This suggests that there is a link between *value* of innovation to the *patent office* chosen for filing. While the *value* of innovation can be tied to the choice of *patent office*, the vice versa is also true. Patent applications filed in international offices through US and PCT route tend to increase patent *value* useful in out-licensing deals and indicates their strategic intent to exploit their high value innovations internationally (Breitzman and Mogee, 2002).

The use of PCT and US offices allow expansion to newer countries and provides opportunities for firms to commercially exploit the value added generics (incremental drugs) market. The established Indian pharmaceutical companies started taking the export route in the 1980s, which expanded rapidly in the mid-1990s. In the 2000s, the focus market of the larger Indian companies was US and other regulated markets with US alone making up 14.2% of India's pharmaceutical exports in 2007 (Chaudhuri, 2007). This is reflected in the increasing use of US patent office for filing patent applications pre-2005 and the use of PCT office post-2005.

The factors that can partly explain the trend in the usage of international offices for filing patent applications are firstly, PCT applications facilitate an efficient way to file patents in different countries and increase territorial presence. Secondly, the increasing use of international offices suggests an increase in the value of innovation and increased confidence of the Indian pharmaceutical companies to patent inventions at global level. Finally, international applications suggest that companies use this route to increase their value of patents and make it commercially attractive to out-license inventions. In this way, the patent filings in international offices serve as a good indicator to assess the value of patents and also suggestive of the strategic direction taken by the companies.

5.2.3 Challenges in the innovation system for new drug discovery research

The changes in the ecosystem after TRIPS and the evidence from patent data provide perspective of the positive changes happening at the macro level and firm level. However, in recent years the Indian pharmaceutical market has witnessed slowdown in growth as a consequence of constraining policies and regulations resulting in erosion of profit margins. The government is using various measures to control pricing and regulate the quality of medicines for public health benefits. The recent implementation of the National Pharmaceutical Pricing Policy 2012 has led to stringent price controls and reduced profit margins (PharmaSummit, 2013). In parallel, the Indian pharmaceutical companies also face regulatory challenges from US FDA and other regulators for compliance related to good manufacturing practices (KPMG, 2015). In addition, the stringent demands to show safety and efficacy in new medicines and changing regulations related to clinical trials are not in favour of industry. The downward trend in the global pharmaceutical industry and cuts in R&D expenditures of global firms has also significantly affected the revenues of the Indian pharmaceutical industry increasingly dependent on the western pharmaceutical companies for contract research business. All these factors are cumulatively leading to reduced revenues and shrinkage in R&D investments by Indian pharmaceutical firms (KPMG, 2015).

Primary research data with key stakeholders in the pharmaceutical sector enables to highlight three main constraining factors in the institutional setup that affect the advancement of research for new medicines: a*)* bureaucracy and funding issues b) poor implementation and monitoring and c) constraining regulations related to clinical trials.

a) Bureaucracy and funding issues: As the industry struggles to cope up with the changes in the macro environment, an increasing concern among both the established and SMEs is to ensure continuous flow of funds for drug research. The government-initiated schemes have been started with the assumption that profit-maximizing firms invest less in the risk laden R&D process. The looming risk of failure of progression of a drug compound to the successive phases of research has made government come up with these initiatives to support private sector in their R&D exercise. However, these initiatives suffer from three grave problems such as *bureaucracy, fluctuations* in R&D budget and *misallocation of funds.*

A major point of discontent among the industry and academics scientists is the degree of bureaucracy prevailing in the system. Respondents are frustrated with the slow, inefficient

processes that prevail in the public departments and deliver poor services. The dependency on extensive paper work and elaborate processes undermines the positivity of these public schemes. Industry professionals say that a simple grant can take up to one to one and half years. This becomes very difficult especially for SMEs if they have to rely on government funds as a funding source (Chief Scientific Officer, Curadev [26]). An academic professor in a leading university of India laments that there is a research proposal, which has been approved by ICMR in 2013 but the money has not been released by Ministry of Health, leading to delay in release of payments to principal investigators (Professor, Jawaharlal Nehru University [12]).

On the other hand, a public official running important schemes feels frustrated in not able to move the complicated bureaucratic machinery forward.

> *"It takes six months to a year for a research proposal to be approved by the committee and get funds (DPRP). The committee meets twice a year, if a project proposal comes for approval after the last meeting took place then this project will be sitting idle and it will get some reviewer's comments only after six months. The review committee will always advise some changes then the ball goes to the institution or the industry because they have to revise and resubmit the proposal. Normally they do not take much time you know they submit in weeks or months and then it comes back. Once everything is done, it will take another three months to sanction the approval. So in DST there are two wheels, two wheels before this cart will move - one wheel what we call the programme division where we are sitting, we are interfacing with the scientist and at the back we have got finance division which does not go into the field and does not interact with other things, they only see the papers. Very often they ask some queries which is passed on to the concerned department and then they would reply to the queries." (Advisor, Department of Science and Technology [20])*

The bureaucracy tends to prolong all matters related to government departments. The process of ordering an instrument in a government research institute takes around a year. It has to pass through a technical bid and a financial bid (Professor, All India Institute of Medical Sciences, [13]). A public research scientist points out that there is a need to centralise the funding of instruments and other infrastructure so as to benefit the entire scientific

community and reduce mismanagement of resources (Scientist, OSDD [22]). There are certain channels, which are redundant. Red tapism is a major barrier and there is a need to revamp the whole system and remove the bureaucratic constraints.

> *"Taking official permission is one thing, going through people who have no knowledge of what science is 'frustrating'. If I have to buy a small machine of five lakhs or ten lakhs it will take me one year to get that. Even if I have to get consumable items, it will take me six months, so my work will be stopped. I have worked in US and UK and there people will not let you wait because you do not have this particular chemical or a particular reagent or instrument." (Professor, All India Institute of Medical Sciences [13])*

There is a consensus among industry professionals and academics that the bureaucracy in the government departments defeats the objectives and there is an urgent need to streamline the process.

> *"People talk a lot, there are good intentions all around, but sometimes the vision of somebody at the top is not translated by the bureaucratic situations." (Scientist , CSO Thinq Pharma [50])*

In recent years, there has been a change in the disbursement of funds from central funding to project based funding that limits the funds available for research and adds to the woes of the researcher. As one principal investigator of a project says:

> *"If you are working in a project and are funded then you have funds available for research. However, if you are working in a project mandated by the institute and if the project has not gone through the planning commission then there is a fund crunch. We are facing this problem as the funds this year have drastically dropped as we have moved from centralised budgeting of the institute to project based mode. This means that the institutes will now get money as per the projects they have. The problem is if the main lab for the project is a biology lab then they get the funds but we chemists who are supporting the project do not get funding. The other concern is the issue of fluctuating funds for R&D. Till 2013, the funding was very good but there was a drastic drop, which makes it very difficult to sustain funds for research." (Scientist, Central Drug Research Institute [16])*

Another issue that severely affects the regular flow of funds is the slowdown in enthusiasm to sustain a programme after few years of inception. Public initiatives are introduced with fanfare and substantial budget money is allocated at the initial stages, but after some years, the initiatives lose their shine.

> *"There was a big talk and large budget was given […] what happened to that? The earlier director general of CSIR suddenly came out with some healthy idea called Open Source Drug Discovery and pumped in huge amount of money, now after five years what has happened? Before that there was a project called New Millennium Indian Technology Leadership Initiative, very good initiative, some good potential candidates came out of that. Now it is in totally different form and not in the same spirit as it was created." (Professor, University of Pune [3])*

On similar lines, an industry professional states that the tendency of the government is to introduce new institutes or new universities instead of ramping up the already existing resources (Senior Management, Invictus Oncology [40]). The propensity to keep shifting the focus on specific disease areas is also not helping either. If a particular policy focuses on tuberculosis then that steers the research area of the scientists in that disease area. After some time if the focus of the government changes to malaria the researchers change the focus of their research to get funds accordingly (Professor, Jamia Hamdard [8]).

The presence of a clique also has an influence on the allocation of research funds. The objectivity and transparency in process of fund allocation is severely lacking and such a funding process limits the funds available for research (Professor, Jawaharlal Nehru University [12]).

> *"I was trying to do something with the government but I realised that if you are a stranger to the system and if you are not blessed by some influential people, your proposal can get rejected and go to somebody and get funded from a very different angle." (Vice President, Lupin [36])*

b) Poor implementation and monitoring of government led initiatives- In a recent press interview of RBI governor of India, when asked to comment on three things most needed to change to make a difference to the Indian economy, he replied:

"Implementation, implementation and implementation." (RBI Governor, Press Interview Jan 20, 2015).

Academics and industry professional point out that the charm of these public initiatives fades when the process of implementation starts. There are several weaknesses in the process of implementation such as delay in project approvals and disbursement of funds, irregular review meetings, lack of transparency, problems in quality of reviewers and quality of outcome assessment.

Industry and academics believe that there ought to be more competent experts experienced in different aspects of drug discovery research to be part of the review committee. Most of the scientists in the committee lack exposure to the drug discovery process, which in turn affects the robust assessment of the project. This also has an important bearing on the type of projects funded under a programme. Projects of dubious scientific merit get funded while scientifically good project proposals get rejected.

The project evaluation is loosely based on the feedback of review committee meetings, which are not held in a scheduled manner. There is a lack of monitoring the project progress through setting targets and evaluation of outcomes. The lack of thoroughness in the evaluation process has made these programmes as funding programmes where the scientists can get away with meagre deliverables.

"At the ground level a lot of distortion happens in project implementation. When we write grants we write lots of things, that the project promises to do but we end up producing two to four papers and some data and that is the end of it. May be one in 10 or 20 projects is good and that is a major weakness of these initiatives." (Professor, Jawaharlal Nehru University [12])

The stakeholders feel that there is a need for a comprehensive evaluation mechanism as part of the programme. There is a need for an external monitoring body that evaluates the effectiveness of such programmes.

A lot of these initiatives, which have been started, are left on the person heading the project. Some initiatives are doing much better than others. Example C-Camp in Bangalore is supporting a lot of projects and doing very

well. But there are no checks on programmes that are not doing well." (Senior Management, Invictus Oncology [40])

Evidence from primary data suggests that these public initiatives suffer from a host of problems in terms of project acceptance, implementation and evaluation process. Implementation is critical to the success of any public initiative programme and there is a need for good governance to optimize the implementation process and an evaluation mechanism to measure if the programme has achieved its objectives.

c) Constraining regulations related to clinical trials – Another challenge which pharmaceutical firms face is the constraining regulations with respect to clinical research. The period after 1990 has seen the rise of clinical trial industry in India. Cost containment pressure on global pharmaceutical firms coupled with conducive factors such as large patient pool in India, highly skilled investigators, diverse genetic pool and ease of recruiting has provided a big boost to the clinical trial industry in India (Maiti and Raghavendra, 2007). However, a series of unethical cases and illegal clinical trials have come to limelight and has fuelled concerns over the efficacy of legislations surrounding the clinical trials (Maiti and Raghavendra, 2007).

Some of the discrepancies include falsified data, noncompliance of GCP guidelines and clinical trials without approval of Drugs Controller General of India (DCGI)[14]. The unethical practices in clinical trials, practices related to payment to kin in case of adverse events and other malpractices led to government bringing in stricter vigilance and regulations, policies to monitor the clinical trial process (PharmaSummit, 2013). The new clinical trial regulations are related to i) reporting of serious adverse events, ii) conditions to be fulfilled by sponsor to conduct clinical trial in India iii) audio visual recording of informed consent process iv) expert committees to review serious adverse events v) specific provisions related to compensation ineffectiveness and placebo controlled trials and vi) Accreditation Standards

[14] Drugs Controller General of India (DCGI) is equivalent to the US Food and Drug Administration USFDA (2014) Novel New Drugs 2013 Summary. In: Cder CfDEaR (ed). and European Medicines Agency (EMEA). The DCGI is the official governing body responsible for all pharmaceutical research and regulatory issues in India described in the Drugs and Cosmetics Rules, 2005 (DCR) Chawan VS, Gawand KV and Phatak AM (2015) Impact of new regulations on clinical trials in India. *International Journal of Clinical Trials* 2(3): 56-58.

for Clinical Trials for Ethics Committee, Investigator and Clinical Trials (Chawan et al., 2015).

The barriers to clinical trials occur at two levels. At the level of regulatory authorities, there has been considerable delays in clinical trial approvals, which is not only affecting the clinical research outsourcing industry but also the pharmaceutical companies engaged in the research of new therapies (PharmaSummit, 2013). It takes around six months to one year to get a clinical trial approval in India whereas it takes only a month to get approval in US, Australia or Canada (Senior Vice President, NCE Research, Piramal [31]).

The new regulations have introduced many more checks in place, which are leading to numerous bureaucratic obstacles. In US, the clinical trial can be started anytime after a month of approval date without the need for any further meetings. But in India, even after the approval, there will be one or two meetings, which take place in a span of 3-4 months only after which work in clinical trials can be initiated. The clinical trial approval process is a multistep and a delayed one, which leads to loss of valuable time for a company engaged in drug development.

The other problem that companies have started encountering after a series of media leaks on unethical practices in clinical trials is the large number of rejections from regulatory authority in India. This has an unfavourable effect on genuine clinical trials. Most of the times, there is lack of transparency for the basis for rejections. Denials are very subjective for which no particular explanation is given by the government authorities. Respondents have cited that such bureaucratic delays are also encountered in the approvals to conduct studies on large animals that require permission from the Central Ethics Committee and the process is not well organised (Professor, Jamia Hamdard [8]).

> *"There is a downward trend in the CRO business for clinical trials partly due to the government of India policy. Animal activism is high and for clinical research, the awareness among Indian public is very narrow [...] government thinks they are using Indian people as guinea pigs. This is very unfortunate and has been propagated by the media and the activists in a very different light. Now even the Drug Controller General of India is not giving licenses to do the clinical research in India specially Phase 1 and Phase 2*

which is creating lots of problems for drug discovery." (Retd. President, Dr. Reddy's [28])

A second level of barrier arises when these regulatory checks are translated to conduct clinical trials on site. In order to prevent the safety of the participants, one of the measures which government has introduced is the mandatory use of audio-video (A-V) recording of all the study subjects for their consent into clinical trials. AV recording is a concern in the Indian setting due to social and cultural factors and confidentiality issues. Most of the respondents get suspicious or feel shy; AV recording is a problem in a country where a large percentage of the population is illiterate and poor (Chauhan et al., 2015).

"Now, if I am a doctor, I cannot talk to you unless you are being videotaped and I say, this is a clinical trial do I have your consent? These are very unreasonable situations. Can you imagine the constraints that impose on an already creaking system? I can understand some of the motivations, because you know there could be always some unscrupulous people who will not explain everything to you and God forbid your health is affected. But I think they went overboard without having the knowledge of what a clinical trial can do." (Scientist , CSO Thinq Pharma [50])

Delays in clinical trial approvals, increase in the number of refusals and stringent policy reforms is leading to dwindling of the clinical research industry in India (KPMG, 2015). These barriers are pushing the companies to undertake clinical trials in foreign countries, which in turn are pushing up R&D costs.

5.3 Summary

The pharmaceutical sector in India is operating in an environment that is witnessing unprecedented change. The chapter elaborated on the important changes in the institutional and regulatory environment in India that took place in two different time periods. The patent data analysis section delves deeper into the patent documents and provides evidence of innovation patterns of the pharmaceutical firms in each of the appropriability regime. The history and current situation of the Indian pharmaceutical industry underlines the main

argument that a potent mix of institutional and regulatory factors is important for the development and progression of an industry.

The institutional environment has positively impacted the new drug research by providing funding assistance and facilitating access to the public research institutions through public private partnership opportunities, strengthening patent policies and IP cells in universities to remove patent related impediments and providing funds to invest in setting up science parks and technology transfer offices. The public partnership schemes examined in detail shows the enthusiasm of the government to provide impetus to collaboration and incentives to 'pair together' and 'innovate'.

While the foregoing mentions about the positivity in the selection environment to increase research and innovation, there are challenges in the institutional environment, which has led to barriers for new drug innovation. The bureaucracy and functioning of the government departments dampens the spirit of these initiatives. The confluence of other factors such as decrease in profitability of pharmaceutical companies, stringent regulatory standards for clinical and animal studies, problems in PPP schemes, insufficient funding and increase in R&D costs have led to slowdown of research activities in India.

> *"In the last 10 or 15 years, people thought things have changed. But, it has gone again into a wrong cycle where you see several difficulties even in conducting clinical trials in India and time delays in getting licenses for running clinical trials. These are all the negative things that hamper scientific research in India and this may be one reason why many of the R&D companies are now currently shutting off activities in India." (Senior Vice President, NCE Research, Piramal [31])*

In addition, the risk involved in drug discovery projects is adding to the woes of the Indian firms. Due to the inherent risk of the drug discovery business and the challenges in the macro environment, commercially oriented firms are losing interest. Few firms have shut their drug discovery operations while others are reducing their activity and moving towards contract research business.

> *"What I have observed is that the outlook of the private sector is short term and commercially motivated. They do not want to take risks involved or put their resources in a much longer period of time to get something substantial.*

They are in a hurry and that is where the mismatch occurs. Even though our department would like to support them but if they see they cannot make money in next three to five years they will close the project." (Advisor, Department of Science and Technology [20])

6 Open Innovation in Indian Pharmaceutical Sector

The institutional and regulatory environment in India has significantly influenced the innovation ecosystem and nature of business activities in the pharmaceutical sector. The selection environment under two different patent laws provided distinct opportunities for the industry to develop and commercialise their innovations. Government has put in efforts to revitalise the institutional framework continually and introduce various policy initiatives to strengthen R&D capability within the country. During the process patent regime, while the Indian pharmaceutical companies were busy etching out their generics businesses, state funded Indian universities primarily continued as teaching institutes. Throughout this period, research activities and patenting at universities remained at ebb. Indian firms followed a closed in-house R&D programme with minimal interaction with universities or pubic research labs. There is a long history of disassociation between academics, industry research and public research labs, rooted in the setup of these institutions and the way they operate. Disconnect between public and private organizations widened over a period of time until the TRIPS patent regime resurrected the innovation scene. The TRIPS patent regime not only brought with it stringent patent laws but also resulted in a shift from research of generic drugs to advanced innovative R&D for new drug research as reflected from the innovative performance of the firms using patent analysis. The recent changes in the macro environment and the complexity of new drug research have necessitated firms to open to external sources.

This chapter reports the findings from the case studies to provide answers to the following research questions:

- How does national innovation system and asset position of a firm influence adoption of open innovation networks between firms and public sector labs & universities?
- How does national innovation system and asset position of a firm influence adoption of open innovation strategies for novel drug research in the Indian pharmaceutical sector?

The cross case analysis and intrinsic case studies of firms peppered with instrumental case studies of public private initiatives enabled to address these research questions. The results of data analysis are presented along two themes:

a) Open innovation networks within the national innovation system – This section explores the type of networks formed between firms, universities and public research labs and factors that positively influence the formation of open innovation networks. This section then tries to map the prevalence of these local innovation networks with the asset profile of the case companies. The concluding part reflects on important barriers that impede the formation of local innovation networks. The major conclusion of this analysis in this section is that local innovation networks are weak and rely mostly on research services such as consulting and fee for service. The public private partnerships to some extent are driven by the strategic motives of firms to seek funding and knowledge. A comparison of strategy between established and SMEs reveals that local innovation networks formed by both types of companies are weak thus attesting that asset position of a firm has little influence on the formation of these networks.
b) Open Innovation strategies used in new drug innovation process – The second section in this chapter examines the *open innovation strategies* used by established and SMEs at different stages of research. The findings identify key *drivers* of open innovation that push an organization to adopt open innovation and explains the four critical factors *(4Rs* – resource supplementation, risk mitigation, retention of control, revenue maximization) that summarises the underlying tension in a firm while opening up to external entities. The open innovation strategies pursued by firms and the innovation networks formed at different stages of research provide the basis for *open innovation pathways* adopted by Indian pharmaceutical firms and leads towards a framework for open innovation.

6.1 Open innovation networks within the national innovation system

In the initial years after independence, the thrust of public policy was on inculcating a culture of research and to promote science. In 1960s, the focus shifted to specific sectors such as agriculture and hone research and innovation in that direction (GOI, 1961). In recent years, the thrust of public initiatives has been to support R&D and bridge the gap between industry and academia. The eighth five-year plan (1992-97) report by the Planning commission of India concedes that significant investments in setting up universities, public research institutes has only resulted in scientists working in silos. The co-operative networks between

science and industry are blaringly lacking in the Indian setup. It was also recognised that despite the tax concessions offered by government, investments by the private sector firms in R&D was significantly low. Mobility of scientists and technologies between academic institutes, government laboratories and industry continued to remain low (GOI, 1992). Historically, these institutions have largely remained divorced from manufacturing enterprises and the functioning of the state machinery has been excessively bureaucratic (Lall, 1992).

At the outset, the empirical research aimed at finding the type of research partnerships formed between industry and public sector institutions. Interview data however revealed that in the Indian scenario the forms of interactions that exist between the industry and science system include few research engagements and many interactions within the local ecosystem for student recruitment, training and other academic related issues. It was hence important to distinguish between knowledge-based research partnerships from other types of academic interactions. The following dichotomy is used to differentiate between the two types of links formed between public research institutions and industry: *non-research networks* and *research networks*. Interactions between industry and public sector institutions for non-research purposes are called *non-research networks* and interactions formed for the purpose of research and knowledge purposes are deemed as *research networks*. The key definitions and salient features of the types of research and non research networks used in this study have been adapted from (Melese et al., 2009; Perkmann and Walsh, 2007).

6.1.1 Non-research networks

In the Indian pharmaceutical context, most of the interactions between university and industry are for academic based non-research purposes. The table below lists the major types of non-research networks formed between industry and academia in the Indian set up specific to the pharmaceutical sector. The types of networks, key terms used to describe different types of networks adhered closely to the study by Perkmann and Walsh (2007) and formed the basis for delineating key network types in the Indian setting. The definitions and key advantages listed emerge from primary research findings.

Table 25: Key forms of non-research networks between industry and public sector institutions existent in India

Types of networks	Definition	Advantages
Human resource transfer	Constitutes interactions between industry and academic institutions that involve aspects such as internship training of students, PhD programmes for industry employees, guest lectures, adjunct faculty for industry professionals, training of students on specific instruments etc.	Promotes bidirectional exchange of information, knowledge and other resources
Informal interaction	Informal networking at conferences, symposiums, workshops etc.	Allows networking opportunities
Use of facilities	Most of the times, SMEs seek access to testing facilities and equipment at national laboratories. In some cases, academic professors might require use of specialised equipment in the industry for their research.	Provides access to facilities and use of machines at cheaper rates
Recruitment tie-ups	Tie-ups for recruitment of students	Saves recruitments costs; strengthens university industry links

The human resource transfer is the most common type of association between Indian universities and pharmaceutical firms. State led Indian universities have stereotypically been perceived as teaching institutions and as a source of human capital for recruitment purposes. The production of skilled science graduates by universities is perceived to be the most important benefit of academic institutions in an economy. Industry has actively engaged with Indian universities for student internships and academic exchange programmes for employees. Companies like Ranbaxy, Lupin and Advinus have agreements with local universities for PhD exchange programmes wherein the employee can engage in research within the company while pursuing PhD on a part time basis.

> *"We have been able to produce five to six Ph.D. students in Advinus and that too of international standards. I think their publication list has gone up to 25 or something, which speaks of the quality of the research that is being done with academics in India. When these scientists work with the academics, they foresee the research opportunities." (Chief Scientific Officer, Advinus [35])*

A significant number of established pharmaceutical firms also provide training to students on certain equipment and technical platforms available at well-equipped laboratories of companies (Vice President, Lupin [36]). Other forms of association include guest lecture invitations of academics as speakers or for mentorship programmes, participation of industry in academic curriculum matters etc. Companies also invite academics as speakers in their conferences where they present their research. In 2014, Daiichi had organised a drug discovery conference in association with Royal Society of Chemistry where scientists from industry and academia were invited to present their research (Associate Director, Daiichi Sankyo India [39]). Such interactions between public and private sectors open doors for future collaborative project or joint research proposal (Chief Scientific Officer, Advinus [35]).

It is also common for universities or public research labs to rent out space or access to facilities. SMEs typically make use of instrumentation and testing facilities available in public research institutions. Jamia Hamdard had rented out an area to a small sized company Hilleman Laboratories specialized in vaccine research (Professor, Jamia Hamdard [8]). In few occasions, Lupin and University of Pune have shared facilities for research purposes (Vice President, Lupin [36]). Curadev also has access to labs and facilities of IIT Kanpur. Academics also seek access to equipment in pharmaceutical companies that are not available in the state funded university labs. A professor in university of Pune mentions that such an interface is useful to further academic research.

> *"I was working on vaccine research project which requires a specialized research facility. In such a case, access to already set up facilities in the industry works. Alternatively, if I have to create such facilities within my university it would require a research grant and it is not worth for one project." (Professor, University of Pune [3])*

6.1.2 Research networks

There are many different channels of engagements between academics and industry for innovation led research. The importance of university–industry research collaborations to further research and innovation is now well documented in various studies (Cockburn and Henderson, 1996, 1997; Cohen et al., 2002). This has led to policy makers in large number of countries to promote collaboration between these two sectors through incentives and R&D

support. It has been seen that these policy initiatives have propelled the formation of open innovation networks but the type of networks formed by firms depend to a great extent on its strategic motives. Research findings point to two important strategic motives that guide firms towards formation of innovation networks.

Types of research networks

In the Indian setup, there are mainly two broad forms of engagements with pubic research labs and universities, firstly, *research services* that refers to academic involvement for consulting on scientific matters or fee for service projects. The second form of engagement is *research partnerships* that refer to integrated long-term research projects with multiyear agreements for drug discovery. The terms research services and research partnerships are based on definitions by Perkmann and Walsh (2007). Other forms of engagements include constitution of scientific advisory boards (SAB) or participation through virtual consortium. Post 2005, government-initiated programmes for facilitating collaborative research projects and to incentivize new drug research in the local innovation system. Within this purview, the different types of networks formed between industry and public research institutions are detailed below in Table 26.

Table 26: Key types of research networks between industry and public research

Types of networks	**Definition**	**Salient features**
Research services	Projects or activities commissioned by industry involves providing expertise and services	• Short time projects • Allows to conduct short term research projects at cheaper rates • Enables academics make relevant contacts with industry and gain funds • Personal networks drive such projects • Works on high reliability and trust basis • Allows to stay focussed to a specific problem area • Helps to avoid bureaucracy • Usually does not result in generation of intellectual property (IP) assets
Scientific advisory boards	Community of scientific experts and researchers on board to guide the drug discovery programme in a firm	• Influencing role in pipeline selection and portfolio management of new drug compounds • Access to science and medical experts
Virtual Research consortium	Consortium of researchers who do academic research and share scientific problems, research ideas on a virtual platform.	• Allows to access interdisciplinary knowledge • Virtual platforms allow access to database of scientists • Resources such as specialised equipment and

	Example: India Innovation Research Centre (IIRC) and Open Source Drug Discovery	databases are shared on partnership basis • OSDD follows a patent free model while IIRC may result in patented research assets
Research partnerships	Inter organisational/interpersonal arrangements for collaborative R&D	• Usually long term agreements of 3 years which might be renewed based on outcome • Enables to gain access to expert knowledge and technology • Revenues for universities • Rewards individual scientists • May result in generation of IP assets or research publications
Public private research partnerships	Research partnerships through public initiative schemes either for funding alone or for research	• Allows to access research grants • Provide a platform for industry and public research scientist to come together • Leads to integrated collaborative projects • May result in generation of IP assets or research publications • Excessively bureaucratic • Monitoring process of project outcomes marred with delays • Low transparency in IP sharing clause • Subject to fluctuating R&D budgets and objectives with a change in government

Research services - Academic consulting and contract research services fall under this category and are the most common form of research networks formed in the Indian set up. A consultancy project usually involves one researcher who provides specialized expertise against payment. Such associations are ad hoc, need based with deliverables aligned against specific objectives.

a) Consultancy projects - Most of the consulting assignments are forged during the drug discovery stage, which deal with problems with highly uncertain outcomes. Most of these partnerships are formed by firms with the intention of seeking a specific answer to a research problem or to seek expertise of an academic in a specific area (Professor, University of Hyderabad [2]).

> *"We sought help from IIT Kanpur from a professor in organic chemistry. But the collaboration was for a very focussed and specific problem. I know 2 or 3 more people that I am very keen on collaborating in the area of stem cells and Alzhemier's." (Chief Scientific Officer, Curadev [26])*

Pharmaceutical professionals in general are in agreement that it is very beneficial to get academic expertise at the drug discovery stage. When working in a specific disease area if some researchers have done a background work, consultation at that stage is very useful to understand the nature of the disease and to know the research, which has been done in that area. Such consultants are specifically useful to make new drug pipeline decisions (Director, Novo Informatics [43]). Interview data reveals that common scientific problems for which consultancy is sought, may vary from issues such as inactivity of a molecule, failure of a molecule in a cell line or animal model, impurity profiling to stability testing, formulation etc.

> *"We have a very active formulation unit and we have provided consultancies to companies like Lupin, Ranbaxy. The proprietary rights remain with the industry but we provide them solution. They then give some grant to the institute and money also." (Professor, NIPER [7])*

The interaction is usually with specialized groups of scientists working in an organization to seek an answer related to a specific research area. As an example, if there is a need to tackle an issue in process engineering, then our pharmaceutics department may contact some of the scientists in leading institutes such as IIT who have experience in such matters (General Manager, Torrent [34]). The basic contention among the interviewees from both the sectors is that research services specially consulting is widespread and is regarded as valuable by both industrial and academic participants.

b) Fee for service projects- More recently, the proportion of fee for service contractual assignments is increasing. The outreach of these services has expanded as evidenced by setting up of biotech parks, spinoffs and dedicated centres to support the innovative efforts of the industry. One such initiative such as C-Camp is already gaining the reputation of providing excellent services at affordable rates, which are of much value more specifically to small and medium sized firms. For instance, Ranbaxy entered into a research agreement with NIPER to explore mechanisms for improving the safety and efficacy profile of a drug. Ranbaxy also tied up with International Centre for Genetic Engineering & Biotechnology (ICGEB) for a project related to profiling the anti-dengue activity of a plant extract. Some of the projects also get funding support from government.

On a general note, research services bring in financial revenues for universities and independent researchers. It also provides networking opportunities, however it has not been regarded by academics as the most intellectual way to interact with the industry. Academics feel that such types of services tend to undermine the contribution of academics by restricting the scope of their research. Such projects rarely result in intellectual property assets. The IP in such cases belongs to the company and the scope of the project does not leave much room for intellectual property generation. Academics have used words such as 'academic slavery' or 'academic prostitution' to describe the nature of such work. On the other hand, industry opines that research services as one of the best way to source in ideas and knowledge from the academic scientists. Industry professionals opine that the key advantages of such interactions are it precludes bureaucracy, reduces chances of intellectual property sharing, minimises possibilities of IP conflict, keep the research activity time bound and enables to provide solutions to a given problem.

Scientific advisory board

An advisory board of scientists is another important channel through which firms source in new ideas and expert advice from the research community. Prominent scientists and academics distinguished in the field of research constitute these boards. Almost all the pharmaceutical companies in India engaged in new drug research have set up an advisory board, which include members from the scientific community as board members. These advisory boards facilitate exchange of scientific ideas, selection of molecules for further development and development of project plans. Such a team of experts provide technical inputs on product portfolios and steer the direction of R&D to discover new drugs. The following quote surmises the role of scientific advisory committee in a company:

> *"The scientific advisory committee in Piramal takes important decisions with regards to progress of all projects the outcome of which is either to continue with the project or shut it down. The other important decision which the committee takes is whether to continue with in-house development of the programme or out-license it." (Senior Vice President, NCE Research, Piramal [31])*

Research consortiums

One of the largest consortium formed as part of government initiative has been the initiation of Open Source Drug Discovery (OSDD) for discovery of novel drugs in neglected diseases (Professor, University of Pune [3]). OSDD provides a virtual platform and has currently more than 8,000 registered users from 130 countries. The consortium based on open source model aims to bring together scientists from universities and public research labs for the common goal of drug discovery. In phase 1 of the programme, the OSDD is emphasising on discovery of drugs for tuberculosis. One of the molecules in-licensed by OSDD from Tuberculosis consortium is now in phase I clinical trials (Scientist, OSDD [22]).

OSDD initiative has managed to generate much interest among the scientists. Most of the researchers see it as a platform where they can translate their research from bench to lab (Scientist, Central Drug Research Institute [16]). However, this initiative has not managed to get the interest of domestic pharmaceutical companies, which are largely absent from this consortium. The Project Director, OSDD [19]) acknowledges that there is a need for more research based pharmaceutical companies to be a part of this project. One reason for this low participation is that most of the Indian companies are not engaged in the research of neglected diseases, which is commercially not an attractive option (Chaudhuri, 2007). Interestingly, pharmaceutical companies like Lupin and Lifecare Innovations are engaged in the research of tuberculosis but these companies are not part of the OSDD community. An important reason for low acceptance of this model among pharmaceutical companies is that it is based on a premise of patent free approach.

> *"OSDD is almost IP neutral. It does not stop anyone from patenting their research. Our main contention is that IP with a monopolistic or exclusivity led approach is of no value in diseases without market…. what we are trying to do is to develop an innovation model which will work in a situation where markets fail to work." (Project Director, OSDD [19])*

Thus, the open source drug innovation model with no patenting options and limited commercialisation opportunities remains as a consortium for university and public research scientists and has failed to attract the interest of local pharmaceutical companies. Despite the absence of industry scientists, the OSDD led by a motivated group of scientists continued to support and nurture the research efforts of many academic researchers and public research

scientists and provide a platform for them to share their scientific discoveries for further development.

Another example of a research consortium is the India Innovation Research Centre (IIRC). The IIRC is a virtual consortium of scientists from across the globe and provides a collaborative environment to share ideas and scientific solutions. In contrast to OSDD, the IIRC models emphasises on protection of intellectual property (IP). Researchers in the community are also encouraged to publish in academic journals. Invictus Oncology has a research partnership with IIRC. The centre is currently in fledgling state but it aims to foster relationships between the scientific community and foster innovation.

Public Private research partnerships

In theory, all research partnerships formed between industry and public research institutions are termed as public private partnerships (PPP). The research partnerships were classified a PPP and examined using the approach described in 4.4.3. Most of these research projects are assisted by public funds from different departments or policies. The TRIPS agreement, which was signed in 1995 and provided a ten-year interim period for developing countries to conform to the requirements, catalysed the initiation of many government funded schemes to support research. Four policy initiatives namely Drugs & Pharmaceutical Research Programme (DPRP), New Millennium Indian Technology Leadership Initiative (NMITLI), Small Business Innovation Research Initiative (SBIRI) and Biotechnology Industry Partnership Programme (BIPP) have been particularly important in India to fund joint research pharmaceutical projects between public and private sector. DPRP is a programme that specifically focuses on funding of research in drugs and pharmaceuticals, on the other hand NMITLI funds a variety of projects across different sectors. BIRAC led schemes SBIRI and BIPP, support biotechnology projects with applied research in pharmaceuticals, biotechnology and agriculture. These public private partnership schemes support research projects at different stages of drug discovery. Policy initiated public private partnerships are further segregated into two types: *funding of stand-alone R&D projects* and *funding of collaborative projects* between government and industry public scientists (Refer Figure **19**). Section 5.1.2 elaborates on these government initiatives in detail.

The public private partnership projects are categorized as follows:

1. Research partnership projects sponsored under the four policy initiatives are referred as '*Policy initiated public private partnerships*' in this dissertation.
2. Joint research projects sponsored by industry or public department funds but not sponsored under the four policy initiatives are categorized as *'Non- Policy Public private research partnerships'*

In recent years, there have been some notable public private partnership projects. The table below shows a count of public private partnerships undertaken by case firms segregated by type of public private partnership.

Table 27: Public private research partnerships formed by Indian pharmaceutical firms

Company Name	**Policy Initiated PPP**										**Non-policy initiated PPP***
	Stand-alone R&D projects					**Collaborative projects**					
	DPRP	**NMITLI**	**BIPP**	**SBIRI**	**Total**	**DPRP**	**NMITLI**	**BIPP**	**SBIRI**	**Total**	
Ranbaxy	3	0	0	0	3	3	0	0	0	3	7
Dr. Reddy's	0		0	0	0	0	0			0	1
Lupin	3		0	0	3	0	2			2	2
Piramal	0		0	0	0	0	0			0	7
Torrent	3		3	0	6	0	0	0	0	0	0
Advinus	1		0	0	1	0	0			0	0
Invictus	0		0	1	1	0	0			0	1
Curadev	0		0	1	1	0	0			0	1
Lifecare*	0		1	1	2	3	0			1	2
Total	10	0	4	3	**17**	6	2	0	0	**8**	**21**

** Projects of Lifecare are incremental drug research projects*

A distinctive pattern, which emerges from the research partnership data is the *less* number of collaborative projects and *more* number of funding projects under the policy initiated programmes. A closer look at the tabular data suggests that such a pattern is uniform for both established and SMEs. This suggests that within policy initiated public private partnerships most of the projects are stand-alone funding projects, which is ironical as one of the main objectives of these programmes is to propel formation of industry and academic networks. The number of non-policy initiated PPP proves that a large number of collaborative projects are based on own initiation efforts for industry and academics. The analysis shows that policy

initiated schemes though have been useful in getting the participation of the industry to get funds for research projects but have not been much successful in their efforts to induce collaboration.

Policy initiated public private partnerships

DPRP: The DPRP programme was one of the first among the new wave of government programmes intended to provide support to private R&D projects and boost academic industry network. It has been functional for the past 20 years and expanded dramatically after the revamp of the programme in 2005. Ranbaxy, Lupin, Torrent (established firms) and Advinus (SME) have availed of funding opportunities under this programme. The big success story of the Drugs & Pharmaceuticals Research Programme (DPRP) programme has been the grant of funds to Ranbaxy for the clinical development of 'Synriam', India's first indigenously developed anti-malarial drug. The new anti malarial drug funded through public-private-partnership of DPRP is the first new chemical entity to be developed and launched by an Indian pharmaceutical company.

Other noteworthy collaborative projects undertaken with an academic partner under this program are a) toxicity and efficacy studies of liposomal amphotericin B (Brand name: KALSOME TM) between Lifecare Innovation and AIIMS and b) development of a nano particle drug for MDR tuberculosis between Lifecare Innovation, IIT Kanpur and PGI Chandigarh etc.

NMITLI: This programme is different from other programmes as it funds only collaborative projects in which government industry scientists work together in a research project. Therefore, the number of stand-alone is reflected as 'Nil' in Table 27. A large project sponsored by NMITLI involved a successful partnership between 12 institutions and pharmaceutical company Lupin that led to the development of new tuberculosis drug LL 3858/4858 (Sudoterb). The project encompassed identification of new targets, new drug delivery systems and application of bio-enhancers as an adjunct to chemotherapy. The molecule LL 3858/4858 (Sudoterb) is currently is in Phase 1 of clinical trials.

Another example is an osteoarthritis herbal public private partnership drug development project supported by NMITLI scheme. The project involved 16 national research hospitals, hospitals and pharmaceutical companies. This project was completed in 5 years and led to the design of few variants of synergistic poly-herbal formulations. Based on clinical trial data,

one drug formulation has been submitted for regulatory approval (Patwardhan, 2014). These two projects appear under the collaborative projects in Table **27**. Primary research findings support the view that the NMITLI programme in recent years has not received as much attention and is less preferred by the industry.

BIRAC: The Department of Biotechnology (DBT) in India set up BIRAC in 2012 to foster research and innovation in the field of biotechnology. BIRAC supports pharmaceutical research through two public initiatives - Small Business Innovation Research Initiative (SBIRI) and Biotechnology Industry Partnership Programme (BIPP). Companies such as Curadev, Invictus, Advinus and Torrent have all participated in BIRAC schemes. BIRAC led initiatives aim at providing capital, facilitating patenting and technology transfer, promoting networks and is popular among SME and established companies.

> *"The DBT plays a very important role and has one of the most forward looking government bodies in Indian science. The Department of Biotechnology has come up with lot of initiatives that would help build relationships, encourage research in India and fund young entrepreneurs through BIRAC. The DBT has really played a frontal role in reducing bureaucracy and improving the collaborations." (Senior Vice President, Piramal [32])*

BIRAC has provided funds to many SMEs like Invictus, Curadev and Lifecare Innovations through the SBIRI scheme. Lifecare innovations won a research grant for Phase I clinical trial of PLG [Poly(dl-lactide-co- glycolide)] for nanoencapsulation of tuberculosis drug. Torrent has utilised the BIRAC scheme for the clinical trials of its new chemical entity TRC 150094 indicated for cardiovascular risk. It has also received grants under the BIPP scheme for a project aimed at development of alternative treatments for heart failure complicated with diabetes mellitus.

In essence, the public private partnership initiatives have resulted in providing funds for research and a platform to facilitate science based networks. The review of research partnership projects shows that firms primarily engage with the policy programmes to get monetary assistance. This is evident from the number of funds provided to stand-alone research projects as compared to joint research projects. DPRP, the oldest programme has been able to attract industry participation largely for funding projects. The analysis of case

companies suggests that four out of nine companies have used BIRAC schemes for standalone research funding projects. NMITLI on the other hand, is getting less popular in recent years for pharmaceutical research. In spite of funding many good successful projects, the programme has been unable to sustain industry interest. One probable reason is the mandatory requirement of this programme to provide funds only for joint projects. The opinion of a professor in a leading pharmaceutical institute of the country supports the proposition.

> *"What I have noticed is that most of the public initiatives did not take the right shape because many proposals require an industrial partner and an academic partner. My personal opinion is that industry seems less responsive as they feel that if it is a profit making successful programme then why not do it ourselves. The industry does not have shortage of money so they think why should we have an academic partner. So despite good initiatives not many good proposals are coming along the way from academia and industry." (Professor and Head of Department, NIPER [6])*

The analysis of public private participation data in Table **27** shows that companies prefer getting into funding agreements from the government rather than using this channel to form collaborative relationships with academics. Companies prefer to seek academic help through contract research and consulting assignments for industry problems.

Non- policy initiated public private research partnerships. These projects are either sponsored by government or industry or jointly sponsored. Table 28 shows sample of public private partnership projects undertaken for new drug discovery work. However, most of these collaborative projects that have occurred between companies and public institutions are ad hoc and do not extend into long-term research relationships. The positive news is that companies have opened up their internal drug discovery programme to external partners as evidenced from the various PPP projects that have taken place in the recent past.

Table 28: Non policy initiated Public private research partnership

Name of company	**Name of collaborative partner**	**Research Objective**
Dr. Reddy's	Madras Diabetes Research Foundation (MDRF), Chennai and Indian Institute of Science, (IISc) Bangalore	To understand the genetics of diabetes and insulin resistance more specifically in the cause and aetiology of Type II diabetes.

Ranbaxy	Anna University	To evaluate a number of medicinal plants as potential sources for novel pharmaceutical agents. The role of Ranbaxy involved lead optimisation, identification of candidates and pre-clinical development on leads.
	University of Saurashtra	Research project for discovery of novel anti-cancer compounds.
	NIPER	Research for anti asthma drugs which involved NIPER synthesising small molecules and Ranbaxy screening these molecules to identify candidates for further development.
	Centre of Biochemical Technology (CBT)	Research collaboration in the area of pharmacogenomics and biological target.
Lupin	Indian Institute of Chemical Technology (IICT)	Agreement for basic research project
	Regional Research Laboratory, Jammu	Research agreement for obtaining leads for diabetes and hepatoprotection from natural resources.
Piramal	Centre for Biochemical Technology	An alliance to focus on new knowledge coming out of the human genome sequence project and utilize genetic material data bank for future requirements.
	Indian Institute of Chemical Biology (IICB)	Basic biomedical research agreement for characterization of anti-cancer and anti-inflammatory molecules from Piper betel leaf extract and identification of their targets by proteomics.
	Indian Institute of Science, Bangalore (IISc)	To identify potential new targets for developing drugs to treat fungal infections.
	National Institute of Immunology (NII)	Research collaboration to discover and develop new chemical entities (NCE's) in the field of inflammation.
	Council of Scientific & Industrial Research (CSIR) and National Institute of Oceanography (NIO)	The collaboration was for screening or chemical analysis of natural product library to use them as sources of novel drugs.
	Anna University	Identification and development of plant extracts in the repository of Centre for Biotechnology Department for the treatment of rheumatoid arthritis and cancer.
	Tata Memorial Centre (TMC)	Collaboration to enable development of preclinical cancer models to enhance understanding of disease biology, treatment response and biomarkers.
Curadev	IIT Kanpur	Memorandum of Understanding for two R&D programmes

Source: Compiled using company websites and press releases

6.1.3 Influence of asset position of firm and propensity for local networks

The central question, which this section aims to answer, is to know if the asset position of a firm plays a role in influencing formation of open innovation networks within the local innovation system. The section uses a variety of primary and secondary data on case

companies highlighting how the firms have used local sources of innovation for new drug research. The results suggest that asset position of a firm has little influence in shaping the local innovation networks. The proclivity of some firms to open up to local source of innovation more than others underscores the role of a firm's dynamic capabilities in shaping these innovation networks.

This section attempts the following:

a) display the firm asset position of case companies

b) describe the connectedness of these companies within the local innovation system

c) demonstrate that open innovation networks are not much influenced by the asset position of a firm but by the dynamic capabilities of firms to form these networks.

Table 29 below shows the asset position of established and SMEs used as cases in this study. The assets are categorized into three types based on Teece et al. (1997) framework: technological, financial and complementary. The measure of technological assets is innovation output as indicated through number of product patent applications filed and pipeline of new chemical entities. Financial assets are measured through consolidated net revenues and R&D intensity while the presence and number of manufacturing plants, R&D labs and strength of marketing force are used as indicators of complementary assets of a firm. R&D intensity of a firm is defined as expenditures by a firm on its research and development (R&D) divided by the firm's sales (Cohen and Levinthal, 1990).

Table 29: Asset position of case companies for the year 2015

Company name	Company related Information		Technological Assets		Financial Assets		Complementary Assets		
	Age of drug discovery	R&D staff	Pipeline of NCE com-pounds*	Number of product patents	Consolidated net revenues USD million#	R&D intensity	Manufac-turing facilities	Marketing capabilities (Sales force number)	Number of R&D Labs
Established Companies									
Case 1-Dr. Red-dy's*	22	1200	15	96	Above 1 billion	~ 12%	25	More than 3000	10
Case 2-Ranbaxy**	22	More than 1000	Not available	100	Above 1 billion	12%	8	4000	5
Case 3-Lupin	14	1400	11	116	Above 1 billion	8.70%	13	5500	2
Case 4-Piramal	15	903	17	57	500 million -1 billion	14%	7	552	1
Case 5-Torrent	17	835	7	40	500 million -1 billion	4.80%	5	5,067	1
Small and Medium Enterprises (SMEs)									
Case 6-Advinus	10	450	14	20	Less than 50 million	100%	These SMEs are research based companies and do not carry out downstream activities such as manufac-		3
Case 7-Curadev	5	34	5	3	Less than 50 million	100%			1
Case 8-	4	Not	2	2	Less than	100%			1

Invictus Oncology		available			50 million		turing or marketing. These assets are not available in these companies.	
Case 9- Lifecare Innovations	~5	Not available	1	6	Less than 50 million	100%		1

* Proprietary pipeline of Aurigene (subsidiary of Dr. Reddy's) is reported
** In 2008, Ranbaxy had transferred all its research assets except for two NCEs to Daiichi Sankyo India Pharma Limited. Daichii also used to develop research assets from its own company headquarters in India. Exact pipeline information was hence not available for reporting purposes.
# Exact revenue figures for SMEs are not available hence the revenues have been shown in a range

Source: Annual reports or company websites for established companies.Company professionals provided the required information for SMEs.

The following section provides a description of firm level cases based on primary and secondary data analysis. The case profiles based on annual reports of the last ten years and primary interview data provides an overview of the nature of business activities, its asset position and important collaborations undertaken by the company. The next section elaborates the cases of established firms and SMEs.

Case 1 - Dr. Reddy's Laboratories

Dr. Reddy's started its new drug research business in 1993. The technological assets of the company include 151 patent applications of which 55 are method patents and 96 are product patent applications filed between 1995-2014. Dr. Reddy's has been one of the pioneer companies to initiate research for discovery and development of new chemical entities. The company conducts new drug research in the area of diabetes, cardiovascular, anti-infectives, inflammation and cancer. The strong generics business provided the capital required for research and development. The company has access to well equipped labs, technology development centres in India and abroad. The R&D intensity of the company is 12% that shows it commitment to conduct research for novel drugs.

> *"Dr. Reddy is someone who pioneered the new drug research programme in India. Dr. Reddy's was the first company to successfully out-license its new drug molecules. We got very good reward in terms of up front payment. It also brought the company brand value […]. It was one of the first Indian pharmaceutical companies to be listed in the New York Stock Exchange." (Retd. President, Dr. Reddy's [28])*

Within the local innovation system, Dr. Reddy's has many non-research collaboration with leading universities and public research institutes. In 2004, it also set up a research

organization Institute of Life Sciences (Ford et al.) through a public–private partnership initiative. As a successful organisation it is sought after by leading academic institutes for student recruitment, consulting and contract research projects. The company has however not participated in any government initiated policy programmes and has not undertaken joint research projects with public institutions for new drug research.

Case 2 - Ranbaxy

Ranbaxy (now Sunpharma) started operations as a distributor of foreign medicines in 1962 and experienced phenomenal growth to emerge as one of the top ranked companies of India with global presence in over 43 countries. Like Dr. Reddy's, Ranbaxy also started its new drug research programme in the early 1990s. The company has multidisciplinary R&D centres with cutting edge enabling technologies for innovative research and 21 manufacturing sites across 8 countries, equipped with state of the art facilities to manufacture generics, differentiated products, OTC product, anti-retrovirals & intermediates. Ranbaxy has filed 241 patent applications, 141 method patents and 100 product patents. The focus of the company for new drug research was in the therapeutic areas of infectious diseases, metabolic diseases, inflammatory/respiratory diseases and oncology.

The company has formed numerous linkages with universities and public research labs for non-research activities like training programmes, student recruitment and supporting student research projects. It has also formed various research partnerships for new drug research with Anna University, NIPER, IICT, Jamia Hamdard and has been an active participant in policy initiated public private partnership schemes. Ranbaxy has had research engagements with various public research institutions at initial stages of drug research for discovery of new compounds, new drug design/development of products and screening/profiling of compounds. It also got funding under the DPRP programme for the clinical development of two of its NCEs – 'Synriam' launched in 2012 and 'RBx 7644', a novel antibiotic drug.

Case 3 - Lupin

Lupin Pharma established in 1968 with headquarters in Mumbai has been ranked in 2015 as the third largest pharmaceutical company in India by revenues. It has a state of the art R&D centre in Pune and 13 manufacturing facilities in India and abroad, approved by leading regulatory authorities. The focus area for new drug research is psoriasis, migraine, anti-

tuberculosis, rheumatoid arthritis and diabetes. The company has a strong pipeline of six new chemical entities in various development stages in these therapeutic areas.

Lupin has filed 213 patent applications during the twenty-year period 1995-2014. Of these, 116 are product patents and 97 are method patents. In the years up to 2001, the company was involved in process-based research for generic drugs. In the late 1990s, the company ramped up research to develop advanced drug delivery based drugs and introduce new formulations of existing drugs.

Lupin is a relatively closed company with focus on in-house R&D and relatively fewer engagements within the local ecosystem.

> *"In Lupin, we did not do as much networking within India with Indian institutes. We are very busy doing our own work but we have started that and we will be doing it more." (Senior Vice President, Lupin [29])*

Despite the inward focus, Lupin has participated in two large public private partnerships with leading research institutes and universities of the country. The outcome was successful and led to the development of a clinical candidate for development. Thereafter, the company has used the schemes to get funding assistance in clinical development of the drug.

The Department of Science and Technology (DST) selected the clinical development programmes for Lupin's migraine and psoriasis molecules for funding and has committed over Rs. 100 million for these projects.

Case 4 - Piramal

Piramal Enterprises, the flagship company of Piramal group is one of the reputed companies in India and in 2011 was ranked amongst the top 50 largest corporations across India by Fortune 500. The company has operations in over 30 countries and brand presence across 100 markets around the world. The company has manufacturing facilities in Canada, UK, US and four facilities within India. It has an R&D centre in Mumbai for API, formulation development and new drug research. Piramal has 90 active patent applications. The company has filed 33 method patents and 57 product patents. The focus area for new drug research is oncology, metabolic disorders, diabetes and inflammation.

The company has been proactive in making significant collaborative agreements with various institutions for new drug research. Most of these alliances were at the drug discovery research aimed to build a repository of knowledge or to enable exploration of a library of molecules, or compounds or gene databank for furthering research. Piramal Life Sciences was one of the first Indian companies to form a public private partnership with nine public research institutes at the pre-drug discovery stage. The project entailed screening of environmental isolates from different ecological niches for active bio-molecules.

> *"An offshoot of the programme was the creation of a national repository for microbes now available in the Pune University. We discovered three NCEs from this programme; we have filed one patent for one NCE while the filing of patent applications is under process for the other two NCEs." (Senior Vice President, NCE Research, Piramal [31]).*

The company was also part of a mega collaborative project with Council of Scientific & Industrial Research (CSIR) and National Institute of Oceanography for the development and screening of natural product library to identify potential sources novel drugs. It has formed various collaborative projects with Anna University, Indian Institute of Science, Bangalore (IISc) and National Institute of Immunology (NII) for discovery and development of new chemical entities.

Case 5 - Torrent

Torrent Pharmaceuticals Ltd is a leading manufacturer of generic drugs in India with a strong international presence spanning 40 countries and over 1,200 product registrations. The company's revenues are mainly from manufacture and sale of generic pharmaceutical products across the globe in key regulated and unregulated markets. Torrent initiated its new drug research programme in 1998 with the setting up of R&D centre in Ahmedabad-Gandhinagar region. The R&D centre, set up at an investment of over USD 40 million with advanced equipment, conforms to international quality standards.

The company has five manufacturing facilities in India. Torrent pharmaceutical has filed 55 patents during the twenty-year period 1995-2014 of which 40 are product patents (13 basic and 27 secondary patents) and 15 are method patents. As an early entrant to the new drug research, the company started filing patents for new drug applications in the late 1990s. The company's efforts to make new drug delivery systems and formulate differentiated generic

drugs are reflected in the method and secondary patent filings. Filing of basic patents was at ebb between 2003 and 2006 and picked up slightly thereafter. Torrent has filed 27 secondary patents and 13 basic product patents.

The company has strategically pursued a closed in-house R&D drug discovery programme with minimal interaction with other companies or universities. The R&D division is currently working on several in-house new chemical entities (NCE) projects in the area of cardiovascular disorders, cerebrovascular disorders and renal disorders. Its two molecules Advanced Glycosylation End-Products (AGE) breaker (TRC 4186) and TRC-150094 (T2 Mimetic) are in clinical development stage in the area of cardio metabolic risks and complications due to diabetes. The company has sought funding assistance through the policy-initiated schemes mostly at drug development stage.

Case 6 - Advinus

Among the SMEs, Advinus is an admirable drug discovery company that was set up in 2005 to capitalize on the drug discovery opportunities in India after TRIPS. It is one of the few companies that managed to get a financial backing by the Tata group of companies, one of the largest business houses in India. The company has research facilities in Pune and Bangalore. The therapeutic areas of focus of the drug discovery programmes are in the area of cardiovascular metabolic diseases, inflammatory and autoimmune diseases and pain/neuro degenerative diseases. Advinus is also working in the discovery of novel therapies for neglected diseases such as leishmaniasis and malaria.

Advinus has filed 20 patent applications for basic product patents and has a pipeline of 14 NCE compounds. Though Advinus has informal networks with Indian universities and public research scientists, it has not formed any research partnerships within the local innovation system. It has sought funding under the DPRP initiative for funding of clinical trials for GKM 001 indicated for Type 2 diabetes.

Case 7 - Curadev

Curadev Pharma, a research based pharmaceutical company engaged in drug discovery and contract research service was formed in January 2010. Curadev has a well-equipped R&D lab at Noida. It is a small research based company which funds its new drug research programme through contract research business. The therapeutic focus of the company is in cancer and

inflammation. Curadev has developed small molecule inhibitors that belong to two classes: IDO specific inhibitors, and IDO/TDO dual inhibitors.

Curadev also has an equity-based arrangement with IIT Kanpur that grants access to infrastructure, lab facilities and expertise of the faculty. The company also draws scientific expertise and guidance for its drugs discovery programme through the Scientific Advisory Board, which comprises of international researchers. The company however has not formed significant research partnerships with local academic and research institutions. It has received funding support from BIRAC under the SIBRI scheme and has filed three patent applications up to 2014, of which two are basic product patents and one is a method patent.

Case 8 - Invictus Oncology

Invictus Oncology is a start-up drug discovery company established in 2011. The focus area of its new drug research program is oncology. It in-licensed a technology from Partner's healthcare that was used to formulate a modified cisplatin, an effective but toxic drug. The company's novel platinum-based supra-molecular therapeutic IO-125 is being developed for the treatment of triple-negative breast cancer and is in late stages of pre-clinical development. Invictus Oncology has filed two secondary patent applications till the year 2014.

Invictus Oncology has formed various scientific collaborations with academicians from leading institutions to form valuable public-private partnerships (PPP). It has a scientific advisory board formed of distinguished scientists and entrepreneurs to guide the drug discovery programme. Invictus Oncology has also formed a research agreement with India Innovation Research Centre (IIRC), a non-profit organization. The company also has plans to form research agreements with All India Institute of Medical Science (AIIMS), National Chemical Laboratory (Hasenclever and Paranhos) and National Institute of Pharmaceutical Education and Research (NIPER), Mohali. BIRAC has provided funding support to Invictus Oncology for its research project under the SBIRI scheme.

Case 9 - Lifecare Innovations

Lifecare innovations Pvt. Ltd. was set up in the year 2000 as a medical biotechnology company with headquarters in Gurgaon, India. It has also setup a R&D centre in Lucknow in close proximity to public research institutes and universities such as Central Drug Research Institute, Centre for Medicinal and Aromatic Plants, Indian Institute for Toxicology

Research, Sanjay Gandhi Postgraduate Institute of Medical Sciences and S J Medical University.

The company has strong networks with public institutions and academics. The company has worked in a public funded collaborative project with University of Delhi, KEM hospital and Seth G S Medical College, Mumbai, which resulted in the development of a successfully marketed drug Amphotericin B. in liposomal formulation for leishmaniasis. In 2006, the company acquired the marketing rights for the novel liposomal formulation of Dithranol (Psorisome) jointly developed by Panjab University, University Institute of Pharmaceutical Sciences (UIPS) and PGIMER.

Lifecare Innovations entered into another collaborative project with DST under the programme Drugs & Pharmaceuticals Research Programme (DPRP) for development of sustained release tuberculosis drug. Under the DPRP programme, the company is engaged in two research partnerships with IIT Kanpur and PGI Chandigarh. The company has also sought funding support for clinical trials for the testing of nanoparticle formulation of anti tubercular drugs (Rifampicin, Isoniazid, and pyrazinamide) under the Biotechnology Industry Partnership Programme (BIPP) scheme. Lifecare Innovations has a new drug in pipeline, ONCO-1 indicated for cancer treatment. The company has filed ten patent applications, of which four are method patents and six are product patents.

In summary, the comparison of established and SME cases shows despite the enthusiasm from government, few firms engage in long-term cooperative projects for research in the Indian ecosystem. The contribution of public science research in the innovative activities of pharmaceutical firms is fairly limited. The findings did not support the contention that young research active small and medium firms engage more within the local innovation as compared to established firms. The general pattern of interaction between university and industry indicate that consulting and fee for service projects dominate the collaborative scene in India. Firms are guided by their strategic objectives to seek knowledge from academic scientists and funds from government schemes and accordingly make choices to open up to the local innovation system. Despite, the increased emphasis by government through their policy efforts, the outcome is ad hoc research partnerships in the area of research for new drugs. A notable pharmaceutical expert commented that

"In my view, there is more fluff than wheat. The projects are not substantial like in Europe and United States. The collaborating partners make an agreement, have a press release, they would say how much money was invested and that is well and good. But the thing is what has come out of these collaborations? [….]. I have not seen anything happen even though there are so many cases where partnerships are being put together, but what has come out of it we don't know yet." (Senior Director, SRI International [49])

6.1.4 Barriers to open innovation within the local innovation system

The Indian innovation system faces special challenges to form science-based networks and the problems that plague the Indian innovation system are much deep rooted. The exploratory research carried out with industry professionals, academic and public research scientists revealed the problems inherent in the ecosystem. This section describes the barriers to open innovation which firms face in forming innovation networks within the local ecosystem. Within the institutional context, the key challenges are:

a) A variety of initiatives have been housed under different departments and ministries, such as Department of Pharmaceuticals, Department of Science and Technology, Department of Biotechnology that makes co-ordinated action difficult (refer Section 5.1.1 for more details). Conflicting priorities of the departments make some programmes more in demand than others. Most of the times with so many initiatives, awareness about these programs is low.

> *"Most of the people are not aware that government spends so much on the programme so it is also Government's duty to increase the outreach and popularise it." (Assistant Director, FICCI [24])*

b) The distinction of universities as 'teaching institutions' versus public research institutes as 'research institutions' have separated teaching from research. Traditionally, universities are viewed as teaching institutions and this perception has failed to form inter research networks between public research labs and universities.

c) The third important challenge is the history of low research within the Indian pharmaceutical sector. The sector was dominated by low-end process research for generic drugs that required little interaction with academic scientists during the

process patent regime. Over a period of time, this led to creation of silos of scientists working in academia, universities and industry.

The inherent problems in the institutional set up have made it difficult to rejuvenate the system despite a shift to a strong patent regime, and positive measures from the government.

> *"When I came to India, I saw that the academic sector and private sector do not see eye to eye. This is very strange to me as abroad this is very common. Somehow those two sectors are moving in their own manner, do not meet each other." (Professor, DRILS [17])*

The predominant issues that have emerged from the interview data to be important reasons for weak innovation networks between industry and public research are: a) low technological opportunities in the public sector b) IP related issues c) trust and cultural issues. The table below show the frequency of codes in the interview text analysis and summarises the top three issues mentioned by respondents.

Table 30: Frequency of important codes from the primary interview data

Important Issues	Codes	Frequency
Low technological opportunities in the public sector	Low research productivity	32%
	Low motivation levels	24%
	Low uptake of public research by industry	20%
IP related issues	Preference by scientists in public sector to disseminate research through publications	18%
	Poor IP infrastructure support	10%
	Patent ownership issues	14%
Trust and cultural issues	History of opportunistic cases	16%
	Different mind-sets	36%
	Tendency to work in silos	28%

Low technological opportunities in the public sector

The disposition of the industry researchers to interact with public researchers depends to a great extent on the available technological opportunities. The knowledge base of the research in the discovery of new chemical entities is still in the initial stage. Post 2005, the host of regulatory and policy initiatives have promoted research activities for new drug research in public research institutions and universities. It has been observed that pharmaceutical firms

with well-established research laboratories have shown little inclination to have research cooperation with universities and there is little evidence of uptake of university research by the industry. One of the reasons for a firm's dissatisfaction with the public research system is the *low availability of technological opportunities.* While the low uptake constitutes a general characteristic of the situation, the explanation for low technological opportunities lies in poor publication record, lack of applied research, lack of experience in new drug research, low level of motivation and lack of regulatory knowledge.

Poor publication record

In the US pharmaceutical industry, lot of drug discovery projects start with a publication or an interesting research project that takes place in an academic lab. This is not common in India as the number and quality of publication is very low. Most of the academic papers are published in journals with low impact factor (Associate Director, Jubilant Chemsys [46]).

An industry veteran commented:

> *'As an onlooker I would say that quality of publications is very poor. It just sounds as a me-too type of thing and there is no breakthrough. Publications in reputed peer reviewed journal is very less, even China has overtaken us." (Retd. President, Dr. Reddy's [28])*

Public research scientists argue that drug discovery is a huge task and research in such a field gets established only after many years of work. A public research scientist opines:

> *"Many universities abroad have the capacity; the scale at which they operate, is several orders of magnitude different from the Indian universities or labs." (Scientist, Indian Institute of Chemical Technology [15])*

Low research productivity

One of the reasons for the low technological opportunities is lack of research with fruitful results. The argument for low research productivity is attributed to the absence of R&D for new drugs in the process patent era in universities and private firms. It is noteworthy that research for novel drugs is not a new phenomenon for public research institutes specifically Central Drug Research Institute that is mandated to conduct basic research for drugs. CDRI

has been operational for more than 60 years but has not been able to develop commercially successful drugs (S. Chaudhuri, 2005). A professor in University of Hyderabad states

> *"The fact is for the past 56 years the new drug discovery effort is ongoing in the country in the laboratories of Central Drug Research Institute but nothing has come up. CDRI did come out with Guggulipid, a natural product based anti obesity agent but you can't call them noticeable success stories. But that was different those things came in 50s and 60s when India was poor. Today, lot of money is available for research [….]so this should translate into some results. The government has pumped in lot of money and the money spent does not commensurate with the output." (Professor, University of Hyderabad [2])*

Another drawback of the national science system research is its inability to support industrial research with relevant knowledge. While the industry is primarily engaged in the research of diseases which are of high commercial value such as oncology, cardiovascular disorders; the public system is primarily engaged in the research of neglected diseases such as tuberculosis, malaria, leishmaniasis which are of low commercial value but pertinent for the population of developing countries. Another concern is the emphasis of public research on basic research. In Scandinavian countries, Japan and Portugal, universities conduct the bulk of basic research while public research institutes focus on applied research. Elsewhere in continental Europe, the basic and applied research coexists in universities and research institutes (OECD, 2002). In case of India both universities and public research labs focus more on basic research.

> *"Scientists in public research institutes are more into basic research than in the drug discovery research. So the attitude they have is that they are more interested in publication and basic research. They have the necessary infrastructure, knowledge and experience as most of the scientists have come from US and have good exposure. But I don't know why they have all turned into pure basic research scientists. I know many scientists in CDRI who have a good understanding and knowledge but said that their director is interested in particular projects, so we are doing that. It is mainly the project selection issue from the ministry, which trickles down to the department and to the respective institutes." (Vice President, Piramal [33])*

Low productivity of the science system

Academics and scientists are in consensus that as far as drug discovery is concerned, there are not many molecules or new chemical entities discovered or researched by Indian scientists. In the university setting, about 75% - 80% conduct research towards getting their PhD. Once the PhD is submitted and students publish their research, additional research work is not undertaken. The percentage of students carrying on further research is only 20-25% (Vice President, Piramal [33]). A company scientist adds that the culture of post doctorate is also not there. Students go to UK and US for post doctorate and then its brain drain (Assistant Director, Ara Healthcare [42]).

India also suffers from limited competence in the field of biology. India has been traditionally strong in chemistry (Vice President, Dabur Research foundation [44]) and also in the field of clinical medicine with the availability of good doctors and surgeons (Retd. President, Dr. Reddy's [28]). With limited competence in biology and limited experience in chemistry, Indian academics have very little to offer to the industry in drug discovery research.

Low motivation levels

Experts and scientists ascribe the low research productivity to low motivation levels. Industry veteran says that the focus for an academic researcher in India is to get a PhD and enjoy life rather than getting into the serious business of teaching and research (Retd. Vice President Formulations, Ranbaxy [27]). A public research scientist attributes the low motivation levels to bureaucracy, which takes a toll on one's patience.

> *"Something, which should take a day, will take about a month or about four months. Many people are getting to their comfort zone by not doing anything. So this is something, which is very dangerous because in a government set up it is very difficult to make a person work. In any country but definitely in India, it has become more of a norm to enjoy the job you are having. So they are not really feeling that they are part of building this nation." (Scientist, Indian Institute of Chemical Technology [15])*

> *"Academics feel that the bifurcation of research and teaching to research institutes and universities have also affected the motivation of academics to*

do research. Very few universities have patent portfolios and this is due to the personal efforts of the researchers." (Professor, Jamia Hamdard [8])

Lack of regulatory knowledge

Industry experts opine that academic researchers lack the necessary knowledge of regulatory guidelines, which affects the usability of research by the industry.

> *"Scientists in universities and public labs have no clue on what does it take to make a drug out of an idea. With respect to the regulatory pharmacology and toxicology studies, they have absolutely no clue. Besides this, they are not well versed with the quality measures that are required. So QA is often not even a department in these organizations. They have absolutely no idea that lot of GMP related studies are required. So none of the data would be useful in a regulatory agency." (Vice President, Dabur Research Foundation [44])*

The academic viewpoint is however different. Academics feel that industry science linkages suffer in India due to low uptake of university research by the industry and indifference on the part of the industry.

Low uptake of public research by industry

Industry has been criticized by academics for not taking up the scientific work done at universities or government institutes.

> *"We had few molecules and lots of patents but there are no takers because nobody is interested in new molecules. We have various collaborations with industry for contractual work or consultancy work but no joint collaborative work for new molecule research is going on." (Professor, NIPER [7])*

On similar lines, a professor in University of Pune who was involved in the NMITLI collaborative project with academic institutions says that the molecule developed under this programme has completed Phase 3. CSIR is trying to out-license the drug but the industry has not come forward to take it. Research interviewees' comment that though the funding by industry for academic research projects has increased in the past 2 to 3 years but pharmaceutical companies are not taking up research work done at the universities or

government institutes. The main reason is low expectations about the outcome of research output of the academic institutions.

> *"Dr. Reddy's used to sponsor lot of academic type of programmes. We had collaboration with Hyderabad University and that was essentially more of academic type of thing. We want some things to be done and they did it. We shared the expenses. As a company we were not expecting huge returns from that investment, it was almost like a charity and we did it." (Retd. President, Dr. Reddy's [28])*

The university system in India also suffers from poorly equipped labs and outdated instruments. The lack of interest from the industry severely cripples funding opportunities for the university researchers. University researchers make efforts to tighten their relation within industry circles by seeking fee for service projects to get funding support. Such interactions not only provide opportunities to make use of academic research but also provide opportunities to receive funds for infrastructure revamp or getting necessary equipment. Academics also feel that if the industry maintains close contact, it will be beneficial to know the technological developments taking place in the industry and enable them to decide on the direction of research. Academics lament the lack of initiative from the institution or industry to provide handholding that would allow making their research usable for commercialization.

> *"Very often our findings are left at the work bench and it is not because we do not foresee the application. This is perhaps because each individual scientist the way he is trained has his own limitations and so the institution can take the lead further in directions required to reach the end user. But that is not happening." (Professor, Jawaharlal Nehru University [12])*

An official in a public support programme feels that academics need assistance not just in the latter stages but even before the project is initiated. From his experience he feels that academics engage in very early basic research projects, which needs to be refined a lot for industry to take interest. Majority of pharmaceutical institutes take part in incremental innovation activities and process based research. Most of the research taken up by academics has no commercial value.

As per the Assistant Director of FICCI [24], the academics fail to undertake two necessary steps before embarking on a research project. One, there is a need for a thorough assessment

on the white areas of the technology. This requires a thorough patent search and needs assessment study which the researchers are not habituated to do. Most of the times, the researcher stumbles upon a research paper or patent either midway or towards the end of the project, which makes them realise the futility of the project. Second, there is a need to estimate the requirements of the project before hand and identify the hiccups and challenges that might come in the way. If there is a funding requirement or a need for special equipment this needs to be estimated beforehand. The academics fail to do contingency planning which leads to hauling the project midway.

A series of policy initiatives reflect the desire of the government to address these issues. Initiatives are focused to provide funds for revamping infrastructure and provide support through handholding schemes to bridge the existing gap between industry and academia. In order to realize this, it is important that academic scientists gear up to brace their research efforts in the right direction to make collaboration possible.

IP related issues

A strong appropriability regime provides two distinct advantages: *opportunities to exploit invention* and providing a *secure environment for information disclosure.* While opportunities to exploit invention promote patenting, secrecy and control over ownership of research assets, a strong legal system provides a secure environment for firms to exchange knowledge and research ideas without worrying about opportunistic behaviour. In this view, 'opportunities to exploit' promotes closed innovation while a 'secure environment' promotes openness in the way firms innovate. It thus becomes pertinent to explore which factors in an appropriability regime outweigh others in the formation of open innovation networks in the pharmaceutical sector. The findings show that three intellectual property related issues act as barriers to open innovation networks a) preference by researchers in public institutions to disseminate research results through publications b) poor infrastructure support and c) patent ownership issues. The figure below is a representation of the important IP related issues that act as barriers to open innovation in the Indian ecosystem.

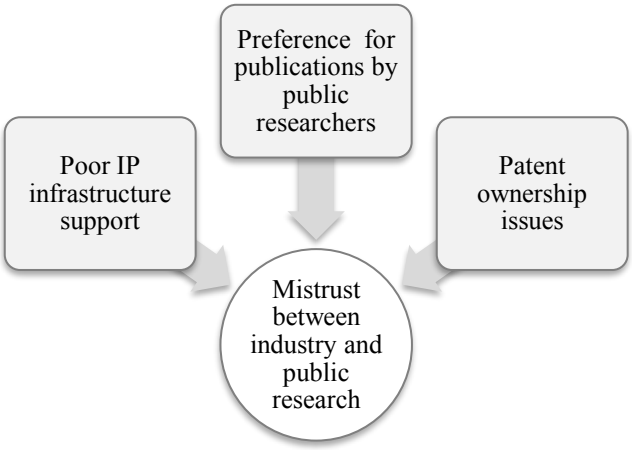


Figure 29: Important IP related barriers

Preference by scientists in public sector to disseminate research through publications

The most pervasive form of appropriability mechanism in pharmaceutical companies is patenting. In sharp contrast to this, researchers in the Indian universities and public labs have the propensity to publish their research work and avoid the patent route. Faculty decisions to publish instead of patent are driven by open science attitude, philanthropic motive to distribute knowledge and for career progression in universities. Academic inventors believe that public research is funded by taxpayers' money and they in turn are obliged to ensure that the fruits of the research flow back to the society. Many academics feel that patenting is in conflict with the open science norms that is associated with rapid disclosure of research results and an environment of knowledge sharing (Partha and David, 1994).

> *"I am not crazy about patents. Patenting is for revenue and recognition. If my clients are happy with my work, that itself is a reward for me." (Professor, University of Mysore [1])*

This difference in opinion between academics and industry causes much friction. In industry, scientists recognize the need to be secretive about research results, which are to be patented and take precautions to prevent information leakage, otherwise, it becomes prior art and the invention will have no value (Retd. Vice President Formulations, Ranbaxy [27]). Another important reason for researchers favouring publications is that in most of the Indian universities and public research labs, the reward system is based on quantity of publications.

> *"For scientists in public research labs, publications are more important for their progress. Companies are not interested in publications; patents and*

research output is more important for our progress." (Vice President, Piramal [33]).

Poor IP infrastructure support

Most of the universities in India do not have a formal infrastructure in place to allow academic researchers to avail opportunities for commercial utilisation of scientific research. Academic scientists are often unaware of how to manage the process of patenting which adds to the impediments in collaborating. A formal patent policy, which encourages universities to protect research results and a patent department to facilitate patenting, are generally missing in most of the Indian universities. Leading institutions in India such as IIT Delhi and NIPER have established a technology transfer department, which enables patenting and facilitates knowledge transfer activity from the university to firms. However, in many of the other Indian universities the concept of patenting is still new.

"Universities are not geared up on intellectual property (IP) part […] as far as IP infrastructure in the university is concerned it is still evolving not developed at this moment." (Retd. Vice President Formulations, Ranbaxy [27])

The government has initiated patent awareness programmes and IP departments are being set up across the nation. National Research Development Council (NRDC) also facilitates patenting to university researchers for a small fee. Biotechnology Industry Research Assistance Council (BIRAC), which has many public private initiatives, feels the need for strengthening the patent infrastructure in universities to remove impediments in collaborative efforts.

"BIRAC has come forward now to help and I think we really have to set up these technology transfer officers and IP officers across the country to help the university researchers. Once they know the value of their IP, they will be more confident in collaborating with the industry. Their only apprehension is that if we work for an industry, our IP will be taken away and we would lose control of our research assets." (Advisor, BIRAC [21])

Increasingly, universities are now realizing the need for patenting and steps are being taken to catch up in this direction.

"The concept of patenting is a new phenomenon here compared to the rest of the world. We have been earlier very conservative when it came to dealing with IP but I suppose we have understood the need for creating and capturing value through formal intellectual property." (FITT, IIT Delhi [10])

Patent ownership issues

Sharing of intellectual property rights poses a bigger problem for cultivating collaborative relationships. The general finding is that firms do not want to share patents with academic institutions. They are willing to collaborate for consultancy projects but not engage in long-term projects that might result in patent sharing agreements. As the director of a public partnership initiative points out, the trend by Indian firms is to in-license a technology or knowledge from academics and undertake in-house research in silo. This allows firms to retain control of their research work (Advisor, Department of Science and Technology [20]). Comments by industry professionals and experts underline the importance placed by firms to retain control of intellectual property assets within the company for potential out-licensing deals.

"The issue is the ownership of the technology, molecules the ownership or any kind of platform they are developing. The transparency is not there on who is going to own? If the assets are coming from a pharmaceutical company, they feel that academic is just doing a service. An academic professor says that he is not doing just a service. He is helping you to understand what a molecule does in the biology field. So he or she might not be willing to give up the understanding." (Senior Director, Pfizer [48])

An industry expert notes that research partnerships are almost non-existent because of IP sharing issues (Expert, Drug Discovery Research).

Trust and cultural issues

Fukuyama (1995) attests that economic activity of a company is conditioned by the level of trust inherent in a society (Fukuyama, 1995). The empirical assessment provided in this section uncovers that lack of trust and cultural issues impede formation of innovation networks in the pharmaceutical ecosystem. Consider the following vignettes from the pharmaceutical innovation system:

"Whenever we present in conferences, the industry people do come and say we are really keen on collaborating with you. But we need to have proper MOUs or statements because ultimately its commercial for them and for me it is my intellectual input, which they can take for nothing and will rake it forever." (Professor, University of Mysore [1])

"It is in the nature of the business. I can't trust anybody in the business I am not in the business of trusting. I am in the business of protecting my assets I can't trust. […]. Intellectual property is all about secrecy and I have to protect that secrecy, its not open source." (Chief Scientific Officer, Curadev [26])

"The apprehension among academics is that if we work with an industry some body will take away our IP and we would not have any control on it." (Advisor, BIRAC [21])

"Universities and government institutes intend to believe that everything that a pharmaceutical company does is only for profit some way they are going to cheat them. […]. Our own nanoxel, which is now commercial, actually came from Delhi University. Of course that was also ridden with certain controversies […] because the university claimed that they did not get due recognition. We as a company made the claim that what you gave was completely modified. Again mistrust. So it did come from collaboration but it wasn't the best of collaborations and the IP was completely ours. That was the part of the deal." (Vice President, Dabur Research Foundation [44])

The common thread that runs through these four apparently unrelated vignettes from different actors in the innovation system – academic, government official, senior management in SME and established firm reveal that there is high level of mistrust between the innovating entities. A professor in Jawaharlal Nehru University remarks that the cultural mould existent within the Indian system acts as a barrier for free interaction, which is required for effective translation of scientific findings into end results. During the process patent regime from 1970 to 2005, there was a long period of disassociation between the public institutions and private industry. Sporadic cases of opportunism, tech transfer issues and different mind-sets have fuelled mistrust between these institutions.

One of the chief problems afflicting the innovation system is the *history of opportunistic cases* and sour collaborations, which has affected the spirit of collaboration. Discussions with academics and firms have pinpointed many cases of opportunistic behaviour where the academics felt cheated as they have not been given their due share. In contrast, an industry professional claims that in the past there were instances where the industry felt cheated, as *technology transfer* from the public sector has not been very smooth. False claims are made during tech transfer issues, which are not reproducible. In some cases, the upfront payment was also made only to realise that the technology was not working (Vice President, Dabur Research Foundation [44]).

The other contributing reason for mistrust is also the different ways of working between public scientists and industry. Academic researchers work at their pace and are *free floating*. On the other hand, the industry works under very tight timelines. There are many cases where the academics have failed to deliver project results (Professor, University of Hyderabad [2]). The laid back attitude of academics and prolonged time taken by public institutions extends the project without yielding significant output (Vice President, Piramal [33]).

An important cultural related issue, which has relevance to this context, is the *tendency of researchers to work in silo*. One of the strong impediments identified in a number of interviews is the inability of the academics to form teams and work in a harmonious manner. The common observation is that academics themselves do not network among each other for collaborative research. A professor of Jamia Hamdard adds that researchers within a university do not collaborate and nor do they share their facilities. As a professor in University of Mysore points out that there are disagreements even for sharing instruments. The challenge lies in integrating academic and industrial factor, even integrating people within academics. A classic analogy shared by an expert sum up the picture.

> *"Indians are very poor team players. Historically, we love working in isolation we work in silence. If you look at Indian classical music, do you see any orchestra? But look at the western classical, everybody has to play in unison so that you build up something." (Associate Director, Jubilant Chemsys [46])*

The arguments advanced so far suggest that mind-set of academics, different ways of functioning, lack of punctuality, history of opportunistic behaviour, proclivity to work in silos

are all barriers to open innovation networks between industry and academia in India. The low technological opportunities and usefulness of research output has raised questions on the quality of research done at the university and the competence of academic research. On the other hand, fear of opportunistic behaviour by the industry and relinquishing control over research assets negatively impacts future collaboration between the entities. The common thread, which runs across all the snippets of data presented shows the fragile innovation networks present between the entities of the innovation system.

6.1.5 Summary

This section provided an overview of the nature of relationships between local innovation entities. The relationships that exist between technology and sciences are complex in the Indian pharmaceutical innovation system. While non-research networks form the bulk of interactions, post 2005 there has been growing interlinkages between industry and university/government labs for research purposes. *A closer introspection provides evidence of predominance of non-research networks and research networks based on consulting/fee for assignment services.* This is in contrast to the research engagements seen elsewhere in the developed part of the world.

Policy initiatives to improve science industry linkages have been high on the policy agenda of the Indian government. However, such initiatives have failed to catalyse the interactions between public and industry. Data analysis based on number of formal public private partnerships initiated through policies reveals that *standalone funding projects* are more in number than projects with an academic partner. The analysis of research partnerships and the interview data point that two strategic motives – *funding* and *knowledge* drive open innovation in firms.

The second level of findings entails a deeper understanding of the problems in the innovation system that mitigates the formation of innovation networks. Three reasons emerged important in deterring the formation of local innovation networks – a) low technological opportunities, b) appropriability related issues and c) trust and cultural issues. In order to mitigate these issues, there is widespread formation of informal *'personal networks'*.

Firms engage with the academic community through personal networks that allows them to build trust through personal interactions and leverage the research expertise. *Trust,* plays an important role in this context as it ensures that collaborative research is done with a person

who is really ‘knowledgeable’ and is dependable. It also provides access to research work of scientists involved in a particular stream of research and circumvents the need for formal contracts and bureaucratic delays. Lastly, such interactions serve as control mechanism to reduce conflicts related to patent sharing and ownership.

The data also demonstrates that *asset position of a firm has little influence on the local innovation networks* formed in the Indian setting. Contrary to the literature that supports the contention that small and medium sized firms are more likely to engage in research partnerships than large pharmaceutical firms, the findings revealed no significant difference in the approach of these pharmaceutical firms in collaborating with local innovation entities. The cases of Indian firms demonstrate that few firms are more open than others and have formed successful collaborative partnerships for research in novel drugs. The differences between the firms in the extent of open innovation networks formed can be attributed to the *dynamic capabilities* of these firms.

6.2 Formulating Open innovation strategies and pathways

This section aims to answer the research question: How does national innovation system and asset position of a firm influence adoption of open innovation strategies for novel drug research in the Indian pharmaceutical sector? This question has been answered by assessment of strategies pursued by firms in drug discovery and drug development stage and comparison of strategies employed by established and SMEs. Indian firms have pursued inbound, outbound and collaborative innovation in different measures. This analysis undertaken in this study unearths two important findings of significance:

a) Openness in companies varies with the stage of drug research. Empirical evidence shows that Indian companies are wary of opening up their firm boundaries at early stages of drug research and open up at later stages to outside partners.
b) The asset profile of a firm plays an influencing role in the type of open innovation strategies pursued and the stage at which firms open its research to outside partners.

The following pages elaborate on the findings from analysis of primary and secondary data to demonstrate that Indian pharmaceutical firms adopt a myriad of possible open innovation strategies for new drug research. The empirical findings reveal four important interrelated factors labelled as 4Rs that play a critical role in shaping openness in these innovating firms. This section concludes with four unique open innovation pathways adopted by Indian firms that is a combination of open innovation networks formed by firms and open strategies pursued at different stages of research. The prominent four open innovation pathways adopted by Indian firms are the outcome of tension between the 4Rs.

6.2.1 Open innovation strategies

Pharmaceutical drug research is divided into two important stages – drug discovery and drug development. The drug discovery process involves discovering a new compound and the drug development phase establishes safety and efficacy of the drug candidate in humans. These two activities require quite different sets of skills and resources (Henderson and Cockburn, 1996). Additionally, they need enormous funds to progress the drug pipeline through different stages of developments. It has been well established through various empirical studies that difference in ownership of assets between large established firms and SMEs and

distinct requirements at each stage of new drug research has a conditioning effect on the boundary decision of firms (Pisano, 1990; Rothaermel and Deeds, 2004). Typically, firms seek external sources across boundaries during the drug discovery stage for exploratory purpose (seeking new knowledge) and during the development stage for exploitation (commercialisation of innovation) (Rothaermel and Deeds, 2004). Taken together, this literature suggests that factors, which affect boundary decisions, are influenced by stage of drug research and the asset profile of firms. This subsection will enumerate how the leading and small and medium scale pharmaceutical firms are using open innovation strategies for the research of innovative drugs in different research stages.

Inbound Innovation

It has been observed that Indian firms engage in open innovation through two ways: *sourcing* and *acquiring*. Sourcing refers to drawing knowledge, ideas, technical knowhow and expertise from external sources of innovation while acquiring refers to obtaining expertise, technology or product through in-licensing or other mechanisms (Dahlander and Gann, 2010).

Sourcing

Sourcing involves non-pecuniary engagements with external partners (Dahlander and Gann, 2010) and there is not much evidence in the primary data for such engagements. However, it is not correct to say that such engagements do not exist at all. Sourcing of research ideas and technical help from local sources of innovation is fairly limited in the Indian scenario. The findings in Section 6.1.4 show that uptake of academic research through industry is quite low. The most prevalent form of research engagements between industry and science involves pecuniary based consulting and fee for services.

Findings reveal that industry scientists consult with their academic professors whenever they require technical help or specific knowledge. The companies may source in research ideas or seek solutions to scientific problems from universities and research institutions. International universities and research institutions are also used sometimes to validate findings or get endorsement for research results.

Another evidence of non-pecuniary engagements is the interaction with scientists through virtual consortiums. In most cases, membership to these consortiums is free or for a nominal fee and serves as a vital platform to engage with researchers for knowledge interactions. At

later stages of research, public funds and other sources of funding are used for further development.

The partnership data provided in Table 31 shows few non-pecuniary sourcing projects undertaken by Indian firms. These findings demonstrate the progression of Indian firms to move from a closed innovation approach to open innovation by sourcing in knowledge and information from outside sources.

Table 31: Sourcing by Indian pharmaceutical firms at drug discovery stage

Company	**Collaborative partner**	**Research Objective**
Established firms		
Ranbaxy	Medicines for Malaria Venture (MMV)	Research collaboration for anti-malarial drug
Small and Medium Enterprises (SMEs)		
Advinus	Geneva-based Drugs for Neglected Diseases initiative (DNDi)	Drug discovery and development for visceral leishmaniasis (kala-azar)
	Genzyme Corporation and Medicines for Malaria Venture (MMV)	The collaboration seeks to develop new, improved treatments for specific patient groups most at risk for malaria (2008)
Invictus	Indian Innovation Research Centre	Research partnership for discovery of cancer drugs

Ranbaxy had formed successful collaboration with the research consortium 'Medicines for Malaria Venture' (MMV) involving researchers from the US, UK, Switzerland and Australia for discovery of anti-malarial drug. Advinus has also formed a research alliance with Medicines for Malaria Venture (MMV) & Genzyme to develop new treatments for malaria. Invictus Oncology, a start-up company, has been novel in its approach of partnering with the scientific community. It has partnered with India Innovation Research Centre (IIRC), a not for profit virtual research institute, which has researchers and scientists from all over the globe. The company hopes to take forward any research output, which comes out of this partnership.

The general opinion among the research community is that companies tend to focus on in-house drug discovery, despite the presence of various options that firms can use within and outside the local innovation system to source in knowledge. Unlike the west, where open innovation models are being experimented through crowd sourcing by Eli Lily, GSK at exploratory phase of drug discovery (Khanna, 2012), Indian firms are relatively closed during

drug discovery stage. Senior management of companies have stressed the point that most of the development related to drug discovery research is carried out internally.

In-licensing

In-licensing is a popular approach used by leading pharmaceutical companies of the world to fill internal project portfolio gaps (Schuhmacher et al., 2013). In the Indian setting, none of the case companies except Ranbaxy has exercised the in-licensing option. However, in recent years, the trend towards opening up to the in-licensing option has been observed. SMEs like Advinus and Invictus Oncology have expressed their interest in opening up to any in-licensing opportunity if it meets the strategic goals of the company. Piramal had evaluated many packages of new molecules for a potential licensing deal though the company could not finalise on any research asset to buy.

> *"In-licensing as an option was also considered. The process was initiated for in-licensing with the idea that if we can get some early stage molecule then we can develop them in-house. We initiated this but we have not finalized any deal till date." (Vice President, Piramal, [33])*

Unlike other companies, Ranbaxy had successfully in-licensed a drug 'arterolane maleate' from Medicines for Malaria Venture (MMV) with a worldwide, royalty-free license to develop and commercialise the compound. The case of Ranbaxy was distinctive as the company was involved in the project from the early stages of research. Arterolane, a new class of compound was invented by a group of scientists from US, UK, Switzerland and Australia, coordinated by the Medicines for Malaria Venture (MMV). Ranbaxy's team of scientists worked in close collaboration with scientists from the University of Nebraska Medical Centre, Monash University and the Swiss Tropical Institute in identifying a candidate for development. The disappointing clinical trials resulted in MMV withdrawing from the project. Subsequently, Ranbaxy in-licensed the compound for further development. The company managed to launch the arterolane in a fixed dose combination with piperaquine (Brand name: Synriam) in 2012. The first NCE launched in the Indian pharmaceutical landscape is thus a successful exemplar of in-licensing combined with in-house R&D development.

In-licensing, however is not a popular innovation strategy in the Indian pharmaceutical scene due to the following reasons: a) perceived risk and b) high cost. Both established and SMEs

have perceived in-licensing strategy to increase risk in a drug discovery project. The inherent risk of a drug discovery project coupled with the risk of investing funds in drug candidates not discovered in-house, makes in-licensing a less preferred option. The lack of experience of purchasing molecules from outside sources also makes in-house R&D a more dependable option.

> *"In case of in-licensing, you are buying somebody's molecule and putting in your own money to develop that to completion. So whenever you are purchasing or in-licensing any molecule, then we need to thoroughly look at what data is there as we are aware of the risk that the project carries. So all the due diligence activities etc., have to be done very carefully before you could in license these projects." (Senior Group Leader, Piramal [30])*

On the other hand, limited financial resources in companies limits their options to in-license.

> *"We are open to in-licensing if there are any interesting molecules but being a start-up company we cannot pay millions of dollars that large pharmaceutical can pay." (Senior Management, Invictus Oncology [40])*

It can be thus concluded that inbound innovation that occurs through *sourcing* innovation or *in-licensing* is not so pervasive among the established firms. The case of Ranbaxy-MMV collaboration, which led to the in-licensing and successful launch of a new chemical entity, is an excellent example of how the in-licensing strategy can be leveraged in favour of the company. However, this has not inspired other companies to leverage collective competence of a network of external scientists through sourcing or in-licensing route. The section on sourcing shows how sourcing has been used in a limited manner within the local innovation environment to access know-how of public research scientists. The evidence from project data and the detailing of problems existent in the local innovation networks point towards the proposition that firms are not using the inbound innovation in early stages of innovation process. Important factors that have been identified in the data analysis as key triggers for closed innovation in the Indian pharmaceutical firms are: *confidence of firms in their in-house research, need for secrecy, avoidance of conflicts related to IP and less reliability on compounds in-licensed from outside sources.* Indian companies are cautious of opening up the innovation process to different sources of innovation in the early stages of discovery. With the multinational companies, the possibility of a takeover also looms large.

"The fact is that large companies have come in and acquired Indian companies. So in that way they were not really true collaborations. Because of these past cases, the Indian companies have also become a little wary of collaborating with multinational companies." (Vice President, Dabur Research Foundation, [44]).

Outbound Innovation

This type of open innovation strategy refers to commercialisation of innovation through selling or out-licensing. In 1997, Dr. Reddy's created history when it became the first Indian company to develop a drug in-house and out-license its two diabetes molecules to Novo Nordisk for further clinical development. It was in early 1990s, that the company had established Dr. Reddy's Research Foundation in Hyderabad and initiated its new drug discovery programme. As part of the out-licensing agreement, the company received an upfront license fee with entitlement for milestone-based payments. However, the agreement hit a roadblock, when Novo Nordisk suspended clinical trials on both compounds due to unsatisfactory results. In yet another out-licensing agreement with Novartis in 2001, Dr. Reddy's licensed out DRF 4158 — a dual-acting insulin sensitizer. In 2003, Novartis also stopped further development of this compound.

These initial setbacks affected the Indian industry in two ways: Firstly, it led to Dr. Reddy's laboratories to introspect and realign its strategy. The company took a strategic decision to out-license molecules at more advanced stages of development (after preclinical stage or initial stage of clinical trials) to gain more confidence about the strength of its innovation. Secondly, it opened the doors for other companies to pursue out-licensing as a viable strategy. Ranbaxy, which also initiated its drug discovery programme in the early 1990s, undertook its first out-licensing deal in 2002. Table 32 lists some of the out-licensing deals stuck by the companies with foreign companies.

Table 32: Out-licensing deals by case companies

Year	Company Name	New Drug Research Phase	Buyer Company	Details of the agreement
Established firms				
2002	Torrent	Early stage Clinical Development	Novartis	• Out-licensing of novel drug compound Advanced Glycation End-Products (AGE) Breaker.

				• Early-stage R&D activity up to pre-defined end-points by Torrent • Option to acquire exclusive global rights for further development and commercialization by Novartis
2002	Ranbaxy	Phase 2	Shwartz Pharmaceuticals	• Ranbaxy out-licensed RBx 258 indicated for the treatment of BPH. • Exclusive rights to develop, market and distribute the product in US, Japan and Europe to buyer • Retention of rights to other markets and entitlement for milestone-based payment apart and upfront fees. • Further development stopped in 2004 by Schwarz Pharma
2007	Ranbaxy	Preclinical stage	Pharmaceutical Product Development (PPD) Inc., USA,	• Acquisition of exclusive worldwide license by PPD to develop, manufacture and market Ranbaxy's novel statin molecule.
Small and Medium Enterprises (SMEs)				
2010	Curadev	Drug discovery stage	US midsized pharmaceutical company	• Development by Curadev till drug target identification. • Transfer of rights to US partner at the candidate selection stage in exchange for milestone payments and royalties.

Indian firms, both established and SMEs have adopted the out-licensing strategy to generate revenues and utilise external partners for further development of research assets. The clinical development cost of the drug is too exorbitant to be funded solely by an Indian pharmaceutical firm.

> *"Earlier our goal was to discover a molecule, develop it into a drug within India, but over the period of years we have changed this pattern. In the last two years, we started trying to package molecules, at different levels for out-licensing…I think the company realized that the financial implications of developing a molecule although 40% lower in India as per global estimate, it is still very huge for an Indian pharmaceutical to sustain for a long time." (Senior Vice President, NCE Research, Piramal [31]).*

The risk for late stage failures has also prompted companies to out-license their molecules at subsequent stages. Interview data suggests that out-licensing emerged as an optional strategy when firms realised that the hiccups of drug discovery and development are much higher than

expected. SMEs, which have drug compounds in early stages of new drug research have emphasised that this is an important strategy, which they would consider in the next phases.

> *"We are working on out-licensing our internal molecules. We have a pipe line of molecules that we are working on out-licensing and hopefully that will happen soon." (Chief Scientific Officer, Advinus [35])*

Out-licensing is a preferred strategy among the Indian companies also because it allows developing molecules in-house in a closed manner, generate revenues and recover costs of research and development. Thus, along with intellectual property rights and ownership of molecule, risk of molecule failing in advanced stages is also transferred out. It also allows the company to earn royalty revenues in case the product is successfully commercialised.

Despite the benefits of out-licensing, the number of deals in recent years have gone down. Companies are now moving to more collaboration based agreements instead of out-licensing for multiple reasons. Firstly, out-licensing limits the licensor's awards by transferring a proportional measure of potential revenues (Reepmeyer, 2006). Additionally, an out-licensing deal at an early stage of drug discovery leads to lesser revenues as compared to molecules, which are out-licensed at advanced stages of development. Yet, the decision to out-license at a later stage requires substantial research effort, more funds, increased risk and binds the company to conduct sole research for a longer time.

Secondly, out-licensing implies relinquishing control over the molecule. This means companies can no longer exercise their control if the partner company decides to shelve the product at latter stages. The case of Torrent illustrates this. In 2002, Torrent out-licensed its novel age breaker compound to Novartis but development for this compound was stopped in 2005. Torrent then acquired back the rights to the drug and decided to develop in-house. Industry experts have mentioned that MNCs have the tendency to purchase patents or discoveries, which are remotely connected to their own discoveries and would then kill the product to avoid any potential competition. This makes companies cautious of out-licensing deals.

Collaborative R&D

The Indian pharmaceutical industry is now witnessing many collaborative deals to gain cost and resource effectiveness, and mitigation of R&D related risks. The most common type of

collaborative R&D agreement formed by the Indian firms is the co-development agreement (Reepmeyer, 2006). The basic premise of such agreements is the ability to utilise the resources of the external partner to develop internally developed molecules. The co-development agreements aim at sharing R&D risks and the synergies of both the partners are expected to lower the risk of the R&D project (Reepmeyer, 2006; Schuhmacher et al., 2016).

Research findings show that Indian companies enter into alliances with foreign firms to get funds for research more specifically for clinical development of the molecules. In recent years, a great number of collaborative deals are being signed in the early drug discovery stage. The co-development alliance has become a norm in the Indian pharmaceutical industry in recent times. The table below shows major co-development agreements formed by the sample Indian firms.

Table 33: Collaboration R&D (Co-development) agreements

Indian Company	**Phase of drug research***	**Year**	**Partner Company**	**Objective of the agreement**
Established firms				
Ranbaxy	Early stage drug discovery	2003	GSK	• Multiyear collaborative deal for research and development of new drugs in the area of respiratory and anti-inflammation.
Dr. Reddy's	Clinical Trials	2005	Rheoscience	• Agreement to jointly develop the NCE 'Balaglitazone' and share the cost of the third phase of clinical trials. • Rheoscience will file for regulatory approval from the US Food and Drug Administration and costs will be shared by Dr Reddy.
Dr. Reddy's	Clinial Trials	2006	Clintec International	• Agreement for co-development of Anti-Cancer Compound DRF 1042 undertaking Phase II and Phase III clinical trials • Dr. Reddy's retains the commercialization rights for the U.S and rest of the world markets excluding most of Europe including major European markets.
Dr. Reddy's	Preclinical stage	2007	Argenta Discovery	• Both parties will jointly develop the selected candidates for treatment of Chronic Obstructive Pulmonary Disease ("COPD") from the pre-clinical stage up to Phase IIa (proof-of-concept). • On successful completion of a Phase IIa trial, the companies may either license-out the candidate or continue further co-development and commercialization.
Dr. Reddy's	Preclinical stage	2008	7TM Pharma	• Agreement to jointly develop pre-selected targets from the pre-clinical stage up to Phase IIa (proof-of-concept). • Companies may either license-out the candidate

				for further development or continue co-development and commercialization.
Torrent	Early stage	2005	AstraZeneca	• Research collaboration agreement aimed at discovering a novel drug candidate for the treatment of hypertension. • Agreement includes success based R&D milestone payments, royalties based on the commercialization of the drug candidate and co-marketing rights in India.
Aurigene**	Early stage drug discovery	2014	Orion Corporation	• Under the terms of the Option Agreement, Aurigene receives upfront payment, licensing fee, milestones and royalties upon exercising the option for rights to Pan BET and Selective BET Bromodomain inhibitors programme. • Orion funds the selective BET programme and Aurigene is eligible for development phase milestones and royalties.
Aurigene**	Early stage drug discovery	2015	Curis, Inc.	• To conduct discovery and preclinical activities, IND-enabling studies and Phase 1 clinical trial. • Clinical development, regulatory and commercialization efforts worldwide, excluding India and Russia.
Small and Medium Enterprises (SMEs)				
Advinus	Drug discovery	2006	Merck	• Advinus receive an upfront payment and potential milestone payments and royalties for developing clinically validated drug candidates related to metabolic disorders. • Merck has the rights to advance to the drug compounds in the later stages of clinical trials.
Advinus	Drug discovery	2008	Ortho-l-Janssen Pharmaceuti-	• Advinus is responsible for drug discovery and early clinical development until the completion of advanced second phase of clinical trials • Advinus receives an upfront payment along with milestone payments besides possible royalties upon commercialization by the partner company (2008)
Advinus	Early stage drug discovery	2014	Takeda Pharmaceuti-Company Limited	• Advinus is responsible for leading the programmes to create optimal IND ready compounds for pre-defined targets in the area of inflammation, CNS and metabolic diseases. • Takeda is responsible for the development and commercialization of these candidates.
Curadev	Early stage drug discovery	2015	Roche	• Research collaboration for Curadev's novel drug molecule indicated for cancer. • Roche will fund future research, development, manufacturing, and commercialization costs and will also provide additional research funding to Curadev for support of the research collaboration.

**Phase of new drug research at the time of formation of research partnership*

*** Subsidiary of Dr. Reddy's Laboratories*

As depicted in the table above, the Indian firms have varied in the way these agreements have been formalised. In the early 2000s, some of the agreements formed by Dr. Reddy's aimed at establishing a partnership to share costs and risks in the clinical development of the molecules. These agreements were formed in late stage clinical trials (Phase 2 and 3). However post 2005, the industry is witnessing a shift in forming strategic partnerships at early stages of drug discovery. Empirical evidence indicates that in all these partnership agreements, Indian firms undertake internal proprietary drug discovery research and then seek a co-development alliance with a foreign multinational firm. A typical arrangement in all these alliances is that the Indian firm undertakes drug discovery research up to a specific stage and the partner company undertakes the clinical development and commercialisation of the molecule.

The rationale of Indian firms to form co-development agreements are a) gain access to capital through upfront fees and milestone based payments b) mitigate risk c) get access to regulatory and marketing capability to enter newer markets d) potential of royalty payments in case of commercialisation, e) get territorial rights in specific markets and f) retain control. The intellectual property right in most of these co-development agreements is transferred to the partner company.

> *"Most of the agreements are co-development where companies undertake research together. In the end, there will be various clauses like, if it comes to phase 1, the partner will give X million and if it goes to phase 2, it will be Y million. There will be also agreement that if the drug comes to the market, the Indian company may have rights to market in India or Asia. Those kinds of agreements are there but IP doesn't rest with the company. The moment they pay milestone based payments or royalty, it means the rights belongs to someone else." (Professor, University of Hyderabad [2])*

Indian firms acknowledge that in most of the cases the agreements with foreign firms are not in equal terms. Despite this, co-development arrangement has become the most popular way of advancing the cost intensive risk prone drug discovery programmes among the Indian pharmaceutical firms.

A comparison of strategies of established and SMEs show that the *asset profile* of a firm shapes the stage at which co-development alliances are formed. Large pharmaceutical firms

such as Dr. Reddy's have carried out research till advanced stages such as Phase 1 and Phase 2 before getting into a co-development partnership. SMEs, on the other hand, constrained by resources aim to start the co-development deal as early as possible in the drug discovery stage. A case in point is the recent deal of Curadev with Roche for the lead immune tolerance inhibitor, which took place in preclinical stage.

The other advantage, which large pharmaceutical firms get, is the right to market the drug in case of commercialisation of the molecule. As Table 33 shows large firms with well established marketing and regulatory capabilities are able to retain commercialisation rights in key prominent markets such as US and India. On the other hand SMEs that are mostly research based companies and lack complementary assets such as marketing and regulatory capability are dependent on partner firms to commercialise their invention.

6.2.2 Summary

This section provides an overview of how the Indian pharmaceutical sector is moving towards an open innovation approach in the research for new drugs. The choice of open innovation strategies demonstrates that various key factors influence a firm's decision to adopt open innovation practices. The key strategic considerations that influences a firm are whether to opt for open or closed innovation model, the type of open innovation strategy to pursue and the stage of drug research at which firms should open up their boundaries for external partners. These critical decisions decide the extent and type of open innovation pursued by a firm. The decision to open up their boundaries is guided by reasons to gain knowledge, funds for research, reduce risk and channelize options for commercialization.

The shift to a strong appropriability regime in India has unlocked various opportunities for firms to commercialize their invention and provide a safe environment for inbound and outbound innovation. The traditional and successful linear model wherein the basic research conducted in public institutions benefits the innovative capacity of firms stands challenged today in the wake of multiple avenues such as bio park, bio clusters, spinoffs, scientific advisory boards, foreign research institutes/universities that has provided new means for firms to use academic knowledge and information. Indian firms realize the need for linkages with external partners to fill in skill deficits and innovation gaps and attest to the importance of open innovation.

Pharmaceutical innovation is complex and there are various influencers, which propel a company to choose one open innovation approach over another. However the most important factor, which has emerged to be of key concern among the firms is the protection of IP. Companies prefer to open up only after their intellectual property is protected and choose those open innovation strategy that allows them to protect their intellectual property, ward off opportunistic behaviour and leverage opportunities to commercialise their innovation. Till then the companies prefer to keep their innovation process closed which explains the minimalistic interactions of the companies at the drug discovery stage.

7 Discussion

The main research question addressed in this dissertation is, how does national innovation system and asset position of a firm influence openness in the Indian pharmaceutical sector for innovation in novel drugs? So far, the analytical focus has centred around three themes – the influence of appropriability regime and institutional policies in stimulating the national innovation system for research in novel drugs, the formation of innovation networks formed within the local innovation system and open innovation strategies adopted by the Indian pharmaceutical firms. The framework of open innovation synthesizes the key findings of this research and brings together the key drivers, underlying factors that determine the openness in firms and the pathways adopted.

The chapter is organized as follows. First a brief overview of open innovation framework is presented. This is followed by a discussion on the relevance of key drivers of open innovation in the Indian context. The next section elaborates the role of four factors or 4Rs in influencing the type of open innovation pathways adopted by firms. The patterns observed in the data enable to identify four different types of open innovation pathways prevalent in the sector. These pathways are presented and described in the last section of this chapter.

7.1 Summary of findings: Framework for Open innovation

The Open Innovation Framework brings together three key *drivers* for open innovation, four *factors* that influence the extent of open innovation and four types of *open innovation pathways* adopted by firms. The Indian pharmaceutical innovation system is moving towards an open innovation model especially for new medicine research and supports the trends of open innovation highlighted in innovation literature (HW Chesbrough, 2003; Kneller, 2010). The case study of Indian pharmaceutical sector shows how innovator companies are using open innovation as a solution to the address the complexities involved in research for novel drugs.

The change in patent regime has brought about important changes in the innovation landscape. It has led to initiation of research for novel drugs by Indian pharmaceutical firms

and growth of new start-up companies for drug discovery research (Chaudhuri, 2007; Kale and Little, 2007). A strong *appropriability regime* and facilitating *institutional environment* go hand in hand in stimulating open innovation. Appropriability regime with strong patent laws stimulates firms to innovate, codify knowledge and capture benefits. The more complex the innovation, the more is the need for the firm to seek patent protection and seek profit from innovative efforts. Strong patent laws also allow sharing information in a secure way important in out-licensing deals or negotiations for co-development agreements. Appropriability regime is hence an important driver for open innovation. The Indian case illustrates this phenomenon perfectly. The shift in patent regime saw firms increase their level of innovation and open up the innovation process to exploit their innovation through various ways.

A facilitating *institutional environment* is imperative to rejuvenate science-based systems and improve the contribution of public research system to innovation. Institutional policies serve as important parameters to stimulate innovation, industry science relationships and promote local innovation networks. Distinctive institutional contexts have shaped science and innovation in India and facilitated technological progress. During the first appropriability regime, the facilitating institutional policies enabled the setting up of a vast institutional R&D infrastructure and fostered the nascent pharmaceutical industry. The institutional environment in the second appropriability regime focused on reshaping the science and technology system and promoting long-term research and innovation.

The shift to a product patent regime and the need for radical research had an effect not only on polices aimed to promote research and innovation but importantly on the incentives to promote collaboration between science and academia for pharmaceutical innovation. Different public policy initiatives have been initiated to stimulate collaboration for research and provide funding support. There have been some notable public private partnerships in the past decade for new drug research. However, the general strength of collaborations within the local innovation system is still weak. The internationalization of R&D and the growth of contract research business have supported the formation of international networks of local Indian companies with research institutions, universities and foreign companies based aboard. Open innovation has thus increased its extent from local innovation network to a complex web of international networks.

When an industry or technology view is new, a variety of strategic approaches for technological innovation are experimented. A firm's strategy outlines its objectives and contours the actions of firms. The theory of dynamic capabilities provides the link between its core capabilities, innovation and the strategy of the firm (Nelson, 1991). Firms within the local innovation system that face the same set of factors differ in their degree of openness. The dynamic capabilities of a firm play a salient role in this respect. It is the *dynamic capabilities* of firms that contours a firm's strategic objective and provides an explanation as to why some firms are more open than others. The central reasoning of this research study is that the macro environmental forces a) appropriability regime b) supportive institutional policies and c) dynamic capabilities at firm level constitute important drivers that push firms to undertake open innovation. In this way, the important drivers identified in this research play an important role in open innovation.

Open innovation allows a firm to formulate combinations of strategies and approaches to undertake innovation. Firms face tension in deciding whether to open up the innovation process to external partners at early stages of research that may lead to probable loss of secrecy, hamper strength of intellectual property rights or remain closed to increase a firm's ability to capture value from innovation. Openness yields reduced development time, and offers incentives to reduce costs, risks and access knowhow. This paradox is surmised through the *4R factors* that work in opposite directions to determine the pathways, which firms choose to follow.

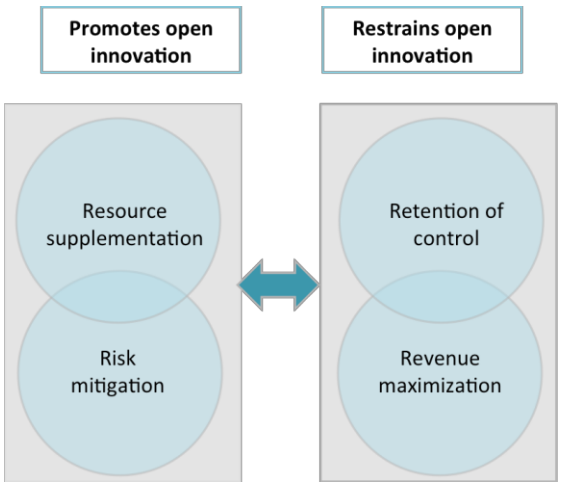
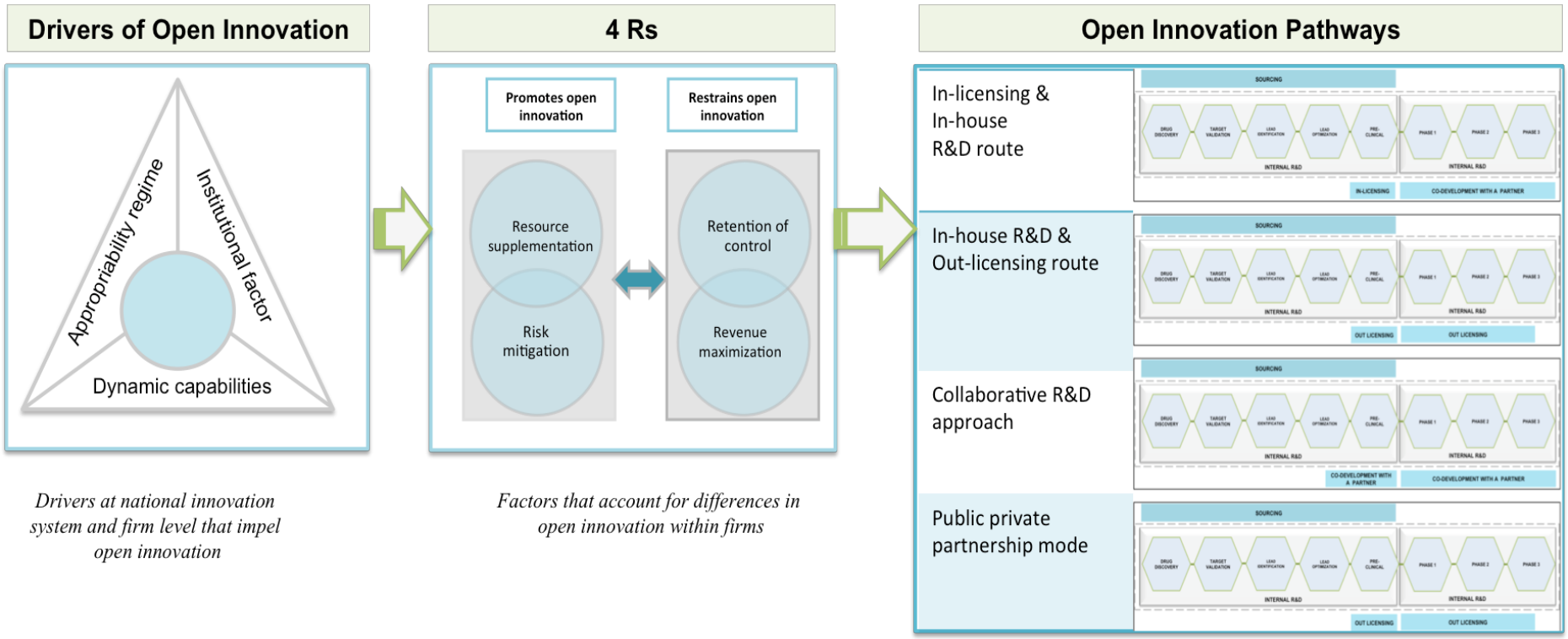


Figure 30:Opposing tensions at firm level as shown through the 4Rs

The type of open innovation strategy pursued by a firm and the level of openness a firm displays within its local ecosystem is influenced by these 4Rs. A strong appropriability

regime may not favour open innovation at all times. During the early stages of drug discovery, when research protection is not guaranteed, companies are wary of open innovation. **Firms pay considerable attention to retain control of their research assets through intellectual property and opt for a strategy that maximises revenues. In the latter stages, the need to supplement resource gaps and mitigate risks steers a firm towards open innovation.** In this way, Indian companies have amalgamated the conventional closed R&D model with open innovation to tackle the challenges that cannot be addressed through the closed innovation route.

The empirical findings of this study lead to an open innovation framework that enables to understand the critical *drivers of open innovation* and *influence of 4Rs* that determine the level of openness and shape the *open innovation pathways* adopted by firms. These pathways are a mix of various open and closed innovation phases and diverse open innovation approaches employed across different stages of research.



Drivers at national innovation system and firm level that impel open innovation

Factors that account for differences in open innovation within firms

Distinct open innovation pathways differentiated by open innovation strategy, local innovation networks and stage of research

Figure 31: Framework for Open Innovation

7.2 Drivers of Open Innovation

The case studies demonstrate that main drivers of open innovation within the local innovation system are strong appropriability regime, facilitating institutional environment and dynamic capabilities of the firms.

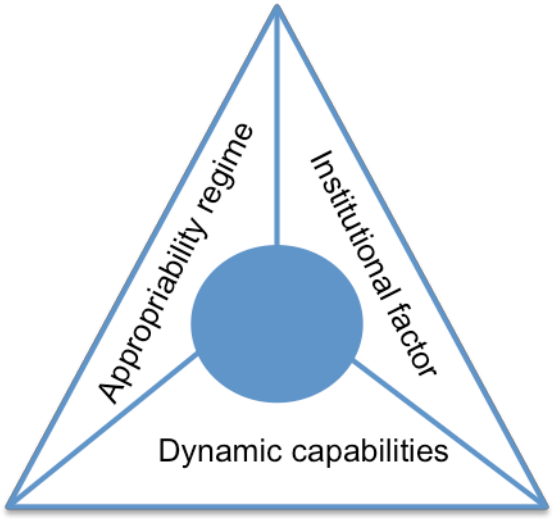


Figure 32: Drivers of Open Innovation

7.2.1 Appropriability Regime

Within the national innovation context, appropriability regime plays an important driver for open innovation. When intellectual protection is guaranteed, inventors use multiple pathways to gain economic returns on their invention (H Chesbrough, 2003b; West, 2006). This was evident in the Indian pharmaceutical sector that shows leaps in technological capability to move in different domains. The shift in patent laws saw a shift in reliance from generic only research and manufacturing activities to undertaking of research for value added generics and new drugs. Another notable feature was the increase in contract research business activities. The technological capabilities of companies have gradually enhanced to allow them to scale up their contract research activities from stand alone research activities to integrated research services. Most of these Indian research based companies focus on multiple drug discovery programs that range from proprietary drug discovery programs to contract research work with various partner firms.

The evidence from patent data supports that the nature of innovation in Indian firms has progressed from process innovations to incremental and radical innovations in the past two decades. This is verified from the less number of process patents and increase in number of secondary product patents and basic product patents filed for new drugs. The ability of the Indian firms to adapt to the challenges and leverage the opportunities at each of the appropriability regimes has significantly influenced the dynamics of innovation. In this way, the Indian pharmaceutical sector resonates more with the latecomer innovator firms of developing countries (Michael Hobday, 1995) as it made the stepwise technological progression from being importers of drugs to manufacturers of simple formulations and progressed towards development of imitation capabilities to produce generic drugs. In the late 1990s, established firms initiated new drug research and made the technological leap towards new product innovation. Post 2005, the sector witnessed the emergence of small research based companies and shift in focus towards research for novel drugs in many public research institutions.

Patenting supports exploitation of innovation and provides opportunity for firms to commercialize their inventions in new territories, thus facilitating globalization of innovations (Archibugi and Michie, 1995). Indian generic companies have always used the internationalization patent route to gain entry into newer markets and to prevent exclusion by competitors (Chaudhuri, 2007). The same strategy is now being used widely for valued added generics and new drug applications. The increase in the number of basic patents filed in PCT and US offices indicates strategy of firm to globalize their inventions. The propensity to patent basic patents over secondary and method patents, indicates firm strategy to globalize high value patents to enhance return on investment. These findings in the Indian sector are in line with the expected notion that in any given appropriability regime, firms choose their appropriability strategy to capture value from their innovation (West 2006). During the process patent regime, the method patents that formed the crux of the generics business dominated the scene. The move towards complex generic formulations to enter new markets and formulate a niche strategy was accompanied by an increase in secondary patents. The shift towards a product patent regime was accompanied by an increase in basic product patent applications. Thus, the Indian industry has formulated a route that moves parallel to appropriability regime.

Another line of study in the organisational theory literature mentions that firms patent their inventions to increase bargaining prowess and avoid potential bargaining problems (Arora and Ceccagnoli, 2006). This is witnessed in the Indian scenario where the shift to a product based patent regime has encouraged firms to increase their patenting activities in order to increase their potential for profit. Patent effectiveness has a positive effect on the patenting and licensing decisions in firms specially when they lack specialized complementary assets required to commercialize new technologies (Arora and Ceccagnoli, 2006). The increase in the number of licensing and collaborative deals for new drug research highlights the willingness of Indian firms to exploit their inventions at varying stages of research. The SME case companies that lack the complementary assets (regulatory, marketing etc) look for out-licensing and early stage collaborative deals that enable them to leverage the resources of partner company. An example is the collaborative deal of Curadev with Roche in the year 2015. Under the terms of the agreement, Roche will fund future research, development, for the company's lead compound for cancer that is preclinical stage of research. Roche provided an upfront payment of $25 million and other milestone payments are linked to future success. Advinus has established similar multiyear collaborative arrangements with other drug discovery partners such as Merck, Takeda pharmaceutical company limited (Takeda), Celgene Global Health (CGH) and J&J.

Established firms too lack the funds to undertake end-to-end development of a molecule and seek ways to raise funds. In the initial years of new drug research business, established firms used to forge co-development alliances at clinical development stage. However, the sustained funds required to progress molecules and failure of molecules has resulted even established firms to seek late stage drug development alliances. These strategies allowed the company to share huge costs involved in clinical development of a molecule and gain market entry into new territories. However, the risk of late stage failures of molecules as was the case with Dr. Reddy's molecules or the termination of advanced molecule by the partner company in the Torrent-Astrazeneca deal has led Indian companies to reconsider their strategic options. Indian companies are now partnering with firms in early stage of research so as to lessen risk and chances of failure. The ability to share funds with a partner and the chance to combine the sales and distribution network of collaborating companies is appealing to both foreign and local firms. In most of these arrangement, the foreign partner gets the IP rights of the molecule while the Indian partner firm benefits from getting research support, sustained funds and ability to commercialize in newer territories. The strong patent laws have also

made it possible to solve the problem of information exchange during licensing that requires information disclosure between buyers and sellers in a secure environment (Besen and Raskind, 1991).

A strong appropriability regime is also an enabler for open innovation as it supports broad networks of innovation (Pisano, 2006). The inbound and outbound strategies adopted by Indian firms support this contention. The new appropriability regime post 2005 witnessed research collaborations for drug discovery between academics and industry scientists that was novel in the Indian innovation space. The collaboration of Lupin with public research institutions to discover a new anti-tubercular molecule for the treatment of tuberculosis, and the collaborative project of Piramal with CSIR and NIO to screen a natural product library for discovery of new chemical entities (NCE's) in the field of inflammation are examples of how entities have come together for a common objective. Section 6.1.2 shows the various types of research interactions that take place between academic and industry scientists. Though research services (fee for service and consulting assignments) based on personal networks dominates the research network environment, the new patent law has opened doors for various other types of research networks such as research partnerships, public private partnerships, scientific advisory boards and virtual consortiums.

7.2.2 Institutional Factor

A strong patent regime alone is not enough to inculcate open innovation within firms. A robust infrastructure of research institutions, research funds, technical manpower and necessary skill set is important to generate innovations and relevant technological opportunities. Post 2005, the Indian government has tried to imbue the science technology system through various initiatives such as increase in R&D budgets, introduction and revamp of existing public private partnership schemes, increase in research grants for scientific research in universities etc. The public private partnership initiatives aim to support R&D through funding support and simulate innovation networks between science and industry. Policy initiatives such as DPRP and NMITLI were overhauled while new initiatives like BIRAC and OSDD were opened to bring together scientists from different institutions for research. Organisations like NRDC have started patent awareness campaigns that aim at facilitating the institution of patent cells in universities and provide assistance to the researchers in the process of patenting. FICCI works closely with industry to provide a platform to connect industry with policy makers and enable commercialization of local

innovation through collaboration with government and foreign academic partners. The initiatives of FICCI have enabled collaborations of Indian scientists with researchers abroad through various innovation programs. In parallel, there have been efforts though government departments to set up patent cells, biotech parks and programs that provide subsidised services to small and medium enterprises to help them sustain their research efforts. These initiatives have collectively sparked the innovation system and promulgated research in the right direction for research through collaboration.

It has been ascertained by many scholars that external linkages of firms within the local innovation system play a decisive role in innovation success (Freeman, 1995; Mowery and Rosenberg, 1979; Mowery and Sampat, 2005). From a policy viewpoint, the promotion of collaborative links between university and industry has become important concerns for the government. In case of the Indian set up, it has been observed that these policy initiatives have been beneficial to some extent in supporting R&D projects and has triggered formation of collaborative R&D projects between government based institutions and private industry. Despite these few occurences, the local innovation networks formed are weak and each of the entities of the innovation is undertaking research in it own direction with little cohesion amongst each other. The policy initiatives by government suffer from problems of bureaucracy, timely disbursal of funds and poor implementation of programs. These problems coupled with low technological opportunities, lack of motivation and IP related concerns at the entity level limit the formation of innovation networks within the local ecosystem. While universities and public research institutions grapple for advanced instruments, sophisticated labs, better infrastructure and fair distribution of research funds, companies are trying to carry out their drug discovery efforts on their own.

Most of the open innovation networks within the local innovation system are for research services and not for long-term research partnerships. There are some very good examples of collaboration where local universities, research institutions and industry have come together for drug research. The example of Piramal's drug discovery project with CSIR and NIO that yielded three NCEs and Lupin's drug discovery project 12 partners with that led to the discovery of a new tuberculosis drug shows the effectiveness of these collaborations. However, such examples have failed to incentivize others and get the necessary attention. Government initiatives often suffer from shifting government priorities and preferences. While NMITLI and OSDD scramble for funds newer initiatives like BIRAC are supported

well by the government. The housing of different initiatives under different ministries and the reliance on only word of mouth as a source of marketing channel has limited the outreach of these programs. The focus of the government to focus on new programs while revamping older ones is not doing justice to the spirit of the programs. The policy initiatives suffer from other weaknesses such as bureaucracy, poor implementation and monitoring of initiatives. Most of these programs have become limited to fund raising programs rather than leading to substantial research output.

Three sets of regulations have particularly proved to be hindering the new drug research efforts of pharmaceutical firms in recent past - regulations related to animal research, clinical trials and drug price control. The price control measures have negatively impacted the profit margins and funds allocated for research. The stringent regulatory requirements to undertake animal studies and clinical trials have resulted in increase in rejection rates, longer processing time and problems in implementation of these studies. While there is no doubt that frequent cases of misuse and allegations of medical misconduct required government should bring out regulatory changes to ensure public safety and reform medical research; such changes have however made it extremely difficult for Indian pharmaceutical firms to undertake trials in India. The delays in getting approvals and practical problems in implementation have resulted in companies shifting animal and clinical trial studies to other countries leading to significant increase in research costs. Despite the measures taken by the government to encourage innovation in the system, the existing problems at the institutional level are doing little to lessen the problems companies face in the research and development of novel drugs.

The journey of Dr. Reddy's Labs and Piramal are two examples that showcase the difficulties encountered by Indian companies to sustain new drug research in India. Both companies are leading generic companies equipped with R&D centers, manufacturing plants both in India and abroad with a vast sales & distribution network. The new drug research was the vision of the owners of these companies; also trained scientists who wanted to reshape the innovation landscape of the Indian pharmaceuticals by indigenously discovering and developing local drugs. The revenues of the generics business were used to fund the new drug research and both companies were successful in lining up a significant pipeline of new drugs. While Dr. Reddy's focused on in-house R&D followed by outbound innovation strategies to commercialize its research, Piramal adopted a mix of inbound and outbound innovation strategies. Dr. Reddy's faced setbacks in sustaining the development of its molecules and

scaled down its operations after many structural changes to its new drug discovery unit. On the other hand, Piramal shut down its new drug discovery operations. The common issues that emerged from the case stories of these companies were difficulty in allocating continued funds for research, constraining regulations, inherent risks of the projects and escalating research costs.

A similar success story was that of Ranbaxy that adopted openness in both drug discovery and development phases. The outreach of the company to local research institutions, academics, research organizations abroad, public private partnership programs is unprecedented in the Indian sector. It formed several collaborations with research institutions such as IICT, NCL, Center of biotechnology and universities such as Jamia Hamdard, NIPER, Anna university and University of Saurashtra to identify drug discovery candidates. It got grants under the DPRP program for the clinical development of two of its NCEs – 'Synriam' launched in 2012 and 'RBx 7644', a novel antibiotic drug. Ranbaxy got embroiled in regulatory problems with USFDA that spiraled and led to the acquisition of the company.

To sum up, Indian companies are finding it difficult to allocate higher funds for research for many reasons. New drug discovery research requires a significant amount of funds to be locked in for many years. Alongside, declining revenues from generics business, increased regulatory constraints, reduced outsourcing business, dampened nature of venture capital business, risky nature of the business and unwillingness of firms to take risks have led to decline in R&D spending. These problems have made the research landscape mundane and caused firms to consider the strategic alternatives of either reducing new drug research spending, or increase focus on contract research and manufacturing business or shut down new drug research business. While Piramal opted out of the new drug business, Dr. Reddy's scaled down is operations and hived off a subsidiary unit Aurigene that mainly undertakes contract research business.

There is hence an urgent need for the government to consider these issues and make the environment conductive for research. In the case of developing countries, national level institutions have played a salient role in overcoming resource limitations enhancing the competitiveness of firms. The interactions of firms with various entities of national innovation system, policies and public research sector are crucial to enable catching up and innovation (Choung et al., 2014). The Indian government has in the past enabled the genesis and growth of the generics industry through various policy initiatives. Post 2005, the efforts

of the government have enabled to create some awareness of patent issues, provide funds for research and create a positive environment for research. Though much needs to be done to solve the constraining issues at the grass root level, the success stories of Ranbaxy's Synriam and Lupin's TB drug that advanced through public private partnerships shows the important role of institutional factors in propelling open innovation. The open source drug discovery (OSDD) initiative has also tried to bring together researchers from different institutions for a common cause. Such initiatives are accompanied by presentations in workshops, panel talks in conferences and have led to numerous positive discussions among researchers in drug discovery conferences. To this end, the institutional factor albeit all their problems and issues have shaken up from the process patent regime to bring about positive changes that enable network formation. In this way, the institutional factor is an important driver for open innovation.

7.2.3 Dynamic Capabilities

The ability for firms to undertake change in strategy due to changes in the macro environment is a testimony of their dynamic capabilities. Open innovation in recent years has emerged to be an important mandate for success and embracing open innovation is a part of the dynamic capabilities of firms (Chesbrough and Bogers, 2014; Teece, 2007). Few large firms such as Ranbaxy, Dr. Reddy's and Piramal have uniquely applied open innovation concepts as compared to others. This can be attributed to the dynamic capabilities of firms that allows firm to create new products and formulate strategies to respond to changing market circumstances (Teece and Pisano, 1994). The theory of dynamic capabilities (Teece et al., 1997) in this way enables to understand the underlying forces that shape different patterns of open innovation witnessed in the Indian firms.

Indian pharmaceutical firms have displayed dynamic capabilities in *sensing* strategic opportunities opened by a change in appropriability regime to innovate, patent and increase their innovation value. Firms have also used the institutional policies in their favour to utilize funding and collaborative opportunities. *This internal capability to shift from closed innovation R&D route and open up their boundaries to external partners in response to changes in the external environment is a testimony of their dynamic capabilities.*

The trends of open innovation among the case companies shows that companies differ in their extent of openness and the type of open innovation strategy pursued for success in new

drug research. This research offers several examples from case studies of SMEs and established firms to show that asset position of a firm does not have a significant influence in the extent of openness. Contrary to the expected notion, the findings of this study did not support the theoretical argument that resource constrained SMEs are more prone to open innovation than established firms. In the western world, the origin and growth of biotechnology industry is based on collaborations and out-licensing deals stuck by biotechnology small firms with incumbent pharmaceutical firms (Rothaermel and Hill, 2005).

Firstly, the analysis of asset position of firms and collaboration data shows that firms vary in their degree of engagements within the local innovation system. Firms like Dr. Reddy's with strong asset position have not engaged in any of the public private partnership schemes nor leveraged the local sources of innovation for new drug research. On the other hand, Ranbaxy and Piramal, leading pharmaceutical companies of India with high asset position have collaborated with the university on many projects and engaged actively with public private partnership programmes. Lupin and Torrent follow a relatively closed innovation approach. Apart from few select collaborative research partnerships with the public institutions, Lupin lags behind in forming university industry relations. Torrent has not engaged in any collaborative public private partnership projects for research purposes.

Secondly, firms differ in their use of open innovation strategies. Firms have differed in their use of in-licensing open strategy. Companies such as Ranbaxy, Piramal, Advinus, Invictus Oncology and Lifecare Innovations have been more experiential in the use of inbound strategy as compared to Torrent, Dr. Reddy's, Lupin and Curadev. However, internalization of external research assets or in-licensing is not practiced widely and is still not a preferred option among the Indian firms. The examples of in-licensing deals are low in the Indian setting but both Piramal and Ranbaxy had explored this strategy to fill its pipeline with new compounds and increase the number of drug discovery programs. The companies then preferred to follow an in-house R&D strategy to develop the molecules. In general, the in-licensing route is perceived to be risky, expensive and firms have largely avoided using this approach.

On the other hand, firms use outbound innovation strategies such as collaboration and out-licensing more often than inbound innovation. In recent years, co-development, research alliances and out-licensing have emerged as common approaches in the complex pharmaceutical innovation and is increasingly being adopted by globally large

pharmaceutical companies such as Eli Lily, Schering, Bayer, Roche or Novartis (Gassmann et al., 2008). In the Indian context too almost all the case companies have engaged either in out licensing, co-development and research alliances. Increasingly, there is a migration towards more and more co-development partnerships with foreign firms as compared to out-licensing deals due the distinct advantages that co-development partnerships offer in terms of risk and revenues sharing. Both SMEs and established firms use these strategies to balance risk, costs and revenue generation. Firms such as Ranbaxy, Dr. Reddy's, Piramal among the established firms and Advinus, Curadev have successfully used a mix of outbound strategies for innovation.

Thirdly, firms vary in their use of open innovation strategy by drug discovery research. The resource mix of a firm plays an important role in influencing the stage at which firms open up to external partners for collaboration and research. SMEs open up their innovation process at a much earlier stage of research than established firms. The licensing agreements of Advinus and Curadev show that most of the deals took place for drug compounds in preclinical stage of research. On the other hand, established firms such as Dr. Reddy's and Lupin opened up to external partners only at the clinical development stage. However, this strategy is changing and the recent deals of Aurigene show that companies are now exploring the collaborations at early stages of research. In any case, the resource profile of a firm is important in influencing the value of these deals. The collaboration deals at early stage of research generates lesser upfront payments and reliance on milestone based payment that is subject to success to passing of the drug compound through successive phases of development.

7.3 Four Influencing factors – The *4Rs*

The empirical evidence from the case studies points towards four important factors that depict the internal tensions firms face when opening up the innovation process to external partners. These four factors are referred to as 4Rs in this dissertation of which two Rs encourage open innovation while two Rs favor closed innovation. The tensions of the four Rs prove decisive for the type of open innovation pathway adopted by a firm.

Need for open innovation

The findings of the Indian case companies showed that firms open up their innovation process for the following reasons: a) knowledge b) need for funds and c) risk mitigation. The need for knowledge and learning in early stages of research and funding requirements has impelled Indian companies to explore open innovation paths. Indian pharmaceutical firms also face the same challenges of the firms in late comer countries in being away from the global centers for science and innovation for enhancing technological capability and having access to national level institutions that are weak technologically and poorly equipped (Mike Hobday, 1995; Michael Hobday, 1995). Learning and access to knowledge plays a critical role for both large and small firms to form the basis for most of the networks in the local ecosystem (Bessant and Tsekouras, 2001).

The complexity for pharmaceutical innovation warrants openness to leverage available knowledge and expertise that may reside outside firms' boundaries. The motives also vary by stage of drug research and by the asset position of firms. While quest for knowledge and learning predominates the initial stages of drug discovery research, risk mitigation and need for funds predominates the drug development stage. Motives to engage with external partners are driven by the need to exploit external sources of knowledge, technologies and supplement internal knowledge base. Funding constraints drive firms to seek support from external sources.

a) Knowledge based partnerships: There is a general consensus among the interviewees about the need for forming teams of multidisciplinary scientists for pharmaceutical innovation. Research based partnerships are crucial for both the entities to close the gap between basic and clinical research. Pharmaceutical companies believe that research in universities is useful in the early stages of drug discovery as it allows to access research carried out by using different strategies and chemical pathways. The companies can then cherry pick and pursue further development work (Chief Scientific Officer, Curadev [26]).

The first point of collaboration in an ideal drug discovery projects starts at the target identification stage with a team of chemists, biologists specifically structural biologists and academicians involved in the exploratory research. Principal investigators spend a lot of time in exploration work, which is extremely useful in early parts of drug discovery research

(Expert, Drug Discovery research). Such collaborations allow leveraging existing knowledge in the system and saves time.

> *"It is important to use the collective intelligence of the researchers of the country to solve the problem of drug discovery. The challenge is that drug discovery is so complex that you need people with very different skill set training and background to come together and solve this problem." (Scientist, OSDD [22]).*

A research engagement with scientists also brings down the development time.

> *"Earlier what was happening was everyone was reinventing the wheel, everyone was trying to build new expertise which, is very time consuming. But now you do what you know best and what you don't know then give it to somebody who knows how to do it. That really speeds up things." (Vice President, Dabur Research Foundation, [44])*

> *"One of the biggest problems of drug discovery is the high attrition rate which increases development time and cost. One of the ways to bring down the attrition rate is to share the failures. Say for example somebody has failed in doing something as per current scenario these things never get published, so they remain on somebody's desktop, laptops or in their lab notebooks. The open source drug discovery is based on this premise that it provides a platform where researchers can share their results, even their failures, within the scientific community." (Scientist, OSDD [22])*

Partnerships are also made with firms for seeking reputation with prestigious partners as it enhances a small scale firm's reputation and also brings legitimacy to research (Koput and Powell, 2000).

> *"My belief is that if something positive comes up here, I need to work with a world leader because if it excites him then my chance of success is much higher. In other models, the collaborations are done depending if we require certain technologies or certain targets to be validated, we would directly link up either with a contract research firm or with a firm in a collaborative manner." (Senior Vice President, NCE Research, Piramal [31])*

It has been recognised by industry scientists that it is imperative to access academic research as it allows comparing the results of different strategies pursued by academic researchers and select a suitable strategy (Retd. Vice President Formulations, Ranbaxy [27]).

> *"What we look for in an academic collaboration is someone who has worked in early part of drug discovery… so that you can test some ideas quickly. But you need to be able to translate that into your organization and make some full discovery programme out of it." (Chief Scientific Officer, Curadev [26])*

b) Funding support: The research partnerships are also formed to raise funds for research. More specifically, government support or co-development partnerships with external partners is sought to mitigate the burden of high research costs involved in the research and development of new drugs. Few companies in India have revenues more than $1 billion while SMEs have net consolidated revenues less than $50 million. Of the total cost involved in new drug research, ~ 70% of the cost is utilised at the clinical development stage. With the cost of R&D expenditure for a new drug hovering more than $1 billion, R&D funding and ability to sustain research of drugs through all stages is a top concern among the Indian pharmaceutical companies. As the director of a spinoff company puts it-

> *"In the field of pharmaceutical research of new drug is a very costly business […] So most of the companies do a part of new drug research. We are doing computational biology, some part in organic synthesis. We are also designing a molecule and involved in synthesis too. But we cannot do wet lab experiments like animal testing, we cannot do cell line testing at this point of time. So we need collaboration to come up with some really good molecule lead in the market. The investment of the money is huge so no one can invest so much money to come up with new drug molecule." (Director, Novo Informatics [43])*

The traditional and successful linear model wherein the basic research conducted in public institutions benefits the innovative capacity of firms stands challenged today in the wake of multiple avenues such as bio park, bio clusters, spinoffs, scientific advisory boards, foreign research institutes/universities that has provided new means for firms to use academic knowledge and information. The internationalisation of R&D (Gassmann and Reepmeyer, 2005) has opened up immense opportunities for the Indian pharmaceutical to network with

universities and research institutes abroad. The contract research outsourcing business has also made it viable for Indian firms to connect with foreign pharmaceutical firms for open innovation. The Indian pharmaceutical industry is now witnessing a growing number of global research alliances formed with universities and research institutes based abroad.

c) Risk mitigation: The initial years of drug discovery research witnessed that Indian companies relied more on in-house R&D and open innovation strategies were pursued mostly at drug development stage. The companies had developed significant capabilities in process research and modular stages of drug discovery and this belief in their scientific capability coupled with low cost of research in India gave them the confidence to carry out in-house research in a closed manner. However, the recent changes in business strategy of firms reflect the need of the firms to reduce risk in research and increase potential to profit from innovation. The increase in R&D expenditures, high attrition rates of new compounds, unlikely return on investment for R&D has led many pharmaceutical firms to tie up with external partners at early stages of drug research. In the past few years, companies have changed their business strategy and have varied in the stage they open up to foreign firms for partnership. The complex nature of research however has made sole dependence on in-house research less appealing. Firms such as Piramal and Ranbaxy had believed that knowledge based collaborations in the initial stages of drug discovery would be useful to gain new knowledge and pursue research in-house. But the complexity of research and high financial costs required to sustain research had made them consider outbound strategies to mitigate risk.

Open innovation paradox

The strong appropriability regime has opened various opportunities for firms to commercialise their invention and also provide an environment, which facilitates safe transactions. Post 2005, Indian firms have ventured into novel drug research and also increased patenting activity. Patenting serves manifold purpose: enables to get ownership of invention b) blocks competition and c) facilitates licensing. The patent analysis shows how firms are increasingly applying for patents in international offices that is reflective of the internationalization strategy of the firms. It also shows the tendency of firms to patent high value patents such as products patents of incremental and radical innovations abroad to enable commercialisation of their products in newer territories. Some of the recent deals of Aurigene, Advinus and Curadev with leading pharmaceutical companies in the world such as

Merck, Roche, Takeda, Celgene Global Health, Curis are successful examples to exemplify how Indian companies have engaged in out-licensing and collaborative research deals for new drug research. Our results concur with Teece's argument that a firm's strategy to profit from innovation is contingent on appropriability regime (Pisano, 2006; Teece, 1986).

However, in order to avail these opportunities, firms need a strong patent portfolio to provide them with a bargaining position. The need for patenting severely limits the information they can share with external entities such as universities and public research labs in research partnerships. Indian firms are also careful in the type of projects they collaborate on so as not to give rise to IP sharing issues. In other words, firms want to retain control of their assets and the related IP to prevent chances of expropriation. This is in line with the *paradox of openness*, which describes the tension between the need for openness for gaining knowledge from external entities and the need for protection and secrecy for commercialization of innovations (Laursen and Salter, 2005b). The choices of the firms to be open become influenced by the choice of appropriability strategy. It is this dilemma that forces Indian firms to be restrictive in their collaborations at early stages of research and focus more on protection of research assets to gain commercial interest from other parties in subsequent stages of drug development.

The empirical evidence also showed that universities and public research labs are more willing to publish over patent due to many reasons: – a) it is in line with the open science norms b) it conforms to existing reward system for career opportunities c) most of the universities lack proper IP policies and patent cell to aid researchers in patenting and technology transfer and d) there is lack of awareness among academics on the commercial avenues attached to patents. These factors cause apprehension of misuse and fear of not getting due credit when collaborating with industry leading to a climate of mistrust. This is in line with the *paradox of disclosure* (Arrow, 1962), which states that once disclosed the information has no value and information cannot be traded without proper patent protection. It is this dilemma, which prevents academics from having interactions with industry scientists, as they fear fraud and misappropriation of their research ideas.

Currently in the Indian setup, the propensity to make use of licensing opportunities and protect research ideas from acts of opportunism outweighs the advantages of openness of collaboration with external sources in early stages of research. It is endorsed that stronger intellectual property regime enable sourcing ideas from external sources of innovation as

opportunistic behaviour can be prevented with legal sanctions (Gallini, 2002; Laursen and Salter, 2005b). The inadequate history of collaborations, environment of mistrust coupled with fewer propensities of academic scientist to patent has contributed to the current spell of poor science based networks. The results of this tension are firms choose those open innovation strategies that allow retaining control of research assets and enhancing their ability to maximize revenue generation.

4 Rs

An important explanation for the choice of these open innovation pathways lies in the four factors described as *4Rs* in this dissertation. Each of the open innovation pathways displays four important forces at work– Resource supplementation (aimed to reduce resource gaps in the firm), Risk mitigation (optimum strategy to reduce technological risk and other risks), Retention of control (prevent loss of control of the research asset) and Revenue maximization (potential revenues that can be earned at different stages of research). These four factors referred as Rs serve as guiding factors to understand the open innovation pathways adopted by the Indian pharmaceutical firms.

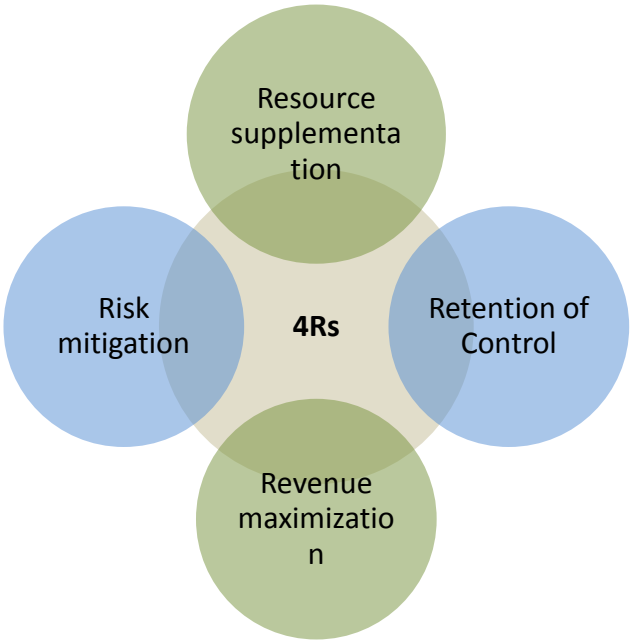


Figure 33: Determining factors of open innovation pathways: 4Rs

Resource supplementation: Resource supplementation refers to an assessment of current asset position, project needs and devising of ways to supplement the resource gaps. The resource constraints in the form of technical competence, funds and complementary assets

(particularly in case of SMEs) compel Indian firms to opt for various strategic pathways. Primary research findings support the argument that the need for resource supplementation is an important factor, which determines the type of open innovation strategy to adopt and the stage of research at which firms need to open up.

> *"From my discussions with many of the Indian discovery companies, they do not have the appetite to spend so much of money for clinical trials. So they take the drug discovery process, identify molecules, most of the GLP toxicology studies, carry out Phase 1 and are ready to partner. They say we have done this much we do not have funds to invest in phase 2 and phase 3 and they are ready to partner. This is the case in 90% of Indian companies." (Senior Director, Pfizer [48])*

The resource supplementation has been one of the most important parameters that guides how firms open up to the external environment.

Risk mitigation- The second most important factor is risk mitigation. The high attrition rates in different stages of drug development and high research cost makes drug discovery a very risky business. Open innovation is considered as recourse to mitigate risk. Risk is lowest in out-licensing deals where rights on drug molecule along with IP are given to the buyer in exchange of lump sum payments. The risk however lies in potential loss of revenues that may occur in case the compound is commercialized or if the foreign firm shelves the project. In case of in-licensing, the risk lies with the purchasing company, if the drug compound purchased fails to progress across different research stages. The collaborative risk-sharing model however enables to share risk at the cost of sharing revenues.

> *"Actually this is a risk based business and all the time risk is there in terms of getting success. So, we have to share this risk together. If we have a collaborative programme, we can share the risk. If we out-license something then risk is 100% on that party and not linked to us. If we in-license, whatever the risk is we have to take care. In terms of collaborative relationship, risk is very less as every aspect is mutually agreed and foreseen further. But in terms of progress of the project, that risk is always there; as you know drug discovery is very risky. As you know very few molecules go further, many of them withdraw in different stages of development. That way*

the risk involved is pretty high in terms of the success." (Senior Vice President, Piramal [32])

Retention of control - The strategic motives of firms to maximise profit through commercialisation of innovations make companies want to retain control of their research assets. Firms assess and use those strategic pathways that enable to leverage benefits of open innovation without compromising on information leakage and cases of opportunism.

Revenue maximisation – The motive of firms to harness commercial benefits from innovation makes way for various open innovation pathways. Initially, out-licensing was perceived as a strategy to bring in quick returns to R&D investment and was the most preferred option. Gradually, Indian firms have realised that more the advanced stage in research, more are the chances of higher revenues. Firms choose that open innovation mechanism that allows maximisation of return on R&D investment. This also provides for an explanation why firms choose to be closed at specific stages of drug research.

The *4Rs* provide the explanation as to why firms differ in their choice of open innovation pathway. Each innovation pathway represents an open innovation pattern configured by the Indian firms.

7.4 Open innovation pathways

Indian pharmaceutical companies have started to harness external sources of innovation to complement internal research by accessing technologies, molecules and R&D projects. While strained relations between science-industry have always existed in India, the move to new drug innovation has necessitated firms to look beyond closed innovation and explore pathways for open innovation.

Empirical findings demonstrate that Indian companies use open innovation pathways to complement their own internal R&D for the research of novel drugs. *In this dissertation, an open innovation pathway is defined as a combination of local innovation networks and open innovation strategies used in different stages of new drug research.* The open innovation pathways adopted by Indian firms can be categorised into four types:

1. In-licensing and in-house R&D

2. Out-licensing after pre-clinical stage
3. In-house R&D and co-development
4. In-house R&D and Public Private Partnership

The categorisation of innovation pathways is based on local innovation networks formed and choice of open innovation strategy by stage of drug research. These open innovation pathways do not imply the lack of in-house R&D, rather these pathways show how Indian companies have supplemented open innovation with internal R&D and are progressing from closed innovation towards open innovation.

In-licensing and in-house R&D pathway

In this open innovation route, pharmaceutical firms in-license innovation from external sources and develop further with internal resources and knowhow. This strategy is preferred by companies as it allows to develop the licensed compound through subsequent stages of research and development in an internal controlled setting. This open innovation pathway has been used by Ranbaxy to successfully commercialise a new chemical entity, Synriam (arterolane in a fixed dose combination with piperaquine phosphate). Ranbaxy in-licensed the drug 'arterolane maleate' from MMV at drug development stage with a worldwide, royalty-free license for this compound. The company then developed the molecule in house. Ranbaxy also collaborated with the government under the Drugs Pharmaceutical Research Programme (DPRP) with DST, to get grants for the clinical development of *Synriam.*

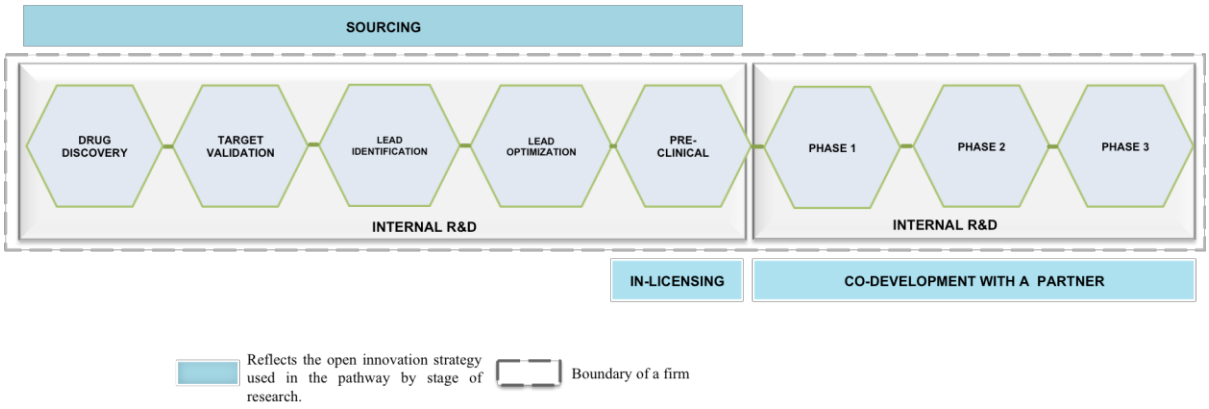


Figure 34: In-licensing and In-house R&D route

Currently, the industry standard for a pharmaceutical company is to predominantly use internal know how, knowledge and resources to conduct R&D. In this open innovation

pathway, inbound innovation is used to acquire the molecule and combine it with in-house research activities to develop the molecule further. Subsequent to this, during the clinical development stage, the company *may* seek external support for further development and commercialisation. In case of Ranbaxy, the company undertook the clinical development of *Synriam* with funding support from the DPRP programme using the in-licensing route pathway.

Ranbaxy has established a convincing open innovation route that supplements the traditional R&D model with in-licensing option. The in-licensing of a drug compound is an expensive strategy to adopt for Indian drug companies and not a preferred option. However, in this particular deal, Ranbaxy, which was already a part of the MMV research venture, was able to in-license the drug 'arterolane maleate' from MMV with a worldwide, royalty-free license for this compound. The case of Ranbaxy provides a testimony on how inbound innovation can be utilised effectively by focussing on the best opportunities to access external innovation.

The in-licensing and in-house pathway is analysed using the 4Rs factors:
Resource supplementation - The in-licensing route is *resource intensive*, as it requires funds for buying a molecule and capital to develop the molecule further. This is hence not a preferred option among SMEs.

Risk mitigation - In terms of *risk* also, this pathway is prone to high risk. One is the technological risk of a drug compound failing in latter stages of development; the other is the risk of not being able to internalise an innovation that has been developed in an outside environment (Gassmann and Enkel, 2004).

Retention of control - This pathway allows retaining full control of the research asset without the need to share intellectual property rights. In this way, the full benefits of commercialisation of innovation can be realised using this open innovation pathway.

Revenue maximization - This innovation pathway benefits immensely in having high potential to reap the *revenues* in case of successful commercialisation. The in-house development ensures that the firm does not have to share the fortune with any external party and this benefit more than offsets the cost incurred to in-license the innovation.

In-house R&D and Out-licensing pathway

The second open innovation pathway adopted by the Indian companies involves in-house R&D during the drug discovery stages to make IND compounds package ready for out-licensing. There are many variations to this path, companies might choose to out-license during pre-clinical stages or even at later stages such as Phase 1 and Phase 2. It has been observed that cash stripped SMEs try to out-license compounds at early stages of drug discovery whereas established firms typically enter into out-licensing deals after preclinical studies or any of the clinical trials stage. More generally, Indian companies prefer to follow a closed innovation approach in the early parts of drug discovery research.

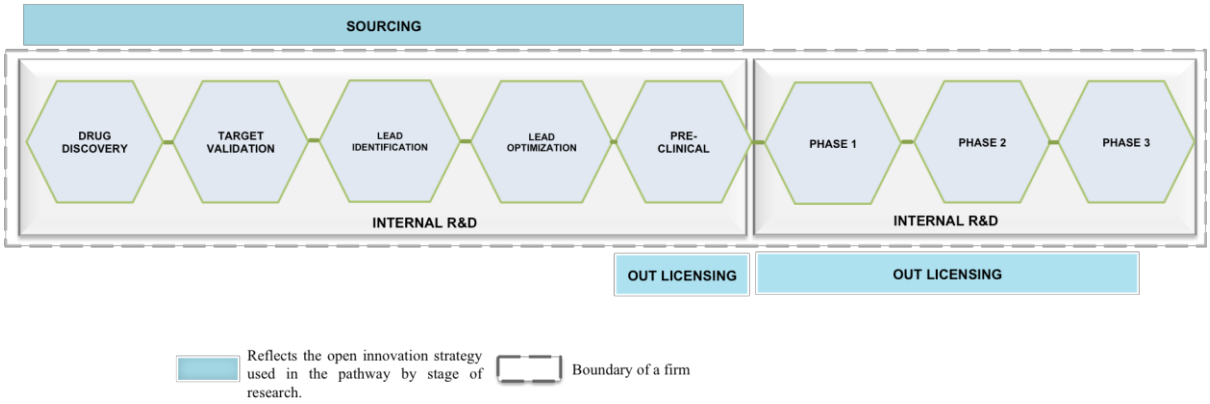


Figure 35: In-house R&D and Out-licensing

Important considerations with respect to the 4Rs involve:

Resource supplementation- The current resource profile of a firm and the need to plug in the resource gap influences a firm's decision to use this strategy. The resource profile also influences the stage of drug research at which outsourcing takes place. SMEs have conceded that out-licensing is an important strategy that would be considered after the molecule reaches a certain stage. Cash rich established firms have the propensity to engage in out-licensing mostly in clinical development stages.

Risk mitigation - In terms of risk, out-licensing is a less risky proposition as the technological risk is transferred out to the external partners. This finding is in line with (HW Chesbrough, 2003) that an important reason for firms to engage in open innovation is to mitigate risk.

Retention of control - The out-licensing strategy suffers from inability to retain control over the research asset. This is by far the biggest drawback of this pathway and makes Indian companies wary of this strategy. The lack of advancement to subsequent stages depends on the external partners. The external partner may choose not to advance the molecules to subsequent stages on reasons of technological failure or any other reason. This also results in significant dent in the potential revenues of the Indian companies that can be earned through royalty-based revenues.

Revenue maximization - Out-licensing is a preferred strategy in the Indian pharmaceutical sector as it allows quick returns to investment. The commercialization rights in select territories and royalty based payments makes out-licensing an attractive deal. However, senior executives observe that the amount of funds, which can be generated post commercialization, is phenomenally higher than what is earned in an out-licensing deal. Additionally, the earlier in the drug research stage the molecules are out-licensed, the lesser the revenues earned. The comparative benefits of out-licensing are much higher than the technological risk associated with internal development of the molecule and this has made it a preferred option among the Indian firms. Ranbaxy, Dr. Reddy's, Torrent and Curadev have used out-licensing in the pharmaceutical space that allowed them to earn quick returns.

The risk of losing potential revenues and inability to retain control influences the choice of this innovation pathway. As the Vice-President of a pharmaceutical company elaborates:

> *"It depends on the company' strategy, if you want 50 million dollars for example or 100 million dollars then this is what it takes to have these out-licensing deals. If the molecule succeeds, then you lose the chance to make a billion dollar, but if you fail then by out-licensing at least the company gained something." (Senior Vice President, Piramal [32])*

The out-licensing strategy has its roots in the quick returns to investment and transferring out of risk to external partner and is one of the favoured open innovation pathways in practice.

> *"Right now, most of the companies which are getting involved in drug discovery are looking at out-licensing anything that they have: technology or the molecules itself. They would like to out-license because if you are looking at completing the drug discovery process and bringing the molecule to*

the market it takes lot of time and it is very very expensive." (Senior Director, Pfizer [48])

Collaborative R&D pathway

A third open innovation route employed by firms is the co-development agreements with foreign companies. Indian pharmaceutical companies have signed several option-based, risk sharing collaborative agreement with foreign companies and such agreements are becoming an integral part of the drug discovery and development process.

Co-development partnerships in India involve research activities undertaken by the Indian firm and clinical development undertaken by the foreign firm. The salient features of the co-development agreement are the upfront payment, milestone payments, commercialization rights in select territories and royalty-based returns. Under such agreements, the Indian pharmaceutical companies take on the discovery and clinical responsibilities depending on the nature of agreement in exchange. The foreign companies have the option to exclusively license novel compounds and IP resulting from these programmes and take responsibility for the clinical development of such compounds and commercialization. These deals may however vary by stage of drug research and co-promotion rights in certain territories.

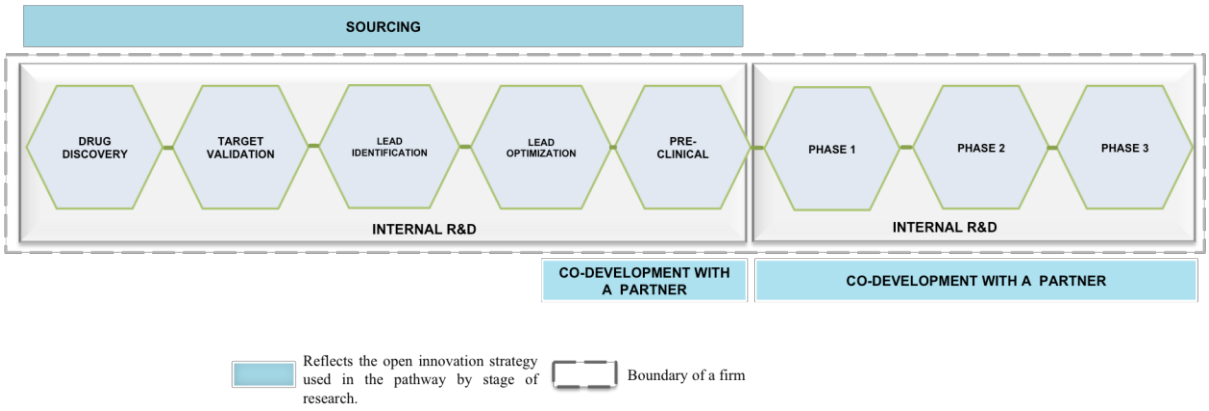


Figure 36: Collaborative R&D approach

This pathway can be analyzed using the 4Rs factors:

Resource supplementation-Like out-licensing, the resource gap influences the decision to employ the strategy and stage of drug research at which agreements are finalized. Co-development agreements allow joint sharing of capabilities and resources and to speed development time.

Risk mitigation– The collaborative route allows sharing R&D related risks with a partner specifically in the clinical development stages. The ability to share risk is a strong reason for firms to use collaboration as a strategic choice.

Retention of control – Indian companies have embraced the collaboration route as the intellectual property rights which the companies take at the early stages of research, allows to structure agreements with an external partner while retaining rights to exercise decision in the progress of the molecule. The ability to take joint development with a partner and share risks and revenues is a winning way to ensure that the company is able to progress its discovery to later stages of development and commercialization. Typically, in such agreements, the intellectual property rights are transferred out to the foreign partner.

Revenue maximization - The ability to earn revenues through upfront and milestone based payments and revenue sharing plays a pivotal role in the choice of this strategy.

Public Private partnership pathway

An emergent open innovation pathway witnessed in the Indian pharmaceutical scenario is the in-house research and development of a drug using the public private partnership route. This approach is more popular for the development of new drugs for neglected diseases, an area which fails to attract drug companies. Companies such as Lupin, Lifecare and Advinus are using the new government incentives to bring new drugs into the market for diseases such as tuberculosis, leishmaniasis, and malaria. Ranbaxy's Synriam, an already commercialised project got grants under the DPRP programme for the clinical trials of 'Synriam' that was commercialised in 2012. Lupin's new drug for tuberculosis LL 3858/4858 (Sudoterb) is an outcome of collaboration with academic and public lab partnership at drug discovery stage. It gets funding support by the NMITLI programme in the clinical trial stage. Lifecare Innovations has mainly worked in the incremental product innovation space and launched significantly improved drugs in the area of leishmaniasis, tuberculosis and psoriasis that have been supported by the government through various initiatives. Another example of the utilisation of this pathway is the case of Advinus that undertook internal development of its molecule ADV- 1002401 (Glucokinase Modulator), a new chemical entity for providing effective oral therapy to patients suffering from Type-2 diabetes mellitus (T2DM). It then took funding support from the DPRP for the early clinical development.

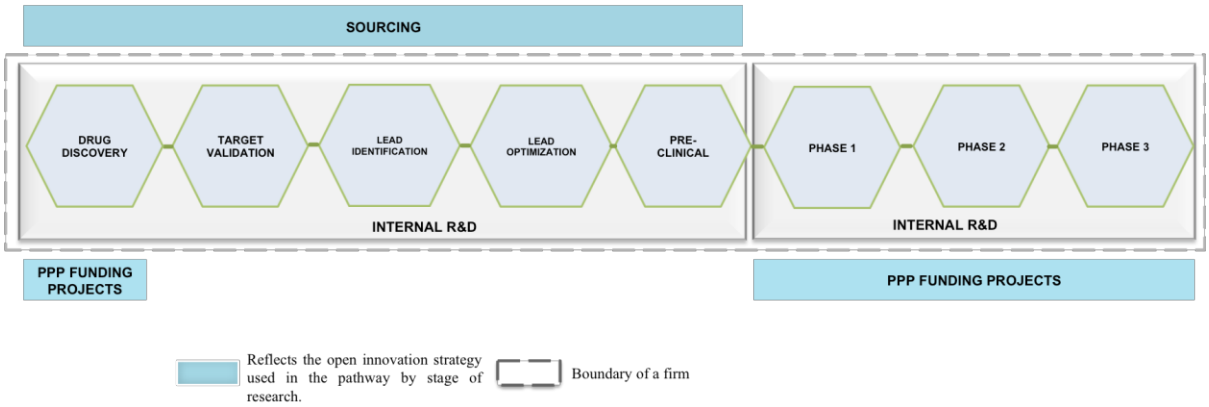


Figure 37: Public Private partnership mode

The 4R factors provide an explanation for the emergence of this pathway.

Resource supplementation- Most of the established firms in India seek open innovation within the local set up to access knowledge and funds. The core of this model is to mobilise government support in getting technical and commercial support from the government. Most of the significant new government R&D incentives are aimed at neglected diseases and facilitate companies to seek scientific support from the public research institutions and also allowing companies to get funds for neglected disease projects.

Risk mitigation –Such an open innovation pathway allows sharing of development risks with the government, specifically in the clinical development stages. Governments across the world are showing considerable interest to share costs and risks for R&D of neglected diseases for public health benefits.

Retention of control - This is by far one of the most important reasons for the utilization of this pathway by Indian firms. Through partnership with public private programmes, companies are able to retain the intellectual property rights within companies.

Revenue maximization - Most of the public private partnership agreements are based on 50:50 fund sharing arrangements. Under such agreements, firms retain full control of research assets and can reap the benefits of commercialization without having any revenue sharing agreement with the government. Typically, firms remain closed for most part of the research stages and open up during the development stages.

In this chapter, the empirical findings are succinctly brought together in an open innovation framework that encapsulates the key tenets of open innovation in the Indian pharmaceutical sector. The open innovation framework reflects how the Indian firms have used various strategic options to overcome the challenges. Firms have devised an impressive variety of open innovation pathways for product innovation. Some of these strategies have been successful and have led to the launch of a new chemical entity and many drug compounds in advanced stages of clinical trials. This chapter shows the problems inherent in the system and the mechanisms the firms have used to evolve over time.

8 Conclusion and Recommendations

This dissertation establishes through case evidence that open innovation is significant in an emerging economy like India that faces many different challenges for undertaking research in innovative medicines. The Indian pharmaceutical industry faces severe constraints in the form of high costs required for R&D of new drugs, stringent regulations related to clinical trials and animal studies, lack of experience in the research of new medicines and skill gap. Indian pharmaceutical companies are now feeling the pressure in the form of failures in the progression of new drug compounds and closure of new drug discovery operations by few incumbents. Few Indian companies have however been able to sustain their drug discovery efforts and are able to respond to the challenges by charting innovation pathways that allow them to leverage the benefits of open innovation to reduce chances of failure. Ranbaxy is the first Indian company to have developed and launched a NCE for malaria. The company could have seen many more successes however the turmoil after 2005, change in ownership, setbacks in the clinical results for out-licensed products had a substantial impact on the progress of its new drug research program. Nevertheless, Ranbaxy is an example of an organisation that utilised its resource strength and strategic agility to launch India's first NCE. To recapitulate, Indian companies have used open innovation strategies in different stages of drug development to adapt to changes, leverage collaborative opportunities and capitalize on its technical strengths to come up with an impressive pipeline of new drug compounds.

This chapter is structured as follows: the first section summarizes the key findings of this research by responding to the research questions along with theoretical reconsiderations. The subsequent section provides the recommendations useful for policy makers and practitioners, highlights the limitations of this study and provides directions for future research.

8.1 Reviewing openness in Indian pharmaceutical sector

This study provides answers to the research question: How does national innovation system and asset position of a firm influence openness in the Indian pharmaceutical sector for innovation in novel drugs? The research findings of this dissertation are summarized in three

central themes: a) Role of national innovation system in shaping the innovation ecosystem b) Open innovation networks within the national innovation system and c) Open innovation strategies used in new drug innovation process. These three themes address the three primary research questions and the embedded research objectives (Refer Table **1**).

Influence of National Innovation system

The study has focused on macro level factors that provides a selection environment to the firm to explore myriad of possibilities, given its sandbox (Prahalad, 2006) of resources and constraints. Indian firms have responded to the opportunities and challenges in the macro environment by venturing to exploit new opportunities such as novel drug and moving from closed innovation towards open innovation. The key findings suggest that the changes institutional and regulatory environment have been beneficial to stimulate innovation and initiate open innovation within and outside the ecosystem. The innovation performance of firms as analyzed through patent data indicates the increase in technological capabilities of firms, reflect the change in nature of innovation and demonstrate the strategic focus of firms to internationalize their R&D. The shift in patent regime brought positive changes in the institutional environment such as new initiatives that aimed to reinvigorate science and innovation in the system. Government has also introduced new mechanisms such as open source drug discovery to propel research for neglected diseases. Through the launch of significant initiatives such as the BIRAC schemes, DPRP and NMITLI, the government aims to create an environment for private sector participation in R&D and create opportunities for public private partnerships.

The changes in the institutional set up show that though the efforts of the government have been positive in creating a positive environment but these efforts are not alone to support a complex technological innovation such as new drug research. A holistic approach is required by the government to propel innovation and achieve significant results. In addition, a highlight of this study is that cultural considerations and trust play a critical role in enabling collaborative relations between scientists from different entities. As a result a blanket approach will not be able to iron out the problems and there is a need for a more customized approach to address these problems. The theory of national innovation systems provides a good framework for this study as it enables to combine all useful elements and relationships that contribute to innovation and competence building (Lundvall et al., 2002). This study enables to get an understanding of national specific differences that is useful to understand its

how open innovation pathways are shaped by a country's institutional, regulatory and cultural factors. An examination insight of the practices of open innovation in the Indian pharmaceutical sector setting is important to identify prerequisites and limits of open innovation. Studies linking NIS and open innovation are lacking (Chesbrough and Bogers, 2014) and are important to make explicate the linkages between institutions and practice (Chesbrough et al., 2008).

Open Innovation Networks

Over the past few years, there has been a dynamic shift in the way pharmaceutical firms in India are tapping into the science and technology system to access knowhow and expertise in specific areas useful for drug research. The findings of the study reveal that within the local innovation system, consulting assignments and fee for service projects based on personal relationships have remained as dominant form of interaction for firms to seek scientific advice from the academia. Such relationships occur on the foundation of *high relational trust* (Gulati and Sytch, 2008; Zaheer et al., 1998) which mitigate the need to get into formal agreements, minimises opportunism, keep conflicts related to IP low and allow access to knowledge from competent reliable partners. In addition to the local innovation system, the internationalisation of R&D has provided access to diverse sources for open innovation such as foreign-based universities, research institutes and firms.

Literature suggests that resource constrained SMEs engage in more alliances than established firms (Koput and Powell, 2000). However, the findings of the case companies did not support this assumption. Few firms such as Ranbaxy, Piramal and Life care Innovations have used many sources of local innovation for drug discovery research while Curadev and Invictus Oncology have formed focused research partnerships with key institutions to allow usage of university knowledge in their innovation activities. On the other hand, Dr. Reddy's, Advinus and Lupin have limited interactions with Indian academic scientists. Barring one public private partnership undertaken by Lupin, the company has relatively followed a closed innovation model. Thus, in the Indian setting, the asset position of a firm has minimal influence on the way firms collaborate with local sources of innovation.

The aim of the government-sponsored policy initiatives to create links between academic and public research institutions with industrial R&D has largely remained unsuccessful. Public private partnership schemes initiated by the government have become a source of funding for

projects but have not been able to trigger research partnerships in the real sense. Despite some promising examples of collaborative research projects of firms with universities and public research labs, the emergent picture is that of disconnected and loose interactions between the entities for new drug innovation.

This research identifies three important reasons to form obstacles in the formation of healthy and adaptive interactions between firms and scientific institutions – low technological opportunities, IP related issues and trust & cultural issues. The nascence of new drug research in India and low scale of research accounts for low technological opportunities in the science system. This impairs linkages as it gives little chance for the industry to exploit scientific discoveries available in the public research institutions. In addition, in any collaborative work the propensity to publish prevails over willingness to patent in universities and public research labs. The reasons to prefer publication over patenting are a) it is in line with the open science norms b) it conforms to existing reward system for career opportunities c) most of the universities lack proper IP policies and patent cell to aid researchers in patenting and technology transfer and d) there is lack of awareness among academics on the commercial avenues attached to patents. Poor patent trends and lack of awareness about patenting among academics cause apprehension of misuse and fear of not getting due credit when collaborating with industry. This is in line with the *paradox of disclosure* (Arrow, 1962), which states that without proper patent protection information cannot be traded. It is this dilemma which restrains academics from opening up to collaborations with industry. On the other hand, firms prefer to keep their R&D work secret in order to facilitate patenting, retain control of their research assets and enable profiting from innovation. This is in line with the *paradox of openness*, which states that the creation of innovations often requires openness to external sources while commercialization of innovations requires appropriability (Laursen and Salter, 2005b). It is this dilemma, which forces Indian firms to be restrictive in their collaborations at early stages of research.

The divergent objectives of the entities in the innovation system make it difficult for the scientists to work together for a common goal. Open innovation networks in the Indian local innovation system thus are contingent on many factors such as personal networks, availability of technological opportunities, appropriability related issues and change in cultural mind-set of industry and academia researchers to enable formation of trust based relationships.

Open innovation strategies

Open innovation in the Indian sector has benefitted greatly from a strong legal system provides secure environment for firms to exchange knowledge and research ideas without worrying about opportunistic behaviour. In addition, the institutional policies initiated by government are important to get funding support and promote collaboration between firms and academic scientists. A strong legal system provides secure environment for firms to exchange knowledge and research ideas without worrying about opportunistic behaviour and in this way promotes inbound innovation in firms and outbound innovation among the public institutions. The benefits of open innovation coupled with a strong appropriability regime have made the environment in pharmaceutical sector conducive to adopt new ways for doing R&D.

Inbound innovation in the Indian scenario occurs through sourcing and acquiring among the Indian firms to bring in knowledge, ideas, expertise or compounds to aid the innovation process. Open innovation literature endorses inbound innovation as a useful approach, which can be applied to procure external discoveries (Chesbrough and Crowther, 2006) and can also be used to seek solutions to technical challenges. However, low technological opportunities available in the system, reliance on in-house R&D and the need to retain control of research assets have driven the Indian companies to follow a closed innovation approach in the initial stages of drug research.

Outbound innovation occurs through out-licensing and co-development arrangements that vary by stage of drug research, payment and commercialization options. The findings show that outbound innovation is more pervasive among the Indian firms as compared to inbound innovation and Indian firms have developed many collaborative arrangements with foreign companies. The asset position of a firm heavily influences the research stage when open innovation is desired. Within the dynamic capabilities framework, the findings suggest that firms are driven by their internal competencies, financial resources, and other assets to adopt various open innovation strategies. The need for knowledge sharing, learning and funds require access to resources (*resource supplementation)*. This coupled with the need to *mitigate risk* in research for new medicines impels firms to open up their innovation process and search for new pathways.

Indian firms use those strategic options that enhance its potential to profit and allow retention of control over research assets. Two factors that deter open innovation in the innovation process include a) revenue maximisation and b) retention of control. These two factors have been identified as the two Rs that curb open innovation within a firm. Compounding these challenges, firms must resolve the dilemma to come up with an optimum open innovation approach to innovate. The 4R factors - **R**esource supplementation, **R**isk mitigation, **R**etention of control and **R**evenue maximization play an underpinning role to enable choice of *open innovation pathways*. A deciding factor in pharmaceutical research is not only to choose whether to open up the innovation process or not but also to choose between various alternative innovative pathways for new drug research.

Three important drivers have been identified in this research that significantly push open innovation in the pharmaceutical sector – *appropriability regime* and *institutional factors* at the selection environment level and *dynamic capabilities* at firm level. The appropriability regime and institutional factors have jointly been crucial to brace up the innovative efforts of companies and set them on the path to technological progress. The dynamic capability of the Indian firms to adapt to the challenges and leverage the opportunities at each of the appropriability regimes has significantly influenced the dynamics of innovation. In this way, the drivers of open innovation significantly influence openness in the pharmaceutical drug discovery and development process while the 4R factors affect the choice of open innovation pathways.

The patterns observed in the empirical data show that firms follow four open innovation pathways that differ by the innovation networks formed and the strategies pursued by firms. Firms consider the tensions of 4Rs and decide on a combination of in-licensing, out-licensing and collaborative strategies, based on stage of research, which leads to the adoption of an open innovation pathway.

8.2 Policy and Management Recommendations

The Indian pharmaceutical sector has significant cost advantages and the challenge lies with the Indian firms in devising and implementing those open innovation strategies that would enable catch up learning and speed up innovation. The study identifies various strategic

options and difficulties that Indian pharmaceutical firms face in making the transition to new drug innovation. The various pathways adopted show how firms come up with strategic approaches to circumvent various hurdles to innovate. The case of the Indian pharmaceutical sector in this way serves as a lesson for other developing countries. The government policy initiatives allows resource supplementation and to some extent in risk mitigation. However, there is a need for a more coherent policy to address the needs of the industry in order to sustain innovation.

Despite the policy initiatives and government support, significant barriers exist in the local innovation system that negatively affects the formation of local open innovation networks between firms and public research institutions. The build up momentum is not sufficient to compensate for the insufficient capacity at the level of universities, lack of applied research at universities/public research labs, and lack of culture of collaborating between academia/public labs and industry. These impediments can be offset by bringing in changes at the grass root level rather than at a policy level. Given the weight of partnerships and the challenges faced by the organizations, there is an urgent need for introspection by the policymakers to adopt an innovation approach more suitable to the Indian needs.

Governments around the world feel that there is a need for national system of supporting institutions to support technical innovation especially in pharmaceuticals (Nelson Richard, 1993). The findings of this study show that private sector firms have been reluctant in using the government initiatives or relying on the national system to propel their innovation forward. With the internationalisation of R&D and access to many sources of innovation, Indian firms are technologically advancing forward by having meaningful partnership with foreign firms, universities and research consortium. In such a scenario, there is a need to revisit the meaningfulness of these public private partnership initiatives. In particular those policy initiated PPP schemes that require a mandatory academic partner for a project to be approved by the government are losing their sheen. Government sponsored PPPs have become easy fund raising schemes and have not yielded much research output (refer Section 6.1.2). The government should instead focus on having separate initiatives to support universities and industry. The following are the recommendations based on the findings of this study:

1. The current need is to revamp the infrastructure of the universities, increase the pace of setting up awareness camps on patenting and to spell out the benefits of collaboration to

the entities in the innovation ecosystem. Currently, there are very few research collaborations taking place between universities and industry. Low awareness of patents among the academics and a looming mistrust is related to the paradox of disclosure. These issues have been elaborated in detail in Section 6.1.4 and underline the need to align public research with industry needs (Cohen et al., 2002). Discrete events are not enough and it entails a strong momentum to enable change at the level of firms, academics and scientists engaged in new drug research. By supporting university research projects and providing funds for public research that is also of use to the industry, the government can facilitate creation of new technological opportunities in the university and research institutes, which will bring industry and academics together for scientific collaborations and increase chances of uptake.

2. There is a need for more concerted efforts to support the setting up of IP departments in universities and raising patent awareness programmes. The preference to publish over patenting their research causes insecurity among academics in interacting with industry scientists and proves as a barrier for research collaborations (Refer Sections 6.1.4). By facilitating patenting and raising awareness, government can help to dispel fears present among the scientific community regarding opportunism and enable to build trust-based relationships.
3. Conferences are an important source of informal networking (Refer Section 6.1.1) however this needs to be scaled up. In 2014 Daiichi had organised a drug discovery conference where scientists from industry and academia were invited to present their research, however such industry-sponsored conferences are limited. There is a need to for creating more opportunities for joint conferences and symposiums that would significantly create networking opportunities and enable the industry and academics to learn about the on-going research in each of these sectors.
4. Government should continue providing funding support to industry based R&D projects. Given the funding constraints faced by both established and SMEs, government should not restrict its initiatives or support only neglected diseases (Refer Section 5.1.2). Most of the companies have their strategic focus on commercially lucrative therapeutic areas such as diabetes, cardiovascular disorders and oncology as described in the case profiles of the companies in Section 6.1.3. In recent years, these diseases are not just diseases of the developed countries but have become significant in the Indian scenario also. Hence, government should widen their focus towards the support of these diseases too alongside providing incentives for firms to conduct commercial research on neglected diseases.

5. An inherent problem with the public initiatives is their dissemination through different departments. Currently in the Indian setup, the Department of Biotechnology, Department of Science and technology and Department of Pharmaceuticals all have different schemes to support specific research objectives. Few schemes are more popular among the others due to word of mouth awareness. As a result, some other existent and new schemes tend to get overshadowed (Refer Section 0). There is hence a need for a common communication platform where the stakeholders can get the necessary information about these initiatives. In this view, there is a need to establish single window clearance for providing grants (Senior Vice President, NCE Research, Piramal [31]) and merging of different agencies under one department to expedite the approval and grant of funds.
6. This study brings to light the state of research in the Indian academic sector and highlights the need for more handholding approach for academic researchers. It is important to support academics in the project initiation stage to undertake research for unmet need and with potential industrial application (Assistant Director, FICCI [24]). Federation of Indian Chambers of Commerce & Industry (FICCI) has taken up a step in right direction in guiding the researchers to undertake projects that are novel and where minimal research has been done. FICCI also puts the academic researchers in touch with industrial collaborators for potential collaborations (Refer Section 6.1.4). There is also a need for a database of researchers and scientists with their research interests that would serve as a single point of reference for collaborations.
7. The findings of the research suggest towards a more professional scrutiny and stricter action by the review committees for policy initiated programs. There have been examples where the project proposal is put in place only to get funds. Though each of the programs has in place a review committee but most of the times the review is not held in time (Refer Section 0). There is a need for a stricter review process to be held in a timely manner to monitor the progress of the research. Furthermore, it is important to enforce accountability for project delivery by putting in place time bound milestones.
8. A positive environment through supportive policies and easy regulations is important to make the process of innovation easier. The stringent regulations for clinical trials to ensure safety of patients has not helped much to make clinical trials transparent but has instead led to curbing of clinical trials in India and transferring them out to foreign locations leading to additional development costs. The bureaucracy process involved in the approval of funding proposals or clinical trials are detrimental to research (Refer

Section 0). There is hence an urgent need to make the government departments less bureaucratic and more science-driven.

The selection environment in India is currently conducive for open innovation and the stance taken by Indian companies has been favourable for innovation. However, Indian companies prefer to look only at foreign sources of innovation and disregard the local sources of innovations as major source of knowledge and expertise. In order to enhance discovery-oriented collaborations between pharmaceutical companies and public research institutions, there is a strong reason for university researchers to change their mind-set and engage in industry-oriented research for novel drugs. Likewise Indian firms should try to harness the knowledge and expertise existing in the local ecosystem for scientific advancement in new medicines.

8.3 Limitations

There are several lines of inquiry left unexamined in this research study. First, the findings are focused in the domain of pharmaceutical innovation industry that faces its unique set for drivers and constraints. Hence, the framework extended in this study is less usable in the other sectors or industries.

Secondly, many of the constraints and barriers highlighted in the Indian economy do not occur in the developed world. More specifically, the Bayh-Dole Act in the US has made possible the utilization and transfer of university research to industry for many industrial applications. The scientific discoveries from public research have contributed significantly to the success of the pharmaceutical industry in the developed world. Therefore, the findings of the study are less likely to be useful to the developed world and would resonate more with the university industry system in other developing countries.

Third, the sample did not include three key pharmaceutical companies – Sun Pharmaceutical industries, Zydus Cadila and Glenmark pharmaceuticals which are also involved in the discovery and development of new chemical entities. In 2014, Sun Pharma acquired Ranbaxy Laboratories and with this merger it has become the largest pharmaceutical company in India, and 5th largest generics company worldwide. Sun Pharma Advanced Research Company (SPARC) conducts research in the area of allergy/ inflammation area. Zydus Cadila, the

fourth largest pharmaceutical company in India has launched Lipaglyn (saroglitazar) in 2013, an NCE that is a breakthrough therapy in the treatment of diabetic dyslipidaemia and hypertriglyceridemia. Glenmark has made significant investments in R&D for drug discovery and development and has a pipeline of seven molecules. The company has struck several out-licensing deals and has three R&D centres for drug discovery and development. All these three companies would have served as excellent cases to be used in this study but could not be included due to access issues. In each of these three companies, many top management officials were contacted but they either did not respond to emails or refused to give an interview. This research study covers five prominent Indian pharmaceutical firms and four SMEs which is a fairly large sample considering that only 10-15 firms are involved in new drug research in India. However, there are limits to the generalisations that can be made from the data obtained and it is appropriate to say that the research is indicative.

A fourth limitation of this research is that only formally reported partnerships of the case companies are used for analysis. In the Indian set up, there are many research interactions between science and academia that rely on personal networks. Many such partnerships are not reported in the media. This research does not claim that all the research based networks formed by case companies are covered. To ensure completeness and offset discrepancy, the data is complemented by a series of semi-structured interviews. Furthermore, interviewee respondents validated the secondary research partnership data.

Lastly, there are advantages and disadvantages related to the fact that I am pharmaceutical professional, with work experience in Indian companies. The familiarity with the context allowed me to grasp the issues, the technical jargon used and was helpful to gather rich data. On the other hand, the subjective bias (Bryman, 2011) could not be completely removed. It was difficult at times to distance away from the subject, remove any previous understanding and to stay open to the current issues of the pharmaceutical sector. This limitation was offset by somehow making the analytical process more explicit.

8.4 Future Research Directions

The strategic lessons learned by Indian firms are important to understand open innovation in a pharmaceutical industry setting. The limitations of the study in terms of time and scope have pointed towards future research in the following directions. This study has identified

that cultural factors play a mitigating role in the establishment of research-based networks within the local innovation system. A future research stream can investigate this line of research further to yield a better understanding of this aspect and enable a shift from stand alone R&D innovation to a more network based socially efficient innovation.

Another future research challenge is to understand the relevance of open source innovation in pharmaceutical innovation. There is a stream of literature, which questions the usefulness of intellectual property protection on innovation (Pisano, 2006) and promotes open source for societal welfare (Baldwin and Von Hippel, 2010). This alternate stream argues that an open source model without IP is much more beneficial to promote innovation, and propel scientific network for social welfare. While the usefulness of open source in high cost pharmaceutical R&D is debatable (Munos, 2010), research that has attempted to reconcile these conflicting views is scarce. A future research agenda can aim to compare the two models for innovation performance. With mounting concerns over high drug prices, access to essential drugs to developing countries and the need for more research on neglected diseases in a product patent regime (Lanjouw, 1998), there is a need to find a suitable model which meets these objectives.

Another line of research can be the expansion of this study to undertake a comparative study with pharmaceutical sectors in other developing economies such as Brazil, Mexico that has well-developed pharmaceutical sectors. The comparison will shed more light into how innovation is taking place in developing countries under constrained resource conditions. It would be interesting to investigate if there are similarities in how open innovation is practiced in these economies and to investigate if the drivers and principles of open innovation framework developed in this study can be evidenced in other economies too.

This study examined an important and unexplored facet of open innovation in understanding the factors that led to the adoption of open innovation for discovery and development of innovative drugs by Indian pharmaceutical firms. The innovative environment in the Indian pharmaceutical sector is rapidly changing with new firms evolving and old firms disappearing from the innovation space. The challenges of pharmaceutical research complexity coupled with the ambition of Indian firms to make use of the opportunities in the commercial environment have led to many open innovation pathways adopted by the firms. Historically, the ability of the Indian firms to adapt to the challenges and leverage the opportunities at each of the appropriability regimes has significantly influenced the dynamics

of innovation. In today's times, those firms that cope up with the critical challenges of drug discovery and development will be successful. The insights into the strategic trends of large pharmaceutical firms and SMEs unveil a framework that may have important implications for organizations to further their innovation agenda. What works and what do not work is a useful lesson to be learnt along the innovation journey of Indian pharmaceutical firms.

Appendix

Table 34: List of Abbreviations and Acronyms

AIIMS	All India Institute of Medical Science
AYUSH	Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha & Homoeopathy
BCIL	Biotech Consortium India Limited
BIPP	Biotechnology Industry Partnership Programme
BIRAC	Biotechnology Industry Research Assistance Council
BISS	Bioincubator Support scheme
CBT	Centre of Biochemical Technology
CCMB	Centre for Cellular Molecular Biology
CDRI	Central Drug Research Institute
CRAMS	Contract Research and Manufacturing Services
CRO	Contract Research Organisation
CRSS	Contract Research and Services Scheme
CSIR	Council of Scientific and Industrial Research
DBT	Department of Biotechnology
DCGI	Drugs Controller General of India
DCR	Drugs and Cosmetics Rules
DNDi	Drugs for Neglected Diseases
DoP	Department of Pharmaceutical
DPCO	Drug Price Control Order
DPRP	Drugs & Pharmaceutical Research
DSIR	Department of Scientific and Industrial Research
DST	Department of Science and Technology
EMEA	European Medicines Agency
EPO	European Patent Office
FERA	Foreign Exchange Regulation Act
FICCI	Federation of Indian Chambers of Commerce and Industry
FIST	Fund for Improvement of S&T Infrastructure
FITT	Foundation for Innovation and Technology Transfer
HAL	Hindustan Antibiotics Limited
ICGEB	International Centre for Genetic Engineering & Biotechnology
ICMR	Indian Council of Medical Research

IDC	Innovating Developing Countries
IDPL	Indian Drugs and Pharmaceuticals Limited
IICB	Indian Institute of Chemical Biology
IICT	Indian Institute of Chemical Technology
IIRC	India Innovation Research Centre
IISc	Indian Institute of Science
IISER	Institute of Science Education and Research
IIT	Indian Institute of Technology
IND	Investigational New Drug Application
iOWH	Institute for One World Health
IP	Intellectual Property
IPAIRS	Indian Patent Database System
JPO	Japan Patent Office
MDRF	Madras Diabetes Research Foundation
MMV	Medicines for Malaria Venture
MRTP	Monopolies and Restrictive Trade Practices Act
MSME	Ministry of Micro, Small & Medium Enterprises
NCE	New Chemical Entity
NCL	National Chemical Laboratory
NDA	New Drug Application
NDDS	Novel Drug Delivery Systems
NII	National Institute of Immunology
NIO	National Institute of Oceanography
NIPER	National Institute of Pharmaceutical Education and Research
NME	New Molecular Entity
NMITLI	New Millennium Indian Technology Leadership Initiative
NRDC	National Research Development Corporation
OSDD	Open Source Drug Discovery
PCT	Patent Cooperation Treaty
PPP	Public Private Partnership
R&D	Research and Development
RAPID	Research Alliance for Product Innovation and Development
SBIRI	Small Business Innovation Research Initiative
SME	Small and Medium Enterprises
SPARC	Sun Pharma Advanced Research Company
SPARSH	Social Innovation Programme for Products Affordable and Relevant to Social Health

TDR	Special Programme for Research and Training in Tropical Diseases
TMC	Tata Memorial Centre
TRIPS	Trade-Related Aspects of Intellectual Property
TSLS	The Synaptic Leap's Schistosomiasis
UIPS	University Institute of Pharmaceutical Sciences
USFDA	US Food and Drug Administration
USPTO	United States and Patent and Trademark Office
WHO	World Health Organization
WIPO	World Intellectual Property Organisation
WTO	World Trade Organisation

Table 35: Details of Interviewee

Inter-view No.	Interviewee and Name of Organization	Date of Interview	Stage of Research Interview
Universities/ Pharmaceutical Academic Institutes			
1.	Professor, University of Mysore	February 2013	Stage 1
2.	Professor, University of Hyderabad	February 2013	Stage 1
3.	Professor, University of Pune	September 2014	Stage 2
4.	Professor, Dr. Bhanuben Nanavati College of Pharmacy	September 2014	Stage 2
5.	Professor, Saurashtra University	September 2014	Stage 2
6.	Professor and Head, National Institute of Pharmaceutical Education and Research - NIPER	September 2014	Stage 2
7.	Professor, National Institute of Pharmaceutical Education and Research - NIPER	September 2014	Stage 2
8.	Professor, Jamia Hamdard	December 2014	Stage 2
9.	Professor, IIT Delhi	December 2014	Stage 2
10.	Foundation for Innovation and Technology Transfer – FITT at IIT Delhi	December 2014	Stage 2
11.	Dean, IIT Delhi	December 2014	Stage 2
12.	Professor, Jawaharlal Nehru University	December 2014	Stage 2
Public Research Institutes			
13.	Professor, All India Institute of Medical Sciences - AIIMS	April 2013	Stage 1
14.	Scientist, National Chemical Laboratory	September 2014	Stage 2
15.	Scientist, Indian Institute of Chemical Technology	September 2014	Stage 2
16.	Scientist, Central Drug Research Institute	September 2014	Stage 2
17.	Professor, Dr. Reddy's Institute of Life Sciences - DRILS	October 2014	Stage 2
18.	Senior Scientist, National Chemical Laboratory	November 2014	Stage 2
Public Department			
19.	Project Director, Open Source Drug Discovery - OSDD	April 2013	Stage 1
20.	Advisor, Department of Science and Technology – DST*	December 2014	Stage 2
21.	Advisor, Biotechnology Industry Research Assistance Council - BIRAC	December 2014	Stage 2
22.	Scientist, Open Source Drug Discovery - OSDD	December 2014	Stage 2
23.	Head, New Millennium Indian Technology Leadership Initiative - NMITLI	December 2014	Stage 2
24.	Assistant Director, The Federation of Indian Chambers of Commerce and Industry – FICCI*	December 2014	Stage 2
25.	Manager, National Research Development Corporation - NRDC	December 2014	Stage 2
Pharmaceutical firms used as cases			
26.	Chief Scientific Officer, Curadev Pharma Private Limited*	February 2013	Stage 1
27.	Retd. Vice President Formulations, Ranbaxy Laboratories Limited	April 2013	Stage 1
28.	Retd. President, Dr. Reddy's Laboratories	April 2013	Stage 1
29.	Senior Vice President, Lupin Limited*	September 2014	Stage 2
30.	Senior Group Leader, Piramal Life Sciences	September 2014	Stage 2
31.	Senior Vice President, NCE Research, Piramal Life Sciences*	September 2014	Stage 2
32.	Senior Vice President, Piramal Life Sciences*	September 2014	Stage 2

33.	Vice President, Piramal Life Sciences	September 2014	Stage 2
34.	General Manager, Torrent Pharmaceuticals Limited	September 2014	Stage 2
35.	Chief Scientific Officer, Advinus*	September 2014	Stage 2
36.	Vice President, Lupin Limited*	October 2014	Stage 2
37.	Associate Director, Dr. Reddy's Laboratories	October 2014	Stage 2
38.	Senior Vice President, Ranbaxy Laboratories Limited	December 2014	Stage 2
39.	Associate Director, Daiichi Sankyo	December 2014	Stage 2
40.	Senior Management, Invictus Oncology	December 2014	Stage 2
41.	Managing Director, Lifecare Innovations*	December 2014	Stage 2
Other Pharmaceutical firms			
42.	Assistant Director, Ara Healthcare (Biopharmaceutical firm)	April 2013	Stage 1
43.	Director, Novo Informatics (Spinoff IIT Delhi)	April 2013	Stage 1
44.	Vice President, Dabur Research Foundation (Contract Research Organization)	April 2013	Stage 1
45.	Vice President, Fresenius Kabi Oncology Limited (Generics company)	April 2013	Stage 1
46.	Associate Director, Jubilant Chemsys (Contract Research Organization)	April 2013	Stage 1
47.	General Manager, Alkem (Generics company with NCE division)	September 2014	Stage 2
48.	Senior Director, Pfizer	September 2014	Stage 2
Other Interviews			
49.	Senior Director, Exploratory Research, Center for Advanced Drug Research, SRI International	September 2014	Stage 2
50.	Chief Scientific Officer, Thinq Pharma, India	September 2014	Stage 2
51.	Ms. Supriya Arun, Certified Pharmaceutical Patent Professional*	September 2014 – October 2015	Stage 2

* Interviewees who validated different sections of the dissertation

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