Typology of Upstream Pharmaceutical Supply Chains

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Masterprogram i industriell ledning och innovation
Abstract

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Antimicrobial resistance (AMR) is the process where the bacteria develop resistance towards the treating effect of an antibiotic drug. AMR poses an alarming threat to human health causing around 700,000 deaths per year around the globe. If appropriate measures to combat the resistance are not taken, the number of deaths globally could increase to around 10 million by the year 2050. There are various factors driving the growth of AMR of which antibiotic shortages are common. A clear insight into the pharmaceutical supply chain is necessary to understand the reasons causing antibiotic unavailability. Ensuring access to medicines is one of the major objectives of pharmaceutical supply chains. Pharmaceutical firms compete in a volatile market to increase their profits. Antibiotics render slim profit margins to pharmaceutical firms; declining profits and increasing costs of production have led to firms outsourcing their operations to suppliers in different geographical locations. This in turn forms complex supply chain structures with various actors of a single drug chain being dispersed across the globe. The complexity in these supply chains lead to antibiotic supply interruptions. National drug shortages drive the risk of AMR, and these shortages are caused when pharmaceutical supply chains are weak or fragile. Therefore, the pharmaceutical supply chains need to be thoroughly analysed. This thesis aims to explore the different possible upstream supply chain structures that could exist in pharmaceutical supply chains. The study also highlights the factors that motivate the firms to choose different supply chain structures. This research is based on the existing literature on pharmaceutical supply chains. Qualitative semi-structured interviews, reports and existing research articles guided the authors in building a typology of upstream pharmaceutical supply chains based on: how different processes are handled by the MAH, the geographical location of operations in the chain, and the sourcing strategy of the Market Authorisation Holder (MAH) who owns the license for the drug. The findings of this study outline how a pharmaceutical firm could possibly structure the upstream supply chain based on its strategies. This study is limited to conceptualizing only the actors involved in the direct supply chain of the focal firm (MAH), further research including actors in the extended supply chain needs to be performed to get deeper insights into pharmaceutical supply chains.

Key words: AMR, antibiotics, pharmaceutical supply chains, upstream pharmaceutical supply chain, supply chain networks, supply network design, supply chain management, vertical integration, outsourcing, off shoring.

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**Popular Science Summary**

We live in an environment where human beings are prone to get affected by a lot of bacterial inflectional diseases. Over the decades, several people have died of such diseases due to the lack of proper remedies. To overcome such an important issue, technological advancements and continuous research in the development of new medicine has helped human beings to combat such life-threatening diseases. Thus, medicine plays an integral part in human life. One such life-saving medicinal substances are antibiotics. Antibiotics are drugs which helps fight bacterial infections in patients. Modern medicine relies on antibiotic drugs to keep patients healthy. It has been identified that bacteria have increased their resistance against antibiotics, due to over usage and misuse of antibiotics.

The complex nature of the pharmaceutical supply chains leads to shortages in the supply of critical antibiotic drugs. Supply chain is the process of transfer of a product from the manufacturer to the customer. Additionally, the complex nature of the supply chains tends to cause shortages and unavailability of antibiotics to the end customer. Further, antibiotics shortages can lead to unavailability of right antibiotic to treat patients which causes life-threatening issues for the patients. For this reason, it is important to identify the pharmaceutical supply chain structures to analyze the causes of shortages of antibiotics.

The primary purpose of the thesis is to define the different types of supply chains that could exist in the upstream pharmaceutical supply chains based on the dimensions such as location, level of vertical integration and number of suppliers. Upstream supply chain involves actors like raw material manufacturers, primary manufacturers, secondary manufacturers and packaging of antibiotics. The thesis also explores the relevant factors that can influence the pharmaceutical firms to adopt different supply chains. The results from the thesis will help the pharmaceutical firms to consider the factors while decision making in order to avoid shortages and improve the availability of drugs for its customers. Further through the thesis, important concerns have been raised through the discussion, which could direct future studies to contribute for securing the pharmaceutical supply chains and mitigate the shortages of antibiotics. Interviews with experts in pharmaceutical supply chains, secondary sources and reports enable the researchers to study this topic.
Acknowledgement

This Master Thesis has been carried out under PLATINEA, a project led by Uppsala University to ensure the demands for antibiotic drugs are continuously identified and met. The interviews from experts within the pharmaceutical industry have guided the authors in developing this research project.

Firstly, we would like to thank PLATINEA, for giving us the opportunity to work with them in fighting against antibiotic resistance for the welfare of public health. Being part of a significant project gave us the motivation and purpose for our work.

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<th>Description</th>
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<tr>
<td>AMR</td>
<td>Antimicrobial resistance</td>
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<tr>
<td>API</td>
<td>Active Pharmaceutical Ingredient</td>
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<tr>
<td>CMO</td>
<td>Contract Manufacturing Organisation</td>
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<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>FDF</td>
<td>Finished Dosage Form</td>
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<tr>
<td>HAI</td>
<td>Hospital Acquired Infections</td>
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<tr>
<td>MAH</td>
<td>Marketing Authorization Holder</td>
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<tr>
<td>MNC</td>
<td>Multinational Corporation</td>
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<tr>
<td>NGO</td>
<td>Non-Governmental Organisation</td>
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<tr>
<td>OTC</td>
<td>Over the counter</td>
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<tr>
<td>PLATINEA</td>
<td>Platform for Innovation of Existing Antibiotics</td>
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<tr>
<td>SCM</td>
<td>Supply Chain Management</td>
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<td>TCE</td>
<td>Transaction cost economics</td>
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1. Introduction

The introduction provides a background on the problems of antibiotic resistance, antibiotic shortages and pharmaceutical supply chains. Section 1.5 explains the need for a typology study and section 1.6 states the purpose and aim of the thesis. The research questions are presented in section 1.7, followed by the limitations of the study in section 1.8.

Antibiotics are critical drugs with special medical value for patients. These drugs are essential in the treatment of infectious diseases. Antibiotic resistance is a global threat; Bacteria develop resistance to the antibiotic drug, causing the effect of the drug to be ineffective on patients. The co-ordinated action of multiple stakeholders is necessary to fight the growing threat of antimicrobial resistance (Roca et al., 2015). One of the driving forces of resistance is antibiotic shortages i.e., the unavailability of an appropriate antibiotic for treating infections. There is a strong correlation between antibiotic resistance and antibiotic shortages (Access to Medicine Foundation, 2018; The Public Health Agency of Sweden, 2017). To understand the reasons causing shortages of drugs, the pharmaceutical supply chains should be analysed.

The pharmaceutical supply chains are a mixture of complex processes, functions and firms who engage in research, development and manufacture of medicines. The supply chains are fragile, fragmented and need to be optimized to improve the responsiveness, increase production and reduce costs (Access to Medicine Foundation, 2018; Shah, 2004; Nagurney et al., 2013). Further, globalization has led to pharmaceutical firms increasingly outsourcing their processes to external firms in different countries. As a result of this, the supply chain structures are becoming more complex. The confidential contracts between the pharmaceutical firms and their suppliers create a lack of transparency in the supply chains (Davies and Lowenberg, 2018). The lack of transparency due to such contracts make it difficult to identify the actors involved in pharmaceutical supply chains. The following sections, section 1.1 to section 1.4 explain the background of the problems in detail.

1.1 Antibiotic resistance

Antibiotics play a crucial role in treating patients with bacterial infections. A negative consequence of improper or excessive use of antibiotics can be antibiotic resistance, which poses a threat to the effectiveness of treatment with existing antibiotics in patients (Access to Medicine Foundation, 2018; Aslam et al., 2018; Nordea Asset Management, 2016; Shibli et al., 2001). Antimicrobial resistance (AMR) is the term used to summarize all the different mechanisms bacteria can acquire to be resistant to antibiotics. AMR has been widely recognized as a growing global health issue. It has been prioritized as one of the major threats to be addressed by various health organisations worldwide, including the World Health Organization (WHO). The global AMR threat shows no signs of decline. The set of causes of resistance are multi-faceted (Aslam et al., 2018). Even though AMR is considered a natural phenomenon, the improper usage and over usage of antibiotics have accelerated the process. It has been estimated that AMR leads to 700,000 deaths annually worldwide of which around 25,000 deaths occur in Europe (Fauci and Alessi, 2018; Access to Medicine Foundation, 2018; Nordea Asset Management, 2016). Statistics show that antibiotic-resistant pathogen-associated hospital-acquired infections (HAIs) are the cause of around 99,000 deaths every year in the United States. Additionally, an economic loss of $35 billion has been recorded annually in the US health care systems due to the ‘productivity loss’ caused by AMR. A
United States non-profit global organisation anticipated a scenario where the world is left with no potent antibiotics to treat patients with bacterial infections and estimated that the global economic burden of this situation could be about $120 trillion. An estimated 444 million people globally could face the threat of succumbing to bacterial infections, with declining birth rates by the year 2050 (Aslam et al., 2018). AMR is a global threat and that the effects are not limited to the patients’ health alone. Severe effects on birth rates, infection rates and economic loss could be recorded.

There are multiple factors that cause the resistance to antimicrobials. One such factor is ‘inappropriate prescribing’. Wrongly prescribed antibiotics may have undefined therapeutic effects on patients, which in turn expose them to complications in following antibiotic therapies. Studies show that antibiotic treatment duration, agent choice and treatment indications are incorrect in 30% to 50% of the cases. In addition, unnecessary or inappropriate prescriptions of antibiotics in intensive care units vary between 30% to 60% (Shibl et al., 2001; Ventola, 2015). Antibiotic shortages also contribute to the growth of antibiotic resistance. The population in underdeveloped and limited-resource environments is prone to higher rates of resistance. Despite the limited access to antibiotics in these countries, the available antibiotics lack proper directions for use, which leads to antibiotic abuse, thus increasing the resistance levels in patients. Millions of people in many countries do not have access to generic antibiotics, and shortages in antibiotic supply chains have been reported frequently (Shibl et al., 2001; Access to Medicine Foundation, 2018).

1.2 Antibiotic shortages

Among the factors causing AMR, ‘antibiotic shortages’ are a common cause. Shortages lead to antibiotics not being able to be dispensed in pharmacies, hospitals and other outlets. A Europe-based survey conducted in 2015 states that patients are given inferior drugs during shortages. More than one third of respondents in the survey said that unavailability led to medication errors. Benzathine penicillin G, a common antibiotic was recorded to be unavailable in 39 out of the 114 countries examined. Between the years of 2001 to 2013, the United States experienced 148 national shortages for antibiotics. Additional shortages were experienced among 22% of other drugs (Access to Medicine Foundation, 2018). These antibiotic shortages fuel the formation of AMR. In case of a shortage of an antibiotic, accompanied by a high demand for it, doctors and physicians tend to prescribe an available, less optimal antibiotic for treatment. The alternative drugs can be less effective compared to the primary treatment and increase the risk of AMR formation in bacteria. When an ineffective antibiotic is used multiple times, the bacteria can, instead of being killed, adapt to it and develop resistance. Therefore, the supply of effective, proper antibiotics must be ensured to provide safety of patients (Fauci and Alessi, 2018; Access to Medicine Foundation, 2018).

1.3 Complex pharmaceutical supply chains

The supply chain networks today are increasingly complex, as most of the businesses tend to outsource their processes to firms in other countries to attain cost leadership and exploit their resources (Harland et al., 2002). This increased complexity of supply chains can lead to supply disruptions, as a small change or minor problem in one of the global links could affect the whole downstream supply chain. These complex supply chains increase the uncertainty of supply, which further makes it difficult to achieve a decent supply chain visibility. Davis and Loewenber (2018)
argue that the reason for shortages in the antibiotic supply chains result from the weak structure of the supply chain. The supply chain for antibiotics is complex and involves several intermediaries that are not explicitly disclosed by pharmaceutical companies, thereby generating a lack of transparency throughout the chain (Davis and Loewenberg, 2018; Nordea Asset Management, 2016).

There are multiple actors involved in the supply chain of every antibiotic. The exit or failure of any one of these actors could lead to supply interruptions. Any issue that arises in the upstream supply chain will have a severe impact on the downstream supply of antibiotics to hospitals, pharmacies and patients. If any of the manufacturers in the supply chain face a problem, there are high chances that it will result in a national shortage. The probability rises in cases where one manufacturer holds a large market share or is the sole manufacturer of a substance (Fox et al., 2014). In addition, the situation is aggravated when healthcare systems face larger demands than the regular order quantity or buy stocks to ensure sufficient supply in shortage situations. Such excess ordering can increase the duration of shortages. Pharmaceutical firms outsource their manufacturing activities to other contract manufacturing organisations (CMOs) based on their make-or-buy decisions. When the firm decides to ‘make’, the activity is carried out in-house. Whereas, when the firm decides to ‘buy’, the activity is outsourced to a CMO. CMOs provide manufacturing services for multiple firms. Pharmaceutical firms order in excess quantities during times of shortages and high demand to ensure safe supply. These large orders placed by the firms cause a ‘bullwhip effect’ in the upper stages of the chain for the particular product (Shah, 2004). For example, if a particular API is out of stock and the firm orders huge quantity of API to the API supplier, the API supplier will order an even higher volume of the particular API which is already out of stock. This increases the duration of shortages, as multiple firms source API from a single supplier. When one firm orders large quantities of a particular material, the other firms also face shortages due to the increased delay of the supplier in processing the large orders.

National shortages can also be caused when pharmaceutical companies prioritize larger profitable markets over smaller ones, when the supply chains are weak or fragile or by inadequate financing in healthcare facilities and unaffordable or expensive products (Access to Medicine Foundation, 2018). Pharmaceutical firms prefer larger markets to sell a higher volume of products and generate higher revenue, which makes smaller markets less attractive to firms. The pharmaceutical supply chains are complex, and the supply chain actors are fragmented with more actors in one part of the chain and lesser number of actors in other parts. The supply chain for a particular drug could be weak owing to the reliability of its supply chain actors. In developing countries or limited-resource countries, shortages could be caused by insufficient financing for healthcare facilities to patients from the government and the lack of economic incentives for pharmaceutical firms. The lack of government funding for medicines in these countries lead to unaffordable prices for drugs.

1.4 Manufacturing practices as risk factors

The different stages in the antibiotic supply chain are fragmented among different players, with multiple players at some stages and very few players in certain vital stages of the chain. One such vital stage is the Active Pharmaceutical Ingredient (API) production. The concentration of API producers is limited to only a few countries, with low production costs, such as India and China. Such overdependence on one or two players can cause accessibility issues and the collapse of the supply chain if there occurs any problem at these sites. For example, an explosion happened in a
Chinese production facility which was the sole API producer of Piperacillin-Tazobactam, a highly important antibiotic, that suddenly became unavailable all over the world (Access to Medicine Foundation, 2018).

A review conducted by the FDA in 2011 on the reasons for drug shortages identified manufacturing issues as the major causes contributing with 43% to the shortages. Shipping or manufacturing delays contribute with 15% each and the lack of API availability contributed with 10% (Fox et al., 2014). These results demonstrate that issues in the upstream antibiotic supply chains are the major cause for drug shortages. To address the reasons behind the shortages due to manufacturing issues, the upstream supply chain of antibiotics has to be analysed. However, this is not easy as the information concerning the pharmaceutical companies’ suppliers are kept confidential. In a previously conducted investigation of 18 pharmaceutical companies, only one company published information about its corresponding third-party manufacturers (Access to Medicine Foundation, 2018). This lack of visibility in antibiotic supply chain makes it difficult to analyse the risks in the supply chain resulting in the supply shortages.

1.5 Why we need a typology

The focus of this thesis is on the upstream pharmaceutical supply chain. The supply chain in the pharmaceutical industry are highly fragmented, complex and have a lack of visibility. The lack of visibility in the supply chains make it difficult to analyse these supply chains. This motivates the need for a typology study to generate the different types of upstream supply chain structures that could exist in the pharmaceutical supply chains by incorporating the various factors that are involved in shaping the different supply chains.

The mechanism in typological theories incorporate the holistic principle of enquiry into organisational research. This principle states that multiple characteristics must be considered in order to understand organisations and how organisational factors fit together (Doty and Glick, 1994). The terms ‘organisation’ and ‘organisational research’ refers to how types are created. Typologies are complex and are more than just classifications. In order to understand the concerns in the upstream supply chain, the diverse involved factors in the upstream supply chain must be considered and organised into typologies. Identifying, conceptualizing and incorporating these factors into the study would increase the understanding of the upstream supply chain and the reasons for particular pattern of supply chain’s existence could possibly be understood.

Typologies refer to inter-related sets of ideal types which are conceptually derived. Multiple ideal types are identified in typologies that represent a specified combination of organisational outcomes which shape or influence the possible obtained outcomes (Doty and Glick, 1994). In terms of antibiotic supply chains for example, a ‘vertically integrated supply chain’ can be an ‘ideal type’ of network structure. The variables that constitute this type could be that the antibiotic product associated with the supply chain could be a branded drug and one manufacturer holds the market with exclusivity. The other constructs or variables that come under this ideal type could be that there is high profitability in the branded drug market which supports vertical integration of all the processes.

These conceptualizations made in the typology study help researchers to theorize beyond the limits of their current empirical world. Researchers can conceptualize the possible types of organisations,
which may not be explicitly known or identified in the empirical world (Doty and Glick, 1994). The flexibility to make such conceptualizations is one of the reasons why it is suitable to our aim to understand the upstream supply chain in spite of its lack of transparency. Such conceptualization help identify the underlying factors that shape the upstream supply chain structures.

1.6 Aim and Purpose

This master thesis has been conducted under PLATINEA (Platform for Innovation of Existing Antibiotics), a two-year project to address the issue of insufficient availability and inappropriate use of antibiotics. The two main goals of PLATINEA are: (1) to improve/secure the availability of important antibiotics and (2) to improve the use of antibiotics. Through this study, we focus on contributing to PLATINEA’s first aim of improving/secureing the availability of antibiotics. In order to improve/secure the availability of antibiotics, the first step is to understand the pharmaceutical supply chains. The focus of this thesis is to understand the upstream pharmaceutical supply chain problems that affect the availability of antibiotics. The upstream supply chain includes the manufacturing processes and problems in the manufacturing of drugs are the cause for 43% of the drug shortages (Fox et al., 2014). The complexity of pharmaceutical supply chains is increasing as an effect of globalisation. This leads to supply chain actors for the supply chain of a single drug to be dispersed around the globe. Previously conducted research in the field of pharmaceutical supply chains contain little to no research on pharmaceutical supply chain structures and how the supply chain structure varies. This research intends to fill this research gap by conducting a study on the upstream pharmaceutical supply chain structures. Further, the data pertaining to upstream pharmaceutical supply chains are not available in a consolidated manner in existing academic articles. This thesis will also serve as a vital source of information regarding the upstream pharmaceutical supply chains.

The main aim of the thesis is to build a typology of the different possible upstream supply chain structures that could exist in the pharmaceutical supply chains. Further, this study also identifies some of the factors which motivate the pharmaceutical firms to adopt the supply chain structures that are identified through the typologies. A typology of the different possible supply chain structures will be conceptualized and organized based on the dimensions used to build the typology. The results of this study shall increase the existing knowledge about upstream supply chains. Though the study is conducted with a goal of contributing to understanding the upstream pharmaceutical supply chains, the results of the study can be applied to a general context.

1.7 Research questions

RQ 1: What are the different dimensions that could be used to build a typology of upstream pharmaceutical supply chains and what are the possible supply chain structures that could exist based on these dimensions?

RQ 2: What are the different factors that motivate the pharmaceutical firms to adopt the supply chain structures that are identified through the typologies?

Addressing the Research questions

The RQ1 was investigated firstly by empirical findings that have been presented in chapter 4 and then analysed with the theoretical concepts that have presented under the chapter 2. Theoretical
concepts such as 2.2.2 Supply chain design, 2.2.3 Vertical integration, 2.2.4 Core competency theory and 2.2.5 Transaction cost economics (TCE) were used to build the typology. These concepts explain the different rationale of the management followed in make-or-buy decisions of a product/service. The dimensions used to build the typology were derived from the concepts in the theories and possible supply chain structures that could exist in the upstream pharmaceutical supply chain have been presented. The analysed results are presented in section 6.1 under chapter 6.

Similarly, RQ 2 was investigated with the empirical findings that have been presented in chapter 4, findings under the section 4.4 Supplier selection, 4.5 Supply chain risks, 4.6 Time to market and 4.7 Competitive strategies. The investigated data has been analysed and the results are presented in section 5.2.

The research was conducted in a qualitative data collection approach. This design enabled the researchers to provide an analysis and answer the research questions. The data collected formed the basis for the conceptualisation of this typology study. The different supply chain structures that were identified under the typology were explained logically by analysing the collected data and complementing them with concepts from the theoretical frame.

1.8 Limitations

The scope of the study is limited to analyse the factors affecting the upstream pharmaceutical supply chain. The distribution(downstream) part of the chain has not been covered in the study. Hence, discussions on other important aspects in supply chain such as purchasing, commercialisation etc. have not been included. Further, the data collected for empirics were based on a unilateral perspective, focussing only on the focal firm’s (MAH) strategies and its effects on the supply chain structure. The supply chains conceptualized in the analysis section does not consider the actors involved in the extended supply chain i.e, suppliers of the focal firm’s suppliers. A total of only ten different upstream pharmaceutical supply chain structures were identified through the study. However, there could be many more possible supply chain structures that could exist in the pharmaceutical supply chains. Some of the supply chain structures identified through this thesis might not be appropriate for certain types of drugs.
2. Literature review

In this chapter, a review of the current literature on pharmaceutical supply chains has been presented under section ‘2.1’. The following section, ‘2.2 Theoretical Framework’, contains a literature review in the field of supply chains, different theories that explain the governance of make-or-buy decisions in an organisation and theories that are used to analyse the external suppliers. These theoretical concepts are used to analyse the empirical data and answer the research questions. The last section, ‘section 2.2.8’ provides a summary of the theoretical framework and explains how the theories have been mobilized in the thesis. This section also explains the connection between the different theories.

2.1 Current Research on Pharmaceutical Supply Chains

Shah (2004) reviews important issues in the design and operation of pharmaceutical supply chains. The author contributes to solving these issues by proposing strategies for the issues identified in the supply chains. The article outlines the general structure of a pharmaceutical supply chain, explaining the activities of the supply chain actors. The author focusses on the main features in the operational issues, strategic and design issues within the pharmaceutical supply chains. Further, Shah (2004) reviews academic research conducted on fields relevant to these issues to discuss the solutions suggested by different researchers. The author suggests solutions to the issues by suggesting improvements in existing processes and improvements in strategic decision-making processes.

The research article by Mehralian et al. (2013) develops an agile pharmaceutical supply chain model to efficiently manage the risks in pharmaceutical supply chains. The authors use the supply chain operations reference (SCOR) model to analyse the three parts of a pharmaceutical supply chain i.e, the supply of API, the FDF manufacturing and the distribution processes. The main findings of the article include the list of factors affecting agility in the different stages of the pharmaceutical supply chain. A list of seven factors were identified under each part, which affects the supply chain agility. Among these seven factors, the most important factors affecting agility were identified as delivery speed, cost reduction, market research and quality.

Mousazadeh et al. (2015) develop a bi-objective mixed integer linear programming (BOMILP) model to solve a network design problem in pharmaceutical supply chains. The model developed by the authors assisted in strategic decision making concerned with the opening of manufacturing and distribution centers permitting optimal material flows. The main aim of the model is to minimize the total costs and satisfy the consumer demand for the drug.

Chris et al. (2010) have discussed the issues in supplier selection for a pharmaceutical supply chain, and they have developed an analytic hierarchy process (AHP) model to quantify strategic supplier selection and evaluate problems. The authors argue that competent suppliers are vital resources in pharmaceutical supply chains and that the lack of good suppliers lead to supply chain performance. The research follows a case study methodology, which studies the case of a U.S based pharmaceutical firm. The AHP model developed by the authors claims to help the decision makers to choose suppliers by ranking alternative suppliers with the importance of their attributes. The study conducted by Huq et al. (2016) explains that the configuration of pharmaceutical supply chains has an impact on the performance of pharmaceutical firms. The author focusses on the
supply chain related disturbance factors to be considered when configuring supply chains. In the article, they have used a multi-phase, mixed-methods approach to identify five important disturbance factors. The factors identified by the authors were quality defects, interruptions in manufacturing processes, difficulties in order processing, delay in product delivery and supplier’s inability to respond to market demand. All the factors identified by the authors were supplier-related disturbance factors.

Breen (2008) claims that drug shortages in pharmacies are caused by the risks in the pharmaceutical supply chain. The author explains that these risks can lead to product discontinuity, shortages, poor performance of firms, dispensing and technological errors. The study aims to understand the nature and prevalence of risks in pharmaceutical supply chains. The author collected data at a workshop conducted with participants from pharmaceutical firms. A total of 35 risks were identified through the workshop, with varying levels of criticality among the identified risks.

The research conducted by Jaberidoost et al. (2013) also focuses on identifying the risks in pharmaceutical supply chains. The authors used databases such as Scopus, PubMed, Web of Science and search engines to collect literature studies in the field of pharmaceutical supply chains. A systematic review of these articles led to identifying 50 main risks and categorised them into seven categories such as supplier issues, strategy issues, financial, logistic, political, regulatory and market issues. The paper concludes that most of the risks identified in the study were internal risks caused by people, processes and functions mismanagement.

The article by Lucker and Seifert (2017) analyses three risk mitigation strategies, dual sourcing, agility capacity and RMI. The authors use a mathematical modelling methodology to model the supply chain of a pharmaceutical firm. The model is based on lowering the total costs incurred by the pharmaceutical firm exposed to disruption risks over a one-year period. The results from modelling suggest that dual sourcing is a better strategy to reduce long disruption times. They further conclude that RMI and agility capacity strategies can be used as substitutes by the firm when dual source of supply is unavailable.

Prasnikar and Skerlj (2006) discuss the importance of time-to-market in pharmaceutical industry for firms. They investigate the managerial factors affecting time-to-market. Through their research, the authors have identified that the factors are related to processes, organisation and measurement. They outline the importance of early supplier involvement and strategic partnering in new product development processes which could have an impact on the market entry and performance.

Capo et al. (2014) understand the different business strategies in pharmaceutical supply chains by observing a network of pharmaceutical firms in the supply chain. The authors follow a case study methodology in their research by studying four different pharmaceutical firms. They have conducted semi-structured interviews to understand the different business models adopted by pharmaceutical firms. The study claims that pharmaceutical firms will be unable to generate value with their current business models in the long run, owing to changing market environments. The article concludes that firms should restructure their business models, involving universities, government and industry actors to ensure an overall functioning of the system.
The current research on pharmaceutical supply chains focus more on supply chain risks, risk mitigation strategies and optimisation of supply chains etc. There exists very limited research on the configuration of upstream pharmaceutical supply chains. The existing research does not outline the different supply chain structures that could exist within the pharmaceutical industry. This thesis aims to fill this research gap by building a typology of upstream pharmaceutical supply chains. Further, this study also highlights the different factors that motivate pharmaceutical firms to adopt various supply chain structures. The outcome of this research would be an increased understanding of how the upstream supply chains could vary and the factors that are considered important by pharmaceutical firms when structuring their upstream supply chains.

2.2 Theoretical Framework

2.2.1 Supply Chain Management

There has been some confusion in reaching a concrete definition of ‘supply chain’ and ‘Supply Chain Management’ (SCM) (Mentzer et al., 2001). La Londe and Masters (1994) defined supply chains as various individual firms playing different roles connecting to each other forming a chain. Roles taken by firms are procurement of raw materials, assemblage of components, transportation of products, and ensuring delivery to the final customer. Christopher (1992) stated that a group of different entities or organisations involved through upstream (i.e., supply) or downstream (i.e., distribution) linkages for different processes performed to deliver the products to the final customer can be termed as a supply chain. Beamon (1998) defines a supply chain as a structured manufacturing process wherein raw materials are transformed into finished products, which are subsequently delivered to the end customers. Mentzer et al., (2001) state that the supply chain is a set of entities involved in the supply and distribution flows of goods, service, finance, and information from a source to a destination. Mentzer et al., (2001) additionally classified the complexity of supply chains. He identified three degrees of supply chain complexity namely ‘direct supply chain’, ‘extended supply chain’ and ‘ultimate supply chain’. A ‘direct supply chain’ includes the company and its immediate suppliers and customers. An ‘extended supply chain’ includes suppliers of the immediate suppliers and customers of the immediate customers. In the ‘ultimate supply chain’, all the actors involved from the procurement of raw materials to the delivery of the products to the end customers are included.

The definition by Mentzer et al. (2001) was chosen as a model for this study. It highlights the vast network of the supply chain and allows categorization of the degree of complexity. It also emphasizes the importance of realizing that the way an organisation chooses to manage its supply chain can create competitive advantages for the organisation. Firms who efficiently manage their supply chains perform better than the competing firms (Mentzer et al., 2001).

The management of the existing supply chains within organisations is termed as supply chain management. In this study, the researchers will largely focus on the antibiotic supply chain of complexity type, ‘direct supply chain’ which will include the immediate suppliers connected to the focal firm in the upstream network (Mentzer et al., 2001). In this thesis, the Market Authorisation Holder (MAH) is referred to as the focal firm, which holds the license to sell the drugs to the market.
2.2.2 Supply Chain Design

Supply chain design concerns questions regarding the location of manufacturing, storage and transportation related facilities (Chopra and Meindl, 2016). Song and Sun (2017) claim that the design of a supply chain aims to shape the supply chain structure and the sequential links among the components of the system. The decision of where to locate the facilities has a long-term impact on the performance of the supply chain as it very expensive to relocate or shut down a facility (Chopra and Meindl, 2016). Many researchers have suggested that the supply chain design is carried out in three phases. Firstly, internal and external environments such as product and market characteristics and sourcing context are identified and understood. Secondly, potential alternatives of the supply chain structure are defined, and a preliminary assessment is conducted. Lastly, a quantitative assessment of the alternative structure is conducted, and a detailed design is created (Song and Sun, 2017). The facility location also sets constraints on how the inventory, transportation and information can be used to reduce the costs or to improve the responsiveness towards the end customer. The development of an appropriate supply chain depends on the individual organisation's objectives ranging from low cost to high responsive nature. The multinational antibiotic companies focus more on the low-cost supply chain goals which leads to the actors in their supply chain being more globally dispersed in low-cost manufacturing locations. Companies which focus more on high responsiveness from actors in their supply chain tend to choose suppliers who are easily accessible. Similarly, Song and Sun (2017) claim that supply chains have become more complicated, especially for multinational companies, owing to additional hurdles like legislation, economic issues, trade barriers in international trade and environmental concerns.

Chopra and Meindl (2006) identified different factors that affect the design of the supply chain network. The strategic factor, technological factor and macroeconomic factors are explained in the following paragraphs. In this study, these factors will be considered to conceptualize the typology of antibiotic supply chains and to understand how these factors influence the configuration of pharmaceutical supply chains.

A firm's competitive strategy has a significant impact on the decisions within the supply chain. Firms that focus on cost leadership will tend to find the lowest cost location for their manufacturing facilities, even though it is far from the markets they serve. Watson et al. (2013) state that the location of the manufacturing plant is considered as one of the critical factors in the success of any supply chain. Further, firms spend 80% of their total investment on the manufacturing plant to manufacture its goods. So, it is important for firms to take a strategic decision on selecting the manufacturing location (Watson et al., 2013). Similarly, Melo et al. (2009) claim that firms spend more time in taking strategic decisions due to huge investment. Further, he adds that the decision should help the firms to have possible adjustments in the chain configuration over a period of time in case there are any interruptions in the chain design. Harrison (1995) states that strategic decisions are important for organisations for their long-term implications. Further, he adds that strategic decisions often occur in the following three situations: (1) Decisions related to product/services, (2) Decisions related to development and implementation of technology for serving the product/services and (3) Decisions related to the differentiation and integration of an organisation structure. Firms that focus on responsiveness tend to locate their facilities closer to the market and may select a high-cost location if the company needs to respond quickly to the market needs. Similarly, this factor can influence the design of the supply chain structure for...
pharmaceutical industries. For example, if a firm wants to achieve cost leadership it might move its manufacturing plant of (API or Formulation) to low-cost manufacturing countries; if the company wants to focus on responsiveness it tends to locate their facilities closer to their market (Chopra and Meindl, 2016).

Characteristics of available production technologies also have a significant impact on the chain design decisions. If the technology for production of products in large quantities is not available within the firm, it tends to utilize the capacities of other suppliers by outsourcing production functions to contract manufacturers. In most cases, such outsourcing operations are combined with significant economies of scale for the focal firm. Such decisions made by the focal firm increases the volume of production but induce changes in the supply chain structure in terms of location. In addition, the inventory management has to be optimized to suit the high volumes produced.

Macroeconomic factors include tariffs, exchange rates, taxes and shipping costs that are not internal to an individual firm. As global trade has increased, macroeconomics factors have had a significant influence on the success or failure of supply chains. Thus, firms take this factor into account when making chain design decisions. Tariffs have a substantial impact on location decisions within a supply chain. If a country has high taxes, companies either tend not to serve the local market or set up manufacturing sites within the country to save on duties. Developing countries often create free trade in which taxes and tariffs are relaxed as long as production is done primarily for export. This characteristic produces a strong incentive for global firms to set up plants in developing countries, which enables them to exploit their low labour costs.

Supplier selection has gained importance in the past few decades as organisations started to focus on its issues of core competence, and to outsource less profitable activities to supply chain partners (Govindan et al., 2013). Also, recent trends in global production have increased both supply chain complexity and have led to changes in the business strategy of organisations. Additionally, it also causes the organisations to move from centralised, vertically integrated, single-site manufacturing locations into geographically distributed locations that collectively benefit and create value for their customers (Kirytopoulos et al., 2008).

The evolution of supplier selection requires a more strategic focus on the buyer-supplier relationship, where close collaborations are necessary, and certain skills and capabilities should be seen by the focal firms while selecting its particular supplier. Since qualified and reliable supplier is one of the key elements in reducing the material cost and achieving on-time deliveries, these are the two important elements plays a vital role in decision making in supply chain management (Kirytopoulos et al., 2008).

2.2.3 Vertical Integration

Vertical integration can be described as the overall scope of different business activities in a supply chain brought under the management of a single company. It is distinct from supply chain integration which has been described as all value adding activities and business process from raw material extraction to the consumption of products by the end user. Different functions which can be carried out by separate firms but handled by a single company owing to its competitive strategy or business model is called vertical integration (Mahoney, 1992; Ellram, 1991). Vertical integration can be realized by two approaches, either vertical financial ownership or vertical
contracts. Vertical financial ownership eliminates the company boundaries through mergers and acquisitions, while vertical contracting includes exclusive dealing and resale price maintenance, which offers a viable alternative to vertical financial ownership. The driving force of vertical integration in strategic and economic theories can be classified into four different categories: transaction cost considerations, strategic considerations, output and/or input price advantages and uncertainties in cost and/or price advantages (Mahoney, 1992). In these categories, the first two categories are more relevant for analysis in this thesis. Transaction cost considerations refers to the considerations made by the firm for making decisions on outsourcing their functions or performing them internally. Strategic considerations are the outcomes of vertically integrating the functions in a firm like barriers to entry, maintaining control over the firm’s functions. Dependency on external actors for resources can give rise to transaction costs such as opportunism, delay in delivery time etc. from external suppliers. This can lead to a higher level of vertical integration in firms. For instance, a firm may choose to vertically integrate its functions to reduce its dependency on external suppliers. As the firm vertically integrates the operations through its supply chain, it creates entry barriers to external actors which are not part of the firm.

Companies also choose to vertically integrate mainly to have better control over their functions. This leads to increased communication among actors in the same organisation which is better than inter-firm communication and lower costs. This power to control the firm’s operations internally also avoids opportunism and externalities that could arise due to quality issues in products handled by external suppliers (Ellram, 1991). From a strategic perspective, vertical integration can implement entry barriers for competitors and lead to excess profits for the manufacturers. For instance, a study revealed that pharmaceutical companies acquire offshore capabilities or supplier firms i.e, ‘captives’ through vertical financial ownerships (Huq et. al, 2016). By acquiring the ownership of such resources, firms gain a better control over their operations and simultaneously avoid transaction costs that could arise from external firms. Additionally, vertical integration can increase rivals’ costs or leave the market thin, thereby restricting the expansion of competitors (Guan and Rehme, 2012; Ellram, 1991). If the operations that are vertically integrated by an organisation are larger than the degree to which it can handle managerially, structurally and technically, there is a risk of diseconomies. Other risks include losing focus on core processes, managerial failure and the risk of technological and financial ownership (Ellram, 1991).

Williamson (1975) argues that becoming dependent on a monopolistic supplier, thus giving space to opportunism, is the reason behind firms not wanting to distribute their operations to suppliers. He further explains that vertically integrated processes can achieve economies of scale and flexibility in situations of uncertainty without opportunistic behavior from other entities. Recurrent processes that require highly specialized assets are more likely to be vertically integrated. In his research on vertical integration, Harrigan (1983) states that vertical integration in a firm takes place when the firm grows and is successful. He continues arguing that the degree of vertical integration is less in highly volatile and uncertain markets. Depending upon the competitive strategy of an organisation, the vertical integration patterns are subjected to change over time (Ellram, 1991).

2.2.4 Core competencies theory

A unique set of skills that differentiate an organisation from the rest of the players in the industry is a vital component to gain a competitive advantage in the market. These set of skills are known as the ‘core competencies’. According to Prahalad and Hamel (1990) core competencies are a
concept in the field of management theory fulfilled when satisfying a set of three criteria. Porter (1986) and Snow and Hrebiniak (1980) argue that firms that concentrate on their unique competence and outsource the other additional operations to different members in the network, thus deintegrating their functions proved to be highly competitive firms and achieved a high degree of flexibility and focus in their operations. An intelligent ‘downscoping’ of the activities of the firm is preferred for implementing this strategic orientation that enables companies to concentrate on their core competencies (Jarillo, 1988; Sydow and Windeler, 1998). Firstly, core competencies are difficult for competitors to imitate, secondly these set of skills can be reused widely for various markets and products and lastly, they must contribute to the benefits experienced by the final consumer and add value to its customers.

Carlos (2003) states that for core competencies to yield a competitive advantage, they must be inimitable, costly or difficult for competitors to imitate. These set of skills are developed over a significant period of time rather than through a single large change. It is important to build core competencies over vertical integration in order to succeed in the global market (Kawshala, 2017). Similarly, Carlos (2003) states that core competencies are an accumulation of knowledge as organisations learn, actualize that learning in competencies and deploy those competencies in their product market strategies. He also argues that competencies are typically embedded in an organisation acquiring a distinct bundle of competencies involving important resource investments such as capital, individuals and management vision.

Core competencies in companies give rise to various decisions, which shape or change the structure of a supply chain. It has been observed that a company could take decisions to focus on their core activities, while outsourcing or offshoring non-core parts of the supply chain (Huq et al., 2016). For example, if the core activity of a focal firm is research, there is a possibility that the company will outsource the API manufacturing and formulation parts of the chain to contract manufacturing organisations (CMOs). This could cause different configurations in the supply chain structure depending on the factors that are considered indecision making.

### 2.2.5 Transaction cost economics

Williamson (2010) explains that transaction cost economics (TCE) is how operations are combined with the governance and organisation of the business. The TCE theory has been elaborated by Williamson based on the previous concepts that have been developed by Coase (1937). The TCE theory contributes to the questions such as ‘why firms are founded’, ‘how are firms governed and structured hierarchically’. Similarly, Schwabe (2013) states that TCE inspects how business partners react to one another from harmful subsidiary indifferent relationships. The theory also acts as an important tool for the firms in ‘make-or-buy’ decisions, where ‘make’ refers to manufacturing the product in-house and ‘buy’ means purchasing the service/product from external suppliers in the market. TCE offers a natural fit within supply chain management research because it centers on make-or-buy decisions (Bremen et al., 2010; Ketchen and Hult, 2007).

A transaction can be defined as the transfer of a semi-manufactured product or service from the upstream to the downstream manufacturing stage. This transaction causes transaction costs in the form of information, communication and coordination. Some examples of transaction costs can be the processes of searching, negotiating, executing etc. The goal of the firm when outsourcing its functions to external actors is to minimise the transaction costs while carrying out transactions
The transaction costs involved in sourcing from external suppliers affect the transaction governance. In general, two extreme modes of transaction governance are differentiated because of variation in transaction cost characteristics i.e., the ‘market’ and the ‘firm’. According to TCE, low transaction costs favour market exchange, i.e. intermediate products are purchased from suppliers, and high transaction costs favour hierarchical governance structure i.e., intermediate products are manufactured in-house by the firm (Bremen et al., 2010). Transaction costs can also affect the level of vertical integration in firms. If the transaction costs involved in sourcing from external suppliers are high, then the firm could vertically integrate the function by having it in-house, or by acquiring firms who specialise in the product/service through vertical financial ownership.

The two critical drivers of TCE are uncertainties caused by cost and external environment, which consist of coordination cost and transaction cost. According to TCE, a firm will outsource its functions if the total cost involved in outsourcing is lower than the costs incurred by the firm in manufacturing or handling the functions internally (Bremen et al., 2010). However, according to Williamson (2010), producing in-house will be the last option, since it is the most complex procedure.

The TCE theory explains that when transaction costs incurred for outsourcing the product/service to an external supplier are high, the firm should favour a hierarchical governance structure i.e., manufacture or handle the product/service in-house. However, when the firm tends to outsource the function to a global supplier situated in a low-cost manufacturing country, the transaction costs involved in the transaction are higher when compared to a local supplier owing to the added efforts in searching, negotiating, executing, monitoring and controlling. The major reasons that lead to higher transaction costs in global transactions are the geographical and cultural distance between the firm and the global supplier. Firms prefer global sourcing despite high transaction costs because sourcing from an external supplier helps firms achieve significant cost savings, higher economies of scale and utilize low-cost labour force in the global market. The transaction costs incurred by a firm when sourcing from a global supplier affects the performance of the sourcing activities in the firm, which could result in the need for a change in the governance structure of the firm. In this context, ‘restructuring the governance structure’ implies that the firm has to relocate its supply chains to regions where the transaction costs are reasonable. This relocation could mean that the firm has to either vertically-integrate its operations or outsource to suppliers in locations which favour lower transaction costs (Bremen et al., 2010).

2.2.6 Strategic Networks

Firms vary in their profits and conduct, which is a vital research question in the field of strategy followed by different firms (Gulati et al., 2000). In today’s world, different companies are interconnected as members of networks in which their relationships are social, professional or exchange with different actors. These networks comprise inter organisational alliances which form a strategic importance for the actors/firms which enter the network of ties, forming alliances, partnerships, long-term relationships and so on. By understanding the relationships within the network, the performance of firms can be understood. (Gulati et al., 2000; Jarillo, 1988; Sydow and Windeler, 1998).
Strategic networks serve as a source of information, markets, technology and resources to focal firms, allowing them to achieve their strategic goals by sharing risks (Jarillo, 1988). Even if firms maintain a close relationship with their suppliers, if there are alternative arrangements with better trading options in terms of quality, quantity, price, time etc., the partnership could be broken (Jarillo, 1988). The nature of the relationship with the supplier should be maintained according to the nature of the commodity sourced from the supplier (Gulati et al., 2000).

Firms embedded in social networks enjoy reduced transaction costs through exchange of services, and as a result of the alliance, there is an increased trust between firms which mitigates the moral hazards existing in the outset. Transaction costs (opportunism, early mover advantages, strategic consideration etc.) enables firms to integrate their operations, allowing them to enjoy economies of scale as well as focus on their core competencies. (Gulati et al., 2000; Jarillo, 1988). Apart from enjoying the economies of scale and reducing the transaction costs, ‘strategic networks’ pursue other goals such as enhanced legitimacy, entering into markets quickly and inter organisational learning (Sydow and Windeler, 1998). These networks help firms to gather valuable information on other firms in the network and identifies each other’s capabilities and resources. ‘Opportunism’ from firms in social networks are reduced, as opportunistic behaviour in a network damages the firm’s reputation in the current alliance, as well as potential alliance partners (Kohtamäki et al., 2014; Gulati et al., 2000).

The network ties that are formed or disbanded by any firm in the network impacts the behaviour of the firm, as well as the other firms that are connected to the firm in the network for subsequent period (Gulati et al., 2000). The companies with higher bargaining power are often higher in the hierarchy and they tend to isolate themselves from “lock-in” effects in the network by refusing to sign exclusive contract alliances, keeping themselves flexible to other potential alliance opportunities. The relationships are formed with mixed motives where the actors expect both private and common benefits. One other network dynamic which has been identified to affect differential returns is the “learning races”. The knowledge/information gained by the actors in the network from the partners they are connected to can be used for their private benefits and there is a possibility that the actors who gain the knowledge exploit the other actors of their assets and exit the alliance (Gulati et al., 2000).

Barnard (1968) argues that the benefits that would be achieved in being a member of the network over time, and the profits reaped through maintaining relationships among other actors. Among mutual benefits that different members of the network would achieve from being a part of the network, private benefits that could be accrued for an individual actor from being a part of the network serves as a purpose for members to enter into networks (Jarillo, 1988 ; Gulati et al., 2000).

2.2.7 Cluster Theory

Regional clusters can be defined as a group of interlinked firms associated with institutions in a certain market or industry that are connected by their similarities bounded within a geographical region (Schiele and Steinle, 2008). These clusters can, for example, be bound within a national region. If a huge concentration of suppliers of automotive parts exists in one country, it forms a national cluster. The firms that belong to a regional cluster are more innovative than firms that are geographically isolated from that cluster. The success of firms embedded in regional clusters is due to their quick access to suppliers, specialized employees and the increased pressure in the
highly competitive local environment in which they operate (Schiele and Steinle, 2008; Karayel, 2017).

Research conducted on clusters reveal that firms which globalize their functions by outsourcing their operations to external suppliers located in foreign regional clusters may experience competitive disadvantages when compared to competitor firms that are a part of the same regional cluster as the suppliers. Clusters are based on the interactions among the actors in it, thus making them a socio-technical system (Porter, 1990; Schiele and Steinle, 2008). A foreign firm which employs a supplier belonging to a regional or national cluster cannot share the same social advantages when compared to a competitor firm who is a member of the same regional cluster as the supplier. For example, consider that there are three actors: 1) An international firm ‘A’ based in Sweden which outsources API from a supplier ‘X’ in India, 2) Supplier ‘X’ who provides API to both firm ‘A’ (Swedish-based) and also to firm ‘B’ (Indian firm), which is located in close physical proximity to supplier ‘X’. When there is high demand for a particular API, and supplier ‘X’ has an insufficient supply of API to serve both the firms, there would be a preference from supplier ‘X’ to satisfy the demands of firm ‘B’. If critical suppliers who are essential for the supply chain process are easily reachable by competitor firms within the regional cluster, these firms gain more competitive advantages than foreign firms. The proximity of the local firm to the critical supplier is essential in managing supplies to ensure the reliability and flexibility of supply (Porter, 1990; Schiele and Steinle, 2008; Karayel, 2017).

Firms grow and benefit from facing strong domestic competitors, pool of aggressive suppliers and local consumer demand. These characteristics in the local environment drive a firm to innovate and upgrade. Porter's diamond of national advantage model explains the reason behind the innovation and competitive advantages that leads to the growth of industries concentrated in a geographical region. He explains four attributes that exist in those environments: factor conditions, demand conditions, strong suppliers and supporting infrastructure in regional proximity (Porter, 1990; Schiele and Steinle, 2008). These are the four important attributes that determine the presence of a regional cluster.

Porter (1990) argues that companies often tend to outsource their functions to other countries overlooking their national diamond while considering strategies for competitive advantage. This is not always the best strategy, and according to Porter, depending on cross-border suppliers is only the second-best solution. Firms can play a vital role in improving the national diamond, by forming clusters with existing suppliers and buyers which helps them to upgrade, and build their competitive advantage (Porter, 1990).

2.2.8 Summary of theoretical framework

The supply chain management theory was chosen to have an introduction about supply chains and their management. The second theoretical strand chosen was supply chain design. This theory enabled us to get insights on how firms design their supply chain and gave an account of the factors that lead to variations in the supply chain design. The vertical integration theory was chosen in order to gain knowledge on when firms follow a vertically integrated chain and to know the different characteristics that complement vertical integration in firms. Transaction cost considerations and strategic considerations are two of the driving forces for vertical integration in firms. The TCE theory was chosen to understand the transaction costs consideration and the core
competencies theory was suitable to gain insights into the strategic considerations. The theory of core competency explains how the core functions of a firm influence its supply chain structure. The TCE theory furthered the understanding in how transaction costs involved in outsourcing functions affect the supply chain decisions, which lead to different supply chain designs. The strategic networks theory explains the consequences of the strategic behaviour of the actors in supply chains and how it affects the supply chain performance. The cluster theory was chosen to understand the effects of sourcing from a global supplier embedded in a regional cluster. This theory also explains how the distance of external supplier the firm creates disadvantages for the MAH. The chosen theories were suitable to analyse the empirical data and to build typologies in antibiotic supply chains.

<table>
<thead>
<tr>
<th>Theories</th>
<th>Useful for thesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supply Chain Design</td>
<td>The theory is used to give an insight about how firms aim to shape their supply chains. It also contributes on how supply chain structure varies based on different factors. Further, ‘supplier selection’ section has been used to elaborate how pharmaceutical firms tend to choose their suppliers, and how such supplier selection influences the supply chain structures.</td>
</tr>
<tr>
<td>Vertical Integration</td>
<td>Used to analyse the empirics and to find when the pharmaceutical companies or MAHs tend to choose a vertically integrated supply chain.</td>
</tr>
<tr>
<td>Core Competencies</td>
<td>Used for analysing the empirical data. The theory has been used to conceptualise different supply chain structures emerging from decisions to outsource the non-core activities, while maintaining the core functions in-house.</td>
</tr>
<tr>
<td>Transaction Cost Economics (TCE)</td>
<td>Used for analysing the empirics to identify how TCE theory influence the supply chain decisions.</td>
</tr>
<tr>
<td>Strategic Networks</td>
<td>Used to understand the behaviour of supply chain actors and their influence on the supply chain.</td>
</tr>
<tr>
<td>Cluster Theory</td>
<td>Used for analysing the empirics and to create discussion on how the MAH’s dependency on sourcing from a cluster-based supplier (who is located far from the MAH) might cause disadvantages and lead to shortages.</td>
</tr>
</tbody>
</table>

*Table 1: Summary of theoretical framework*
3. Methodology

This chapter describes the methodology used for conducting the research. It begins with an overview of the methodology that has been used, followed by the approach of the study that was adopted. Further, it describes the design of the research study and explains the reasons for selecting the research methods used. Finally, the ethical aspects that has been followed throughout the research, and during data collection is explained.

3.1 Research Methodology

This thesis follows a qualitative approach combined with a literature review in order to obtain better findings. According to Bryman and Bell (2011), qualitative analysis is characterized by two methods: interviews and observations. This thesis is based on interviews with experts within the pharmaceutical industries who are well aware of pharmaceutical supply chains. The reason why no observations could be done were due to the confidentiality and non-transparency of the supply chain processes in pharmaceutical firms. Interviews were essential methods to get a deep understanding of the complex supply chain processes in the pharmaceutical industry. Further, data was gathered from secondary sources to complement the data from the interviews. The data collected from the interviews are personal perspectives of the interviewees on the subject. This subjective approach could be biased based on the interviewees’ experiences. The researchers conducted interviews with three experts in pharmaceutical supply chains. Section 3.4, ‘Interviews’ explain the methods followed in the interviews.

3.2 Research Approach

The research study approach was an explorative qualitative type, due to the fact that exploratory research is considered as an appropriate first step to gain insight on a particular topic because this approach is considered flexible with respect to methods (Churchill, 1999). In addition, Ghauri and Gronhaug (2010) claims that research study that follows a qualitative approach, utilizes an explorative orientation and aims to develop a theoretical perspective. An exploratory research is conducted on a subject which has not been researched earlier, and when the research subject lacks clarity. There has been no previous research conducted exclusively on ‘upstream pharmaceutical supply chains’ and the upstream pharmaceutical supply chain structures have not been defined previously in research. The researchers followed an exploratory research type to increase the understanding on the subject. Different configurations of upstream supply chain networks that could exist within the antibiotic supply chains were explored by the researchers. Also, the various factors that influence the pharmaceutical firms to adopt different supply chain structures were identified.

Further, an inductive approach was used for this thesis where data collection was the first step. According to Bryman and Bell (2011), an inductive approach is where theory is generated out of the research, which is the case in this thesis. In this thesis, a typology of upstream antibiotic supply chains is developed, and theory is generated in the logic used to build the typologies. Moreover, inductive research method has been used so that the primary data interacts with the secondary data. Both primary and secondary data sources were used to collect data for this research. Primary data was collected from the interviewees and secondary data was collected form of literature review and reports. The participants were selected based on their experience and knowledge of supply chains in the pharmaceutical industry.
3.3 Data Collection

The data collection has been done using two sources which are primary and secondary sources. The primary data collection used are interviews as it was the best way to get a deep understanding about the topic. The secondary data, in the form of literature review and reports, enables a better understanding of the concepts that lie behind the empirics.

![Data Collection Method](image)

*Figure 1: Data Collection Method*

3.4 Interviews

According to Bryman and Bell (2011), interviews are a prominent method for data collection in qualitative research. It helps in gaining deeper knowledge and understanding how people perceive a phenomenon. In this research study semi-structured interview method were adopted for the data collection, as it involves a set of open-ended questions allowing the interviewee to respond spontaneously and in-depth (Ryan et al., 2009). Semi-structured interviews are aimed at exploration of in-depth experiences of the interviewee and the meanings that are attributed to these experiences. These forms of interviews are considered a useful tool in situations where limited knowledge exists or known about the topic of interest (Adams, 2010). Similarly, in this study there has been limited knowledge exists about the upstream pharmaceutical supply chain, in order to gain more insights semi-structured interview has been selected.

In this study three subject matter experts were selected based on their high knowledge and experience in dealing with purchasing and supply chain of pharmaceutical industries as shown in Table 1. According to Bryman and Bell (2011), a semi structured interview is an interview where the interviewer has a series of questions that are more in general form and has the freedom to sequence it upon their desire. Furthermore, the interviewer has the latitude to ask further follow-up questions to the interviewees’ responses to get more insights. This nature of semi-structured...
interviews motivated the researchers to prepare the interview guide in a semi-structured manner. By posing semi-structured questions to the interviewees, the researchers could achieve the required data from the interviewees on a particular subject.

The first step of the method for the study is to develop an interview guide containing list of questions prepared by the researchers. The interview guide is prepared in such a way that it contained questions that would likely yield more information about the topic of the study which helps in addressing the aim and purpose of the research. Further, the responses by the participants were followed up with lead questions during interviews to extract more insights from the participants. Two of the interviews were conducted through Zoom and one interview was carried out in a face-to-face manner. All the interviews were recorded with participants’ approval and were transcribed. Recording the interviews made it easy to code the interviews. Same questions were asked to all the participants and two of the interviewees were not able to answer some questions due to their lack of knowledge on the particular subject. Asking the same questions to different participants helped the researchers collect different views of the participants on the same topic. The data collected from the participants varied based on their personal experiences in upstream pharmaceutical supply chains.

<table>
<thead>
<tr>
<th>Interviewee</th>
<th>Position</th>
<th>Company</th>
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<tr>
<td><strong>Interviewee X</strong></td>
<td>The interviewee has been working mostly in sustainability issues in supply chains for pharmaceuticals for the last 4 years. Currently working at Company C.</td>
<td>The interviewee works in a Multinational pharmaceutical company which is one of the largest antibiotic producers in the world.</td>
</tr>
<tr>
<td><strong>Interviewee Y</strong></td>
<td>The interviewee has experience in antibiotic supply chains having worked for many years in the purchasing department for a non-profit organization.</td>
<td>The non-profit organization works in providing healthcare products to the poor children and people all over the world.</td>
</tr>
<tr>
<td><strong>Interviewee Z</strong></td>
<td>The interviewee works as a production expert for antibiotics manufacturing and research center for the past seven years, especially in new drug development.</td>
<td>The research center works in development of new drug, which has been working towards implementing innovation in manufacturing process.</td>
</tr>
</tbody>
</table>

*Table 2: Information about Interviewees*

**Information power**

The concept ‘information power’ can be used to evaluate the sample size in qualitative research. This concept claims that a lower sample size is sufficient for the study, provided the sample hold adequate relevant information for the actual study (Malterud, et al., 2015). The information power of the sample is determined based on five factors: (1) Aim of the study, (2) Sample specificity, (3) Established theory, (4) Quality of dialogue and (5) Analysis strategy.
1) **Aim of the study:**

A high level of information power can be obtained from a small sample size, if the aim of the study is narrow (Malterud et al., 2015). In this study, the aim is narrowed down to identify the possible antibiotic supply chain structures in the upstream supply chain. The study is limited to identifying the factors which cause complex configurations in the upstream supply chain network. Malterud et al. (2015) claim that a study based on the interviews of a few participants is sufficient to provide access to a high level of information power when the aim is narrow.

2) **Sample specificity:**

Sample specificity refers to the specificity of experience and knowledge carried by the participants included in the sample. Participants containing characteristics that are highly precise (specific) for the aim of the study can contribute data with high information power (Malterud et al., 2015). The interviewees included in the sample for this thesis are antibiotic supply chain experts with over four years of experience in the field of study. The participants chosen are specific to the different fields within the study explored by the researchers.

3) **Established theory:**

The level of existing theoretical background relevant to the study guides the adequate sample size. If the study is supported by relevant theoretical background, high information power from a smaller sample size is sufficient for analysis (Malterud et al., 2015). This thesis is assisted by previously established theories like supply chain management, core competency theory etc. which are specific for the analysis of the thesis. Hence, a high level of information power could be obtained from the smaller sample size supported by relevant theories.

4) **Quality of dialogue:**

The quality of dialogue is important to achieve a high level of information power. Sufficient information power can be achieved when a study is supported with strong and clear communication between the researcher and participants for the study (Malterud et al., 2015). The interviews held for this study were semi-structured interviews with clear interactions between the researchers and the participants. The questions asked were open-ended questions which allowed the researchers to extract much information concerning the topic of discussion from the interviewees.

5) **Analysis strategy:**

The strategy followed to analyse the study is related to the information power. This thesis is an exploratory analysis in which the aim is to present specific patterns relevant to the study, but not to cover the whole phenomena. This study aims to identify the possible pharmaceutical supply chains that could exist in the upstream supply chain and to identify the factors causing the different configurations. An exploratory analysis with a few chosen participants who are well-articulated, with information specific to the aim of the study are sufficient to obtain a high level of information power (Malterud et al., 2015).
The condition for the presence of high level of information power in this thesis can be explained by analysing the five factors and its relevance with this study.

3.5 Data interpretation and analysis

The data collected through the interviews were interpreted and organized by coding the transcribed interviews. The themes that emerged from the transcriptions were labelled and the data collected from the interviews were presented under each theme. Further, secondary sources were also used to complement the primary data. Information was gathered from scientific articles on the themes and merged them with the primary data under each theme. This followed a narrative approach on the theme which incorporated data collected from both sources. For the analysis section, the data in the empirical section was analysed with the theoretical strands in the theoretical framework, so as to establish a link between the empirics and theory. This enabled the researchers to build a typology of upstream antibiotic supply chains.

3.6 Internal Validity

Internal Validity deals with the concern if actually a research measures what it intends to do. For example, if a particular variable X is actually affected by Y and not by any other variable like Z. The researchers intend to build a typology of upstream antibiotic supply chains. The logic used to build the typologies were based on the grounded theory. The use of grounded theory and empirical data together in guiding the logic of typologies strengthen the internal validity of the research. The researchers answered the research questions that were formulated by them.

3.7 External Validity

External Validity deals with the generalisation of the study which means how it can be transferred to other areas of research. The results from the study can be partly generalisable to other areas of research. The study explains the nature of relationship and strategic behaviour of the supply chain actors which affect the performance of the antibiotic supply chains. These aspects of the study can be generalisable to supply chains in other industries as well, which are dependent on suppliers for their products. Further, the typologies that have been conceptualised were built based on the different decision-making factors in the pharmaceutical industry. Hence, the typologies can be generalised to industries which follow similar patterns in decision-making and have the same parameters while choosing their supply chain actors.

3.8 Reliability

Reliability concerns the question of whether a result can be repeated. Reliability plays an important role for quantitative studies compared to qualitative studies. The reason being that qualitative studies consists of interviews and observations which are subjective and depends from person to person (Bryman and Bell, 2011). Since this thesis is a qualitative study based on interviews, therefore the reliability would be low and replicating the research would be difficult. Further, this study is a fairly conceptual work. If other researchers follow the same logic applied to build the typologies by the researchers of this study, then the same results could be achieved. Also, data collection from the interviews could vary from one study to another based on the different viewpoints and responses from the interviews.
3.9 Ethics

Ethics plays an important role in any kind of research. During interviews, there are certain implications that must be considered. Bryman and Bell (2011), provides several ethical guidelines that need to be followed while interviewing someone. It is important to ensure that the study does not harm any participants and ensure there is no ‘lack of informed consent’. The covert method of study is not followed throughout the research. Before conducting the interview, the participants were well informed about the topic and what kind of study was being carried out. They were also informed of how the information obtained from the interviews would be used in this thesis. All the questions posed during the interviews were created in order to get more information, and at the same time, not making the interviewees uncomfortable with any private questions. Respecting the privacy of the interviewees has been considered highly while carrying out the research. Before the commencement of the interview, the interviewees were asked whether the interviews could be recorded or not. All the participants agreed to have their interviews recorded. Further, the participants wanted their name to remain anonymous and so, the researchers refer to them as ‘interviewee X, interviewee Y and interviewee Z’ respecting their concern for anonymity. The data obtained for the empirics section were gathered from scientific articles and reports on the pharmaceutical supply chains. The researchers have responsibly made use of the information by properly citing the source of the reports and articles.
In the following chapter, the field material used to analyse and obtained findings will be presented. The findings come from different kinds of sources: journals, interviews, and secondary data. In this chapter, sections 4.1 gives an empirical background on the pharmaceutical industry with an outline of the pharmaceutical supply chain. Sections 4.2 and 4.3 explain the two main manufacturing processes followed in the supply chain. Further, the data gathered on important themes that emerged from coding the interviews are presented from section 4.4 through section 4.8.

4.1 Pharmaceutical Industry

The pharmaceutical industry is a complex web of operations, processes and different actors involved within the supply chain network. There are different players in the pharmaceutical industry who are responsible for the production and distribution of drugs sold in the market: 1) The big multinationals, who are based on research and development, having a global presence in the branded drug market. These companies have their manufacturing sites at different geographical locations, 2) The generic manufacturers, who produce off-patent drugs and over the counter (OTC) drugs, 3) Local Manufacturing companies who produce both generic and branded drugs. These operations are carried out under a license or a contract, 4) Contract manufacturers producing intermediates, APIs, or carry out the manufacturing functions to get the FDF (Finished Dosage Form) by offering outsourcing services to other firms. They do not own a product portfolio, 5) Small biotechnology companies who focus on drug discovery. These are mostly start-ups, with limited resources that do not facilitate the manufacture of the drug internally (Shah, 2004).

Within the pharmaceutical industry, there are two different types of drug manufacturers namely the branded drug manufacturers and the generic drug manufacturers. The generic and branded drug producing companies follow similar processes in the supply chain, but there are differences in the financial incentives for the stakeholders in the generic and branded drug market (Association for Accessible Medicines, 2017).

Branded drug manufacturers produce new drugs in the market and protect the drug with a patent, to prevent other manufacturers from producing a similar drug. These drugs are known as branded or originator drugs. However, when the patent of the drugs reaches the expiry stage, other manufacturers can apply to the European Medicine Agency (EMA), Food and Drug Administration (FDA) and other regulatory agencies to manufacture the bio-equivalent of the branded drugs. These generic drugs are produced with the same API and has the same dosage levels for usage as the branded drugs. (Association for Accessible Medicines, 2017).

Firms that produce branded drugs must invest in the research and development process of the new drug, which can be costly and includes substantial risks. But once the drug is released into the market, there are no competitors for the product until the patent expires. In this period, branded drug manufacturers have greater control over the price of the drug, and they reap the benefits of the competition-free market, to recoup the costs involved in the R&D process. Hence, for branded drug manufacturers, the high unit price of the product plays an important role in maximizing the revenue. In the branded drug market, there is high profits for the MAH (Association for Accessible Medicines, 2017; Interviewee X). The branded manufacturer has a set time plan for the drug and
there is more time to carry out operations. This is because the branded drug manufacturers manufacture new drugs and there are no competitors in the market. Hence, they follow a time plan for the product development process of the drug in the pipeline. Whereas, the generic drug manufacturers manufacture the bioequivalent drugs of the branded drugs and there are multiple competitors for the same product. The branded drug manufacturers invest more time in upfront sales. There is no major need to optimise the process, other than cutting costs (Interviewee X).

Generic manufacturers need to invest to make sure that their drug is bioequivalent to the branded drug and maintain capacity for production by incorporating new manufacturing lines. The generics also have to meet the requirements established by the EMA, FDA and other regulatory agencies in terms of strength, purity, quality and potency. Since the generic market is composed of identical products, here, the competition is based on the supply cost and agility. Generic firms cannot regulate the price of the drug like the branded firms as there are many players in the market; they maximize their revenue with volume of the drugs, rather the price (Interviewee Y). Generic drug manufacturers have to act very quickly to opportunities and follow rapid decision making. The generic drug companies cannot afford to invest longer periods of time into thinking about a project because of the huge competition in the generic market. Facilities and resources, for example, ‘manpower’ are less in generic companies when compared to patented manufacturers (Interviewee X).

The pharmaceutical supply chain is highly sensitive and complicated, where customer service level in the upstream supply chains is of high importance, as it directly impacts the safety and health of the patients (Shah, 2004; Mehrian et al, 2013). Many pharmaceutical industries hold a large inventory to ensure 100% supply. However, to ensure the availability of drugs at all times involves huge costs, unless the supply chain is focused and streamlined to the requirements and demands of the customers. The main problems faced by the industry are marketing time, R&D, stringent government regulations, decreasing patent life, supply chain issues and increasing cost (Mehralian et al., 2013).

Pharmaceutical companies invest heavily in over-dimensional manufacturing sites in order to ensure capacity. This resulted in the shift from companies having local manufacturing facilities to a global supply chain network, resulting in complex coordination issues and constraints in capacity. The global supply chain involves different actors for each function along the chain. The different nodes in the supply chain mostly are unaware of the resource constraints in the other nodes which causes supply disruptions (Shah, 2004).

The general pharmaceutical supply chain resembles the structure in Figure 2. The upstream supply chain for pharmaceutical drugs starts with the sourcing of raw materials, which is the first stage after the research and development process. The next stage will be the API production of the drug, which is the primary manufacturing process. The secondary manufacturing process consists of the manufacturing of the finished dosage form (FDF) and the packaging and labelling of the product as shown in Figure 2. After the packaging process is complete, the product reaches either the Market Authorisation Holder (MAH) or the distribution centers (Shah, 2004; Interviewee Z). There are different stakeholders involved in the upstream supply chain, starting with the raw materials producer, intermediates supplier, API producer and FDF producer. These different actors are linked together by the focal firm. The actors in the supply chain should coordinate with the other actors in the supply chain to ensure the supply of the drug (Mehralian et al, 2013).
4.2 Primary Manufacturing

The primary manufacturing site in pharmaceutical industry is responsible for producing API (Active Pharmaceutical Ingredient). This manufacturing process involves several chemical processes. For antibiotics, it can vary from synthesis process, fermentation process or a mixture of both, which varies depending upon the final drug ingredients (Mousazadeh et al., 2015). The primary manufacturing process is long and requires many processing shifts, and since it involves several stages to produce the API, considerable inventories are often held between the stages. Further, the materials from an intermediate stage should often pass through the quality check before being approved for the downstream process. This can lead to additional delays in the system and lead to problems in downstream process in meeting the market demand (Shah, 2004).

Shah (2004) explains that traditional process technology involves batch production and has flexible pipework, whereas when there are any downtimes in the equipment, it affects the total supply chain because the agility to react to demand is too low. But, the application of automated manufacturing processes has rectified the problem of downtimes and has increased the responsiveness when the market demand fluctuates (Shah, 2004).

Further, due to the complexity and long manufacturing process involved in the manufacturing process, the focal firms look forward to outsourcing API production to contract manufacturers. The process of outsourcing in the pharmaceutical industry is growing and the research oriented MAHs are concentrating on the discovery and development of existing drugs or new drugs. This external participation of third parties and suppliers leads to extended supply chain coordination problems and further makes the supply chain more complex and long (Shah, 2004).
4.3 Secondary Manufacturing

The secondary manufacturers manufacture the final drug by combining and processing the API with inactive ingredients which are also called as excipients. They also take up the responsibility of processing and packaging the final product. Depending upon the form of the final product (e.g., tablets, syringes, or capsules), the production requires different types of equipment and process changes and will be manufactured in different locations (Shah, 2004). According to Mousazadeh et al. (2015), secondary manufacturing facilities are located in a different location from the primary manufacturing; the number of secondary manufacturers are more than the primary manufacturers. After production and packaging, the distribution stage begins. This process will depend on whether the product is manufactured in-house or outsourced. Sometimes the API is outsourced, and the formulation is done in-house, or the entire product is outsourced, and MAH receives the final product. The product will then be transferred to a market warehouse or a distribution center, and from there, it will be transferred to a wholesaler. Finally, the drug will be ready to be commercialized, which can be either sent to hospitals or retail pharmacies (Shah, 2004).

4.4 Supplier selection

Supplier selection in the pharmaceutical industry depends on various characteristics that the external supplier should possess. The focal firm (MAH) will consider the following characteristics while choosing suppliers.

4.4.1 Quality

The pharmaceutical companies consider quality as an important criterion while selecting the supplier. Primarily, because of strong regulatory quality checks by the FDA, EMA and other regulatory agencies as they demand high quality from the drug manufacturers in their respective products. It forces the pharmaceutical firms to select the suppliers who hold the supplier’s certification and suppliers with proven records of world-class service for providing quality raw materials (Chris et al., 2010). Quality of raw material and components requirements are considered as important factors in the pharmaceutical industry, given that the industry is a highly regulated industry.

Interviewee X explained that the MAH checks the supplier’s previous records to check whether the supplier had any bad reputation with regards to the quality of the product and manufacturing systems. According to interviewee X, pharmaceutical industry prioritizes quality standards as a high possible risk factor. For instance, a focal firm would establish a relationship with a supplier and set the requirements for the quality. However, there needs to be regular interaction with the suppliers in order to monitor if they follow the steps for quality as mentioned in the contract or whether they deviate from the standard agreement. Maintaining regular interactions with external suppliers are difficult when the contract manufacturing organizations (CMOs) are located far from the MAH’s location (Interviewee X).

Further, there are instances where companies tend to lose revenues in massive margins caused by supply chain disturbances such as manufacturing and quality issues from the supplier. For example, Johnson and Johnson lost over $900 million in revenue in 2010 due to supply chain disturbances.
disturbance related to manufacturing and quality issues (Huq et al., 2016). Such issues lead to product recalls from the regulatory agencies or the MAH firms when certain criteria for manufacturing standards are not met. These product recalls incur severe financial losses for the MAH firm.

### 4.4.2 Regulatory Compliance (RC)

Rules and regulations considerations have become a vital factor in the pharmaceutical industry and also while choosing the supplier by the focal firm. The two main reasons behind the regulatory intervention are to guarantee and improve patient health and safety and to limit the expenditure for people in buying the drug (Atella et al., 2008). These regulations have forced the focal firms to maintain interactions with the various actors of the supply chain. Especially, the generic pharmaceutical industry is under increased pressure, because of the strict rules and regulations devised by the FDA, EMA and other regulatory agencies. This forces the focal firm to comply with the rules and regulations governing the quality of its active pharmaceutical ingredients (Chris et al., 2010). This also means the generic pharmaceutical manufacturers are more interested in selecting the suppliers, who comply with FDA rules and regulations and have knowledge of existing laws and regulations. The drug regulation process takes time and is an expensive process.

Interviewee X explains that focal firms (MAHs) do have risk with regulatory issues with supplier selection. For instance, the interviewee explained a personal experience with a supplier in China, where the supplier had promised to manufacture the product without violating the regulation. But the supplier had been confronted for violating the rules and regulations of manufacturing in the country. If there is any inspection made by authorities of the particular country and if they find the respective supplier guilty, it can lead to a shutdown of the supplier manufacturing unit. Further, it will cause huge problems to the focal firm in meeting the market demand and also it affects the brand name of the focal firm. Interviewee Y explained that selecting suppliers from a country that has less stringent regulations on manufacturers helps the firm in cost reduction by utilizing the cheap labour force in the country. Also, the interviewee states that the selection of good supplier leads to help the focal firm to know about the supplier firm’s operating markets and has the opportunity to tap into those new markets (Interviewee X; Interviewee Y).

### 4.4.3 Cost

Cost has been considered as one of the most important aspects in the supplier selection criteria irrespective of the industries. For instance, outsourcing the product to suppliers in India and China helps the focal firm to avoid spending on production cost like investing in new machineries, labour cost and also avoid maintenance cost. However, it will increase the transaction costs such as the cost of obtaining accurate market information, negotiating and concluding separate contracts (Xu, 2010).

### 4.4.4 Service

Supplier service is crucial for any manufacturing firm. Pharmaceutical focal firms expect the suppliers to provide high-quality products. The supplier services should include on-time delivery of the product, ease of communication and other value-added services (Chris et al., 2010). Value-added services are provided by some suppliers, which may include additional services that the
supplier provides to add value to the focal firm. For example, a supplier which provided the FDF manufacturing for MAH can also package and label the product. Here the packaging and labelling becomes the value-added service. Further, Interviewee X stated that during supplier selection, the focal firms (MAHs) also check whether a supplier delivers the product on time.

### 4.4.5 Selection based on location

The geographical location of suppliers are essential factors in the pharmaceutical industry that impact the delivery lead time, transportation and logistics costs. During the supplier selection process, firms should ensure the location of supplier should be far from the natural calamities’ region. Because if the supplier is exposed to any natural calamities, it leads to disruption in the supply of drugs to the focal firm (Mwikali and Kavale, 2012).

Interviewee Z explains that the MAH’s competitive strategy has a significant impact on the selection of location for the operations. Interviewee Z explains that if the focal firms focus on cost leadership, it will tend to favour the lowest cost location for their manufacturing facilities, even if it is far from the market they serve. On the contrary, firms that focus on responsiveness tend to locate their facilities closer to the market and may select a high-cost location if the company need to respond quickly to the market needs. However, Interviewee X remarks that when the focal firms decide to choose a supplier from a low-cost manufacturing country which is far from the focal firm, the MAH also tends to check how good the supplier is supplying the good on time. Interviewee X also adds that sometimes focal firms (MAHs) buy an established contract manufacturer in a low-cost manufacturing location, so that they could act as their subsidiary. The main reason for this would be to ensure uninterrupted supply of drugs and this practice has been prominent in Europe for the last two decades (Interviewee X; Interviewee Z).

From the findings from (Berger, 2017), it has been observed that more than 80% of German and global manufacturers are highly dependent on intermediate and API from non-EU countries like China and India. Also, India and China are considered as main countries of origin of intermediates and API. This is due to the rising costs of manufacturing local intermediates and API in the EU, which arise from the strict regulations and practices to be followed in manufacturing for Western European countries. Whereas in China and India, liberalization of laws has reduced tensions of strict audits. Further, setting up a manufacturing plant needs a lot of investments and extra cost might be involved like machine breakdown cost, maintenance cost. Therefore, most EU manufacturers outsource the API manufacturing and intermediates manufacturing (Berger, 2017).

Huq et al. (2016) have identified the general supply chain model of a pharmaceutical multinational corporation, where they devise supply chain structures based on the MAH’s strategy. The three different types of supply chains are insource nearshore, outsource nearshore and outsource offshore (India/China). In insource nearshore, almost all the activities take place in the same country and there will be no outsourcing, companies go for such supply chain location in order to avoid a potential increase in risks caused by an extended supply chain. Whereas, a company might choose nearshore outsourcing, if the company needs to outsource only certain steps in the supply chain in order to reduce certain manufacturing process in the supply chain. For instance, if we assume that the MNC is in Western Europe, the company could outsource some of its manufacturing process nearshore in Eastern European countries with cheap labour like, Poland, Czech Republic or Bulgaria. Also, companies choose to nearshore in order to have easy access to
the supplier if something goes wrong. Finally, some Western companies tend to offshore the entire process to Asian countries like India and China. The companies that tend to choose such an outsourcing strategy in order to utilize the low production cost for the drug and also due to the rising cost of R&D and declining drug outputs also due strict rules and audits (Huq et al., 2016).

4.5 Supply Chain Risks

The pharmaceutical supply chain structure is so complex that a detailed analysis of the entire supply chain actors comprising the network of buyers and suppliers is required to critically analyses the prevalent risks in the Pharmaceutical supply chain (Breen, 2008). Through the examination study of pharmaceutical supply chain conducted by Breen (2008), she identified as much as 35 prevalent risks in the pharmaceutical supply chain with varying risk criticality, among the 35 risks, the most critical risks were found to be ‘fragmentation of supply chain’, ‘lack of visibility’, ‘inappropriate forecasting of customer demand’ and the ‘inability to meet demand’. The findings from the study show that a lack of uniformity in decision making found in the pharmaceutical supply chains lead to such problems, and suggest that a co-ordinating body that recognises the interconnectivity of all the actors in the supply chain, which handles the meetings, implements strategy and targets would benefit the entire supply chain. Certain operational and functional risks within the supply chain were found to be within the control of the industry that could be avoided or battled with appropriate mitigation strategies. The study also points out that there is no risk assessment carried out on the suppliers to find the level of risks associated in a contractual relationship with respective suppliers, though one of the key risks that could lead to a disruption in supply is a supplier risk (Breen, 2008).

A systematic review of pharmaceutical supply chain (PSC) risks conducted by Jaberidoost et al. (2013) confirms Breen’s (2008) statement that out of 50 identified risks in the PSC, 20 were assigned to supply and supplier risks. The review paper explains that many of the risks identified in the study were internal risks caused by processes, people and mismanagement in firms which could be mitigated by suitable strategies (Jaberidoost et al., 2013). Consideration of such supply chain risk will be influential factors while configuring supply chains networks. Risks involved in outsourcing processes to suppliers come in different forms among which the ‘quality defects’ is the most important risk. Quality based risks are of increasing concern in Western and Eastern European countries (Huq et al., 2016).

Unforeseen/random interruptions in production at the supplier’s facility can also be a risk factor for the focal firm. These risks can be power breakdowns, labour strikes, natural disasters etc. Lack of proper communication between the supply chain actors in the network contributes to supply chain disruption, as a wrongly interpreted message at one of the suppliers could affect the processes of other actors in the chain (Huq et al., 2016). Interviewee X mentioned that some of the suppliers release the wastewater from the factories into the water bodies, which could lead to environmental disturbances. This damage the reputation of the focal firm (Interviewee X).

4.6 Time to market and lead time

“Time-to-market” is one of the most important drivers in the pharmaceutical industry. Firms compete to achieve faster lead times in their process and decision making in order to reap significant profits in the early life of a drug (Shah, 2004). It has been estimated that a manufacturer
who enhances the production time by 19% can save up to 100 million US dollars; a firm could lose 1 million US dollar every day the drug delivery is delayed from its release into the market (Mehralian et al., 2013). ‘Dual sourcing’ is one of the strategies used by pharmaceutical firms to mitigate supply chain disruption risks and secure their supply chains. They establish and qualify a second manufacturer for a particular function in the chain, if the first manufacturer is prone to disruption; this allows the firms to continue production if a disruption occurs in the chain (Lucker and Seifert, 2017). The cycle-time or the lead time in the upstream supply chain is the period between the completion of a function and the initiation of the next function in the chain. If the lead times for the completion of a particular function in the chain are too long, say, for example, the formulation process, the focal firm can establish a second manufacturer to carry out the operations in order to ensure that they stay ahead in the competitive market (Interviewee X).

Being first in the market to release the generic version of a branded drug is an important factor that determines the success of a generic drug manufacturing firm and time-to-market is a vital source for comparative advantages for the generic drug manufacturers. The lead times are measured for all the actors participating in the chain, and it has been identified that the lead time and time-to-market are significantly longer if the API and the formulation process are handled internally, than it is outsourced to other actors. When these processes are being outsourced to an external actor, there is more involvement from suppliers and less involvement from the focal company and the internal resources can be utilised for other functions like the firm’s core operations or research and development (Prasnikar and Skerlj, 2005).

A study in the pharmaceutical supply chains reveals that if the lead time of the packaging processes are doubled, the results of the performance of the drug in the market are significantly affected proving that lead time is a critical factor for the launch of a drug. The suppliers for packaging should be selected based on their lead times rather than the price, as the delivery of the products is more important in this context, compared to discounts and ordering costs. When the operations for FDF are carried out in house, without a CMO (Contract Manufacturing Organisation), the volume produced is much less and there are fewer products which can be sold to customers at the launch time of the product (Hansen and Grunow, 2015). Though the study by Hanson and Grunow (2015) argues that the presence of CMO for the FDF process is necessary in the pharmaceutical supply chain of a drug to achieve higher volumes, this entirely depends on the size of the focal firm (MAH). The scenario explained in the study could be possible when the MAH is a small pharmaceutical firm which focuses more on the R&D of the drug and has limited resource capabilities to manufacture large volumes of drugs. Large pharmaceutical firms that own extensive manufacturing facilities for the FDF process of their drugs can achieve large output volumes.

Three supply chain experts who were interviewed in our data collection process mentioned that lead time is an important factor for focal firms to choose more than one source of supply for the functions within the chain. Interviewee X explained that this strategy is often employed by firms to have shorter lead times, but the paperwork and documentation involved in maintaining two suppliers for the same function is high, and also the focal firm has to conduct double inspection at the suppliers to make sure they maintain the standard requirements for manufacturing processes. Both interviewees X and Y mentioned that dual sourcing is a common mitigation strategy to ensure secure supply, but at the same time they also mentioned that the documentation involved is complex. Interviewee Y added that the security threat and the cost incurred for maintaining two CMOs would be high.
4.7 Competitive Strategies

Business models for pharmaceutical firms are subjected to modification over time, as firms are continuously looking for methods to manage the functions in the supply chain efficiently and effectively, without affecting the performance of their research and manufacturing functions. The effect of this has led to changes in the business models of not only the focal firm, but also some of the other actors involved in the supply chain (Capo et al., 2014). Pharmaceutical firms restructure their supply chains with the goal of reducing costs and maximizing productivity, in order to sustain the competition in the industry. The change in the business model enables the firms to survive in the industry, by complementing each other’s functions within the network.

Traditionally, pharmaceutical companies followed vertical integration, where they owned the facilities and capacity for production of each function within the chain, which increased the costs and led to underutilization of their resources. The vertically integrated pharmaceutical supply chains did not favor any profitability returns, nor an increase in concentration. (Capo et al., 2014; Temin, 1979). In the modern Pharmaceutical industry, the focal firm makes strategic choices to restructure the organization of their supply chain to achieve competitive advantages. Pharmaceutical firms tend to outsource their production operations to CMOs, combining the secondary manufacturing process (formulation) with the packaging and labelling process. This strategic action allows the focal firm to recover investments made in underused production capacities, while attaining an increased volume and flexible production through CMOs. The choices made by focal firms to maintain overseas suppliers is directly linked to performance, and they are expected to recover their investments made in research and development (Leask and Parker, 2007). Focal companies (MAHs) change the nature of the relationship they maintain with the suppliers based on their services. If the CMO delivers highly value-added services, and at the same time offer low costs and increase in efficiency, then they maintain close relationships with these suppliers and foster a ‘win-win’ strategic perspective for the actors involved in the network (Capo et al., 2014; Leask and Parker, 2007).

Focal firms can act as “virtual manufacturers”, by taking up the role of mere coordinators in the supply chain, where they own none of the production capacities, and rather externalise (outsource) the functions of the supply chain from production to distribution. Though there are minor risks associated with this strategy, small research oriented pharmaceutical firms with no significant manufacturing capacities tend to follow this niche strategy on the basis of flexible costs and access to new technologies and competences. Being a virtual manufacturer requires the focal firm to have a network of reliable suppliers, with strong coordination capabilities and the ability to manage relationships with their supplier network (Capo et al., 2014).

Focal firms use their supply network as a source to gain knowledge on the areas they lack, and interorganizational knowledge transfers take place in all the members of the network. Through the networks, companies that are not self-sufficient absorb the required skills and resources from their network partners, thus enhancing learning about new developments within the processes and also strengthening their internal competencies (Capo et al., 2014).

The current trend in pharmaceutical supply chains today for the firms is to streamline their portfolio and focus on their core competencies, by shrinking their number of factories internally and increasing their suppliers for other operations. These suppliers have expertise in the areas they
provide services and they know how to make the process more efficient, which in turn helps the firm to reduce unwanted manufacturing processes (Interviewee X). To enter new markets where the focal firms do not have distribution or sales channels, they out-license their drugs to other partner firms to sell the product. This is carried out through joint ventures and co-ownerships with partner firms who work closely with the focal firm (Interviewee X; Interviewee Y).

Moreover, firms outsource their operations increasingly to achieve economies of scale and flexible production advantages, there are some operations which the focal firms prefer to handle internally: Branded drug manufacturers keep the production in-house when they do not want to disclose the ingredients of the drug. When the drugs are sterile drugs or advanced, the technology needed to manufacture the drug is owned by the firm and the operation is carried out internally (Interviewee X). Based on their business model, some pharmaceutical firms own even the API production in order to secure their supply, as the API production is more prone to supply disruption risks (Interviewee Y).

Large multinational pharmaceutical firms indulge in the ‘mergers and acquisitions’ practice by buying or merging with other firms to support huge operations. If the demand in the market for a drug is high, then the firms have to produce huge volumes to meet the market demand. Another form of this practice arises when a firm wants to expand their core competence capacities. For instance, if a firm whose core competence is API manufacturing, then they would try to acquire other firms which expertise in API manufacturing and utilise the acquired firm’s resources like workforce, technologies etc. (Interviewee Y).
5. Analysis

In this section, the analysis of empirical data is presented. This section brings up results relevant to both the research questions addressed in this study. In section 5.1, a typology of upstream pharmaceutical supply chains has been built and a total of ten different upstream antibiotic supply chain structures that could exist have been conceptualised by analysing the empirical data with the theories chosen for this study. Section 5.2 explains the five different factors that motivate the MAH to choose different supply chain structures.

5.1 RQ 1: What are the different dimensions that could be used to build a typology of upstream pharmaceutical supply chains and what are the possible supply chain structures that could exist based on these dimensions?

The typology is built using three different dimensions: 1) The level of vertical integration in the supply chain based on how firms handle their operations, 2) The geographical location of the supply chain actors guided by the outsourcing strategies followed by firms and 3) The number of suppliers involved in a particular outsourced function guided by the sourcing strategy of the MAH. The possible supply chain structures that could exist are presented in the following sections.

5.1.1 Based on how the operations are handled

The first dimension used to build the typology is the ‘level of vertical integration’ in the focal firm (MAH). This dimension deals with how and when pharmaceutical firms handle their functions internally and when they tend to outsource certain operations. Based on the empirical findings from primary and secondary sources, we have conceptualised four different upstream supply chains that could exist depending upon how pharmaceutical firms handle their operations. It has been observed from the interviews that the raw materials are sourced from countries like China and India (Interviewee X; Interviewee Y; Interviewee Z). Hence, for all the chains, we have assumed that raw materials for production have been purchased from India or China.

‘Chain 1’ as depicted above is a vertically integrated chain, where all the functions in the upstream supply chain such as the API manufacturing, FDF manufacturing and packaging are carried out internally by the MAH/ focal firm as shown in Figure 3. Firms tend to handle their different functions internally when they want to ensure a higher level of control over their operations. By vertically integrating their activities, companies reduce the possible risk of opportunism that could
arise from other external actors. Companies tend to vertically integrate when operating in volatile markets when they grow in size and are successful (Ellram 1991; Mahoney 1992). In a TCE theory perspective, make-or-buy decisions in companies are usually made based on the costs that the firm would incur in making transactions with external actors. If the total investment of the firm in handling the operations in-house is lesser than the costs involved in outsourcing the operations to external suppliers, the firm might as well decide to carry out the functions internally (Bremen et al., 2010). The theories go in line with our empirical findings from the primary and secondary sources. The data from the interviews suggest that a vertically integrated supply chain could exist when the focal firm wants to keep the information regarding the ingredients of the drug within the company. Companies who vertically integrate their functions rely on high volumes of production, to achieve economies of scale, to reap the benefits of the huge investments made to integrate their operations vertically. Large multinationals or branded drug manufacturers tend to vertically integrate their operations when the drug is relatively new (Interviewee Y).

In ‘chain 2’, the API is manufactured internally by the focal firm (MAH), whereas all the other functions in the upstream chain are outsourced to external suppliers as shown in Figure 4. After the upstream supply chain processes are complete, the MAH launches the product in the market. Firms tend to handle certain core operations internally and outsource less profitable activities. These core operations are a unique skill set of the firms, which cannot be imitated by their competitors. The core competencies yield a competitive advantage for the firm. Hence firms focus on their core operations and utilise their resources to optimise their core functions, by outsourcing non-core activities (Govindan et al., 2013; Carolis, 2003). In this supply chain, it has been assumed that API production is the core competence of the firm, which is carried out internally and the other activities (FDF manufacturing and packaging) are outsourced. The theories tend to support interviewees' views that in the current trend of pharmaceutical supply chains firms tend to streamline their portfolio and focus on their core competencies, by shrinking their number of factories internally and increasing their suppliers for other operations (Interviewee X). Core activities could vary for different pharmaceutical firms, and hence, there could be different supply chain structures based on the core competency of the focal firm. For example, If the core activities of a focal firm are FDF manufacturing and packaging, then they would tend to handle these functions internally, and externalise manufacturing of the API.

![Figure 4: Chain 2](image-url)
In ‘chain 3’, all the steps in API production are outsourced by the focal firm (MAH) and only the last stage of the synthesis is carried out internally by the firm as shown in Figure 5. The theory of vertical integration suggests that the recurring activities within the chain which require specialised assets are more likely to be carried out internally by the focal firm (Ellram, 1991). The findings from the interviews go in line with the theory, as interviewee X mentioned that the production of sterile drugs are highly advanced, and these processes are mostly handled internally by the MAH. The interviewee further added that there could be suppliers involved throughout the API production, and the last step is performed internally as shown in Figure 5 (Interviewee X). Hence, in chain 3, we have conceptualised based on the findings that the focal firm will perform the last step of API production in-house. Whereas, the FDF manufacturing and packaging can be performed either internally or externalised based on the core competencies of the firm.

The virtual manufacturer chain or ‘chain 4’ is a completely outsourced chain, where all the operations like API manufacturing, FDF manufacturing and packaging are outsourced. In such a supply chain, the focal firms act as a virtual manufacturer, where the focal firm takes up the role of coordinator, where they don’t have responsibilities of any manufacturing operations. Instead, they outsource the entire process of the supply chain from production to distribution. Generally, focal firms that have no manufacturing capabilities and small research-oriented pharmaceutical companies tend to follow such a niche strategy. Being a virtual manufacturer in the supply chain,
the focal firms tend to have a strong network of reliable suppliers with strong coordination capabilities with various actors in the supply chain network (Capo et al., 2014).

5.1.2 Based on Location

The ‘geographical location’ of external suppliers is the second dimension that has been used to build the typology in antibiotic supply chains. This dimension deals with how and when the pharmaceutical firms inshore, offshore and nearshore. Based on the findings from the primary and secondary sources, we have conceptualised three different upstream supply chain that could exist within the second typology.

![Diagram of Chain 5 - Inshore](image)

**Figure 7: Chain 5 - Inshore**

In ‘chain 5’ as depicted in Figure 7, all the activities are carried out in the country the focal firm is located. We assume that the focal firm (MAH) is located in Sweden. Based on the strategy of the focal firm, it can either perform all the functions internally or outsource certain activities to external suppliers based in Sweden. The focal firm could handle all the operations internally if they want to avoid the possible risks of the extended supply chain, for example, supply disruption, opportunism from suppliers etc. If the focal firm chooses to outsource certain activities to external suppliers, they want suppliers in Sweden, as the supplier location would be relatively near to the focal firm, rather than to suppliers that are located outside the national border. One of the interviewees mentioned that the location of the supplier is an essential barrier for inspection. If the suppliers are located far away from the focal firm, they cannot conduct regular inspections at the supplier’s manufacturing site (Interviewee Y).

![Diagram of Chain 6 - Nearshore](image)

**Figure 8: Chain 6 - Nearshore**
The ‘chain 6’ or nearshore chain is based on the nearshore outsourcing strategy. In this chain, the API and FDF manufacturing activities are outsourced to Eastern European countries like the Czech Republic, Poland, Russia etc. as shown in figure 8. These locations have relatively low-cost labour when compared to Sweden, and the focal firm (MAH) can easily visit the supplier’s site as it is located closer to the focal firm’s country of origin when compared to other Asian suppliers. Moreover, these countries share similarities in culture with the focal firm and also have relatively less stringent regulations (Huq et al., 2016). These are the reasons that could be considered while decision-making to outsource the functions to Eastern European countries by the focal firm.

![Diagram of Offshore Supply Chain]

**Figure 9: Chain 7 - Offshore**

The ‘Chain 7’ has been conceptualised based on the offshore outsourcing strategy, where the focal firm outsources the activities to Asian countries (India, China) as shown in Figure 9. By moving their operations to external suppliers in Asian countries, the focal firm achieves economies of scale through the low-cost labour in these developing countries. Large multinationals tend to outsource their functions to Asian countries to recover the vast investments of R&D they make in Europe. The risks that could arise from outsourcing services to overseas Asian suppliers are higher than the benefits. The distance between the focal firm and the supplier is a hindrance for the firm to conduct inspections on the suppliers to ensure they follow Good Manufacturing Practices (GMP). Further, the regulatory processes to release the drug in these countries are lower, if some part of the manufacturing happens in the country (Huq et al., 2016).

The supply chain network design claims that the supply chain networks today have become more complicated for MNCs because of the legislative issues and economic issues. Further, it also adds that the decision of where to outsource their activities or offshore their processes have a long-term impact on the performance of the firm. Firms may choose locations that are far from them to leverage low-cost benefits, and on the other hand, if they expect to have better interactions with their partners for high responsiveness, they may choose easily accessible locations (Chopra and Meindl, 2006; Song and Sun, 2017). The factors that are mentioned in the literature are in line with how pharmaceutical companies choose their locations to carry out their functions, either externally or internally. In a strategic networks’ perspective, the motive of the focal firm can also be to enter the Asian market, and by forming strategic alliances with external suppliers, they release their drug into the market.

### 5.1.3 Based on Sourcing

The ‘sourcing strategy’ (i.e., single or dual sourcing) followed by the focal firm (MAH) is the third dimension that has been used to build the typology of antibiotic supply chains. This dimension
explains how the upstream pharmaceutical supply chain structure changes with respect to the number of actors that could be involved in each step within the chain. It also gives an account on the favourable conditions that motivate the MAH to have more than one source of supply. Based on the findings from the primary sources and secondary sources, three different supply chain structures that could exist have been conceptualised. We have assumed that only two actors could exist in each outsourced step. This assumption is based on the interviewees’ comments, that the documentation process involved in having multiple suppliers is high and that the MAH often tries to reduce the entry of new suppliers into the chain.

In ‘chain 8’, the focal firm tends to outsource its API manufacturing to two contract manufacturers as shown in figure 10 and the rest of the operations will be either outsourced or manufactured inhouse. Firms tend to do such operations to meet the market demand and to increase the economics of scale.

Similarly, two chains, ‘chain 9’ and ‘chain 10’ have been conceptualized based on different possible configurations depending upon the strategy of the company and its core competencies. If the firm’s core operations are API manufacturing, then it tends to hold the API manufacturing inhouse and outsources the rest of the activities like FDF Manufacturing and packaging to two or more contract manufacturers as shown in figure 11.
If the firms tends to increase the volume of production inorder to meet the customer demand then it tends to connect with two or more API and FDF manufacturers in order to speed up the production rate. This could lead to complex supply chain structures involving more actors as shown in ‘chain 10’ (Figure 12).

Figure 12: Chain 10

From the empirical data it has been found that dual sourcing is often followed in the pharmaceutical industries, to avoid disruptions, to reduce the risk of availability and to secure their supply in the supply chain. The findings were found to be in tandem with theories by Lucker and Seifert (2017), as they claim that dual sourcing is one of the strategies that firms follow to mitigate supply chain disruption risks. Also, they add that the focal firm tends to establish and qualify an additional contract manufacturer for a particular function in the chain. This gives scope for firms to continue production if a supply disruption occurs in the chain.

In such situations, firms tend to maintain close relationships with their suppliers. Further, the firm tends to work with suppliers they have known and already have a relationship with, because, it is much easier for them to have a partnership with the actors they already know than to add new partners in the supply network (Interviewee X; Interviewee Y). These findings complement with study by Capo et al. (2014) and Leask and Parker (2007), where they argue that focal companies change the nature of the relationship they maintain with the suppliers based on their services.

Thus to conclude from the findings firms tends to choose multiple sourcing to increase the rate of production volume to meet the market demands, the number of sources varies based on the market need and firms relationship with suppliers and also reliability of suppliers in supplying the drugs on time, to avoid supply disruptions.

5.2 RQ 2: What are the different factors that motivate the pharmaceutical firms to adopt the supply chain structures that are identified through the typology?

5.2.1 Regulatory issues

One of the factors that drives the MAH to adopt different supply chain structure was found to be regulations. This factor has an influence on the configuration of the supply chain structure based
Firms tend to offshore their manufacturing process to developing countries with less stringent regulations like India, China and other Latin countries rather than doing it in-house. The environmental laws and regulations in Asian countries are liberal than European regulations. (Interviewee Y). Precise regulatory checks conducted by auditing agencies in Europe have set high expectations in manufacturing processes to be followed by the suppliers. The high standards for manufacturing set in Europe require costly investments (Berger, 2017). Hence, manufacturing operations are offshored mainly by pharmaceutical firms to countries with liberal regulatory standards. These factors influence firms to adapt supply chain structures as shown in ‘chain 7’ i.e, the offshore chain where the firms outsource the entire manufacturing process and handle the packaging and distribution process within the firm. Also, firms can follow ‘chain 4’ i.e, the virtual manufacturer chain where the MAH outsources the complete manufacturing processes to external suppliers in Asian countries, and the focal firms take up the role of coordinating among the actors to make sure the drugs reach the end customer at the right time.

However, with regards to the manufacturing process efficiency, the pharmaceutical industry has always lacked in comparison with other industries. This is because the pharmaceutical industry is highly regulated in nature, where each operational process needs to be documented and be approved by the regulatory agencies. So, the pharmaceutical industry generally involves much documentation, which is a time taking process if many suppliers are included in the chain (Interviewee Z). In such cases, when the firm wants to avoid the time-taking documentation process, a vertically integrated supply chain would be preferred as shown in ‘chain 1’. By this, the number of actors in the chain will be largely reduced with favourable conditions for the documentation process.

5.2.2 Lead time

The supplier lead time is important for the MAH to ensure that the product reaches the market on time and to maintain its competitive advantage by achieving early time-to-market for drugs. The findings from our study suggest that lead time is one of the critical factors that gives rise to various supply chain structures. Supplier lead times influence the MAH to follow the supply chain structures that are identified in the third typology i.e, chain 8, chain 9 and chain 10. Firms tend to achieve faster lead times in their process and decision making to achieve significant profits in the early stage of a drug (Shah,2004). This was found to be in line with the empirics gathered during our research. If firms want to satisfy the demand in the market it serves, then the focal firm tend to establish a secondary manufacturer to carry its operations, to ensure that they stay ahead in the competitive market. Dual sourcing is a common mitigation strategy by the firm to ensure a secure supply (Interviewee X; Interviewee Y; Interviewee Z). The secondary manufacturer may either be API manufacturer or FDF Manufacturer, based on the company's need. Moreover, sometimes firms can hire two or more secondary manufacturers; it depends on the market and the demand it has to serve. In such a situation, firms follow the supply chain structures that were conceptualised based on the third dimension i.e, the sourcing strategy of the MAH.

Further, from the findings of Prasnikar and Skerlj (2005), it has been found that lead time and time to market are significantly longer if the API and formulation process are performed internally by a firm which has limited resource capabilities. The study also claims that a delay in process times could affect the performance of the drug in the market. This can lead to the focal firm’s inability to meet market demand. Thus, it is one of the reasons the pharmaceutical industry outsources the
manufacturing process to more secondary manufactures. Moreover, from the findings from our interview during our research, it has been observed that firms set up their manufacturing plants in various geographical locations to meet the demand and to speed up the production rate.

5.2.3 Cost

Cost is one of the most important factors that influence the variations in the supply chain structures. Firms which have the strategy of cost leadership will tend to outsource most of its operations to the supplier who provides low cost manufacturing services. Companies tend to outsource their manufacturing processes to the supplier, even though the supplier is located far from the market it serves (Chopra and Meindl, 2016). Similarly, interviewees mentioned that if the companies want to attain low cost manufacturing benefits, to meet the goals of the company, they tend to offshore the manufacturing process. This often happens in generic drug manufacturing industry. Whereas, a patent drug manufacturer has a set time plan for the drug, and there is more time to carry out the operations. They tend to invest more time in upfront sales, and there is no major need to optimize the process other than cost-cutting. Firms could follow the supply chain structure as mentioned in ‘chain 4’ where the focal firm (MAH) acts as a virtual manufacturer and outsources all its upstream supply chain functions to avoid the manufacturing cost, maintenance cost or any investment cost. The company only takes up coordinating all the actors in the supply chain. Focal firms (MAHs) also follow supply chain structures as shown in ‘chain 7’, i.e the offshore outsourcing chain, where the MAH outsources most of the manufacturing processes and holds just a single manufacturing process in-house. The MAH follows the supply chain structure in chain 7 to achieve high economies of scale by outsourcing its functions to suppliers in Asian countries with low-cost labour.

5.2.4 Supply risk

The pharmaceutical industry considers risk as a vital factor during the time of decision making, to either outsource or insource as it influences the availability of drugs in the market. Form the study conducted by Breen (2008) it has been observed, that there are 35 prevalent risks in the pharmaceutical supply chain, with varying risks like lack of visibility of supply chain, inappropriate forecasting of customer demand. Also, findings from the study show that lack of uniformity in decision making in pharmaceuticals supply chain leads to various problems and firms will tend to concentrate more during the decision making also the firms will have a mitigation strategy if something goes wrong (Breen, 2008). The results of the study conducted by Breen (2008) complemented our findings in the interviews. One of the interviewees claimed that if the drug is life-critical and people are dependent on it, and if anything goes wrong in the supply of antibiotics to the customer, it will tend to affect the reputation of the particular firm (Interviewee X). So, in such situation firms will spend much time in supplier selection, that the supplier can deliver the drugs at the right time. If the supplier fails to provide the product at the promised time, it will lead to a massive problem for the focal firm. In such cases, the firms try to avoid outsourcing and hold the entire process in house. In such a scenario, the MAH could follow ‘chain 1’, the fully vertically integrated supply chain structure.

However, if the focal firm tends to share its risk, then the firms tend to outsource the operations. In such scenarios, firms tend to choose suppliers who are reliable in delivering the drug and are ready to have strategic alliances and partnerships. In such situations, there is a possibility that the
MAH follows the supply chain structure as shown in the virtual manufacturer chain i.e, ‘chain 4’. In the virtual manufacturer chain, the MAH is heavily reliant on its suppliers as it holds no manufacturing capabilities to manufacture the drug. The third dimension used for building the typology explains that MAHs adopt the dual sourcing strategy to reduce the risk of availability and secure the supply in their supply chain. This leads the focal firms (MAHs) to follow the supply chain structures depicted in the third typology i.e, ‘chain 8’, ‘chain 9’ and ‘chain 10’.

5.2.5 Quality

Quality is another factor which motivates the MAHs to adopt different supply chain structures by motivating the MAH to select suppliers based on their quality. The pharmaceutical industry is highly regulated, because of the strong regulatory checks by the FDA, EMA and all other regulatory agencies. They demand high-quality from the drug manufacturing companies, as the products affect the life of patients. So it forces the focal firms to select the suppliers who have a good reputation of providing the products with high quality (Chris et al., 2010). Further, our findings from the interview states that the pharmaceutical industry prioritizes quality as an essential risk factor and tend to select the supplier who tends to have proper quality checks. If the suppliers are suitable in terms of quality, then the focal firm will outsource their products and tend to follow the supply chain structures as shown in ‘chain 2’ and ‘chain 4’ which falls under the first dimension used to build the typology. Even though if the outsource their product to suppliers in Asian countries who have a good quality check, the focal firm has to conduct a double inspection at the suppliers to make sure they maintain the standard requirements for manufacturing processes.

However, since the pharmaceutical industry is more regulated and involves stringent audits from the regulatory agencies, there are examples in which firms lose revenues in massive margin due to supply chain disturbance from manufacturing and quality issues. Johnson and Johnson lost over $900 million in revenue in 2010 owing to supply chain disturbance related to manufacturing and quality issues (Huq et al., 2016). So, if the firms want to avoid such risks due to quality, then they will tend to hold the manufacturing process in-house. So, in such situations, firms follow the vertically integrated supply chains, as shown in ‘chain 1’.
6. Discussion

In this chapter, interpretation of our findings in connection to the previously reviewed theory is presented. This section is carried out by applying critical thinking to the problems that have been identified during the study. The discussion is carried out in three sections: ‘The effects of concentration of API production in few countries, ‘influence of strategic behaviour of supply chain actors on the supply chain’ and ‘Do pharmaceutical firms need a different outsourcing strategy?’

6.1 The effects of the concentration of API production in few countries

The pharmaceutical supply chains are comprised of different actors, each performing a specific function in the supply chain that adds value to the end customer. Among the different functions in the chain, the API manufacturing is the most important process in the chain. The API manufacturing takes long lead times and has low responsiveness from the supplier (Shah, 2004; Mousazadeh et al, 2015). The API manufacturing process is largely outsourced by the focal firm to Asian countries like India and China. Interviewee Z mentioned that majority of the suppliers producing the active ingredients are located in India or China and the multinationals in Europe outsource their API production process to these countries to attain cost leadership through low-cost labour and low-cost manufacturing facilities. The Rolands Berger report claims that more than 80% of the global antibiotic manufacturers are highly dependent on India and China for intermediates and API, due to the rising costs of production of API in Europe (Berger, 2017).

An analysis of the pharmaceutical supply chains conducted by Breen (2008) claims that the pharmaceutical supply chain is fragile. One of the critical risks in the supply chain was the ‘supplier’s inability to meet demand’ (Breen, 2008). To understand the reason behind this problem, there should be a clear picture of what happens at the supplier’s end which leads to such shortages.

The primary data collected from the pharmaceutical supply chain experts briefly explain the API market in these developing countries. The actors in the supply chain (for example, an API supplier) handle operations for their customers like the focal firm in discussion and also for other firms that outsource their services to the supplier. Both interviewees X and Y also mentioned that it could be possible that the supplier who offers outsourcing services for the focal firm produces API for itself and also to other companies in order to maximize its capacity utilization. This forms a market itself and when the supplier faces a limitation in capacity or shortages in API, conflicts arise among the actors and the suppliers choose to produce API for the firms that they prefer over the other firms who use the same supplier. Moreover, interviewee Y describes the Indian and Chinese pharmaceutical market structures to be highly volatile with high growth rate in the past few years. The interviewee further added that pharmaceutical firms in Europe used to outsource their non-core functions to India or China. Performing certain functions in the chain for other pharmaceutical firms used to be the major focus of suppliers in these developing countries. Today, the pharmaceutical industry structure in these countries have transformed largely and they have started producing finished products. This causes a huge disruption in the market due to the competition between the two markets i.e, the domestic market in Asian countries with local antibiotic producers against the global markets which offshore their functions to Asian countries. He also adds that during the times of shortages in API, the supplier would try to satisfy the national demand as their portfolios are meant to serve local markets (Interviewee X; Interviewee Y).
The data collected from the interviews about the environment of the suppliers in developing countries suggest that these suppliers supply API for cross-border firms as well as firms in the same country or region as the supplier. With this data, we could consider that the suppliers in the developing countries who provide services for firms based in Europe could be members of regional pharmaceutical clusters.

According to the cluster theory, remote firms which outsource services to a supplier who is embedded in a regional cluster will not have a close relationship with the supplier when compared to the other firms that are located in proximity to the supplier. The literature on the behaviour of firms embedded in clusters stresses the importance of geographical proximity of the firms to their suppliers. Firms closely located to their suppliers tend to operate in the same environment and also have cultural similarities. Domestic buyer-supplier relationships are more positive than cross-border relationships, and the domestic firm has a better probability of being the preferred customer to the supplier. Physical proximity promotes the growth of firms embedded in clusters through their frequent interactions and social bonds (Schiele and Steinle, 2008; Kuah, 2002). This implies that when there is a shortage in the API, the supplier tends to satisfy the demand of the local buyer. For example, consider that there are three actors: 1) An international firm ‘A’ based in Sweden which outsources its API production to a supplier ‘X’ in India, 2) Supplier ‘X’ who provides API to both firm ‘A’ (Swedish-based) and also to firm ‘B’ (Indian firm), which is located in close physical proximity to supplier ‘X’. When there is high demand for a particular API, and supplier ‘X’ has an insufficient supply of API to serve both the firms, there would be a preference to satisfy the demands of firm ‘B’. In a transaction cost economics perspective, we can consider the competitive disadvantage that firm ‘A’ incurs compared to firm ‘B’ as one of the transaction costs involved in outsourcing its functions to an overseas supplier embedded in a regional cluster. The high dependency on overseas suppliers leads to a situation where the supplier becomes a critical resource for the firm and not just another actor in the chain.

Pharmaceutical firms based in Europe largely outsource their functions to external suppliers located outside national borders. The competitive strategy of the focal firm to attain cost leadership motivates the firm to outsource its services to low-cost manufacturing countries despite the geographical distance between the firm and its supplier. From the interviews, it was also identified that the focal firms decide to outsource most of its functions to recoup the large investments made by the firms in the research and development process of the drug. Porter (1990) argues that firms should depend upon competitive domestic suppliers over highly qualified foreign suppliers. He further elaborates this view that the international success of companies depends upon their home environment. The focal firm can play a vital role in improving the home environment by forming clusters among the local buyers, suppliers and other channels. The company can develop the home cluster and help the members of the cluster upgrade their competencies to extend their own competitive advantages (Porter, 1990; Schiele and Steinle, 2008). The growing dependency of pharmaceutical firms on overseas suppliers for APIs poses a threat to the focal firm, due to the possibility of opportunism from the supplier when there is only a limited supply to satisfy the market demand.

The discussion raises two important questions which could be considered for future research. Should pharmaceutical firms based in Europe reduce their growing dependency on foreign suppliers? Can developing regional clusters within the geographical boundaries of the firm
strengthen the reliability of their supply chain? Above questions should be considered by firms while making decisions on outsourcing their outsourcing activities.

6.2 Influence of strategic behaviour of supply chain actors on the supply chain

Globalisation has made supply chain networks and operations more complex, by allowing companies to exploit economies of scale by manufacturing in low-cost manufacturing countries. Further, globalisation has also made markets more complex and fragmented due to increased competition. Consequently, one important issue in developing and managing international supply chains is to increase responsiveness and at the same time. But firms are more concerned in achieving cost-efficiency (Hilletofth, 2008). Similarly, Interviewee Z said that in pharmaceutical industries, firms tend to choose the manufacturing location based on the strategy of the company. If the company wants to achieve cost leadership, it tends to outsource its functions to low-cost manufacturing countries. Whereas, if the firm wants to achieve responsiveness, it tends to either nearshore or hire more CMOs to attain its market demand.

So the firm needs to choose the strategy that fits its goal. One of the important strategies that the pharmaceutical industry follows is cost leadership. For this, the firms tend to have strategic alliances with suppliers. However, the focal firms (MAHs) tend to maintain either strong or weak relationships with the suppliers depending on the profitability of the relationship (Gulati et al., 2000). Interviewee Y and Sydow and Windeler (1998) claim that apart from utilising the lost cost benefits, firms tend to have strategic alliances to gain access to enter into new markets. The findings from the interview also claim that MAHs form strong relationships with global suppliers in potential markets. The MAH could later release its drug into that market through the supplier. From Roland Berger report, it has been observed that over 80% of the API manufacturing process has been outsourced to suppliers. This shows very high dependency of the focal firm on the suppliers. However, too much dependence on suppliers can lead to a dependency risk (Jarillo, 1988). To complement this statement, the strategic networks theory also adds that even when the firm maintains close ties with its suppliers, the suppliers could break the relationship with the firm when it finds potential alliance opportunities. This will lead to shortages for the focal firm in meeting its demands in the market.

In such a scenario, the MAH with higher bargaining power tends to isolate itself from the supplier's demands and keep themselves flexible to other potential alliance opportunities to avoid shortages and provide continuous supply for its customers. Therefore, companies need to rethink a strategy which is highly flexible in nature, to prevent shortages because it is a severe problem in the pharmaceutical industry owing to the life-critical nature of the drug.

6.3 Do pharmaceutical companies need a different outsourcing strategy?

The pharmaceutical industry is highly competitive, and firms adapt many competitive strategies to stay ahead of their competitors, reduce costs and generate more profits. One such competitive strategy followed by pharmaceutical firms is the ‘offshore outsourcing’ strategy. By outsourcing their non-core processes offshore, pharmaceutical firms leverage economies of scale, through the low-cost manufacturing services in Asian countries, particularly India and China (Leask and Parker, 2007; Capo et al, 2014; Interviewee X; Interviewee Y). It has been found that the API manufacturing or the primary manufacturing processes are mostly outsourced to these countries
and yet, the API manufacturing is the most critical process which is the least responsive part of the supply chain (Berger, 2017; Shah, 2004).

The offshore outsourcing strategy followed by pharmaceutical firms increase their profit potentials and enable them to create a competitive advantage in the market. This strategy is presumed to be the best way for firms to recoup their expenses on research and development process based in Europe. Further, the suppliers in these countries are specialised in the API production process, which enables the firms create value by focussing on core competencies and maintaining decent quality levels in the non-core process by outsourcing them to expert suppliers (Interviewee X; Interviewee Y). From these findings and with the trend in pharmaceutical firms to streamline their processes internally and increase their external suppliers globally, we could assume that the outsourcing strategy would be increasingly followed by the MAHs in the Western pharmaceutical industry.

According to interviewee Y, the economic structure in the pharmaceutical industry in Asian countries, where most of the API production is concentrated, is increasingly changing. He further explains stating that, in the past, developed countries in Europe used to outsource non-core activities to India or China and that these countries used to focus on providing manufacturing services for pharmaceutical firms in Europe. But now, these countries have started producing finished pharmaceutical drugs, i.e, pharmaceutical firms in Asia and Western Europe are sourcing from the same set of suppliers. This causes a disruption in the market, and at times of shortages, when there is a spike in demand for a particular drug, the suppliers tend to satisfy national/local demands. This disruption has led to the entry of new entrants with heavy vertical integration without much dependence on third parties (Interviewee Y).

From the findings, we could assume that offshore outsourcing as a competitive advantage generated wealth for the pharmaceutical firms based in Europe when the pharmaceutical market in India and China were mainly focussing on providing manufacturing services for pharmaceutical firms in developed countries. When the market economy of these developing countries shifted to producing finished products, offshore outsourcing started facing its limitations due to the competition between firms in both the markets. Does this imply that the offshore outsourcing system has reached its limits due to the extreme offshoring by the Western pharmaceutical firms to Asian countries? If this is the scenario, there will be increasing shortages for drugs, where the pharmaceutical firms in Europe are highly dependent on their external supplier. Pharmaceutical firms based in Western countries are in need of new strategies to stay competitive in the market. Could ‘vertical integration’ or more ‘nearshore outsourcing’ replace the offshore outsourcing strategy?

The TCE theory states that the transaction costs for a firm which outsources to global suppliers located far from their reach are high. However, research conducted by Bremen et al. (2010) on TCE and global sourcing claim that despite high transaction costs involved in global outsourcing, firms tend to outsource their services to global suppliers. The important factor that drives companies to take these decisions is the low-cost services offered in the global market. High transaction costs also affect the performance of the sourcing activities in firms. The firms will have to restructure their governance structure to reduce the transaction costs either by handling the function in-house or by nearshoring operations to suppliers in locations which do not lead to high transaction costs (Bremen et al.,2010). Interviewee Y also stated that the pharmaceutical firms are
vertically integrating their operations, as the global outsourcing operations are affecting the performance of the firms (Interviewee Y). The findings from the interview goes in line with the TCE theory. In that case, the supply chain structure followed by the MAH will be similar to ‘chain 1’ i.e, the fully vertically integrated chain according to our typology. If the MAH offshores its functions to Eastern European suppliers to achieve economies of scale, then the supply chain will represent ‘chain 6’ i.e, the nearshore outsourcing chain which was conceptualised in the second typology.
7. Conclusion

In this chapter, conclusions from the study are presented. Firstly, a summary about aim and results obtained through the study will be presented. Secondly, the academic contributions, policy implications, ethical and societal considerations that emerged are presented. Lastly, suggestions for future work will be presented.

The thesis aimed to build a typology of upstream pharmaceutical supply chains and also to identify the possible upstream supply chains that could exist in the pharmaceutical industry. Through this study, ten upstream pharmaceutical supply chain structures that could exist have been identified based on three dimensions that were used to construct the typology. The first dimension used to build the typology is based on how pharmaceutical firms (MAHs) handle their operations, the second dimension that enables to build the typology is based on the geographical location of the upstream supply chain actors and the third dimension identifies supply chains that could exist based on the sourcing strategy adopted by the MAHs. Further, it has been found that five factors motivate the pharmaceutical firms (MAHs) to adopt different supply chain structures: regulatory issues, lead time, cost, supply risks and quality. However, the factors influencing the supply chain structures might vary if the data collection involves a large sample size. The findings from the study contribute to the existing academic field of pharmaceutical supply chains. Furthermore, the study will be useful for pharmaceutical firms since the study gives an insight into the upstream pharmaceutical supply chain and how the supply chain structure varies. This research also contributes to valuable data on the upstream pharmaceutical supply chain and increases the understanding of the upstream chain.

7.1 Academic contribution, Policy Implications, Ethical and Societal considerations

Academic contribution

The study has contributed to the existing theory and literature on pharmaceutical supply chains. Further, this study has laid a foundation for future studies regarding upstream pharmaceutical supply chains as there is limited research on this topic in existing research. Apart from serving as a vital source of information on the upstream pharmaceutical supply chains, this research also presents a visualisation of the upstream pharmaceutical supply chain structures and how these structures could vary based on the strategies of pharmaceutical firms (MAHs). Moreover, the factors that have been identified through the study will guide the pharmaceutical companies to reconsider their decisions on whether to outsource or manufacture its products in-house. In addition, the thesis also highlights the underlying problems in the upstream pharmaceutical supply chains which could lead to drug shortages. The possible reasons for drug shortages faced by Western pharmaceutical firms were proposed in the ‘Discussion’ section by applying critical thinking, connecting the problems with the theories and bringing forth important questions to be addressed by future researchers.

Policy implications

Policy implications can be directed to improve the availability of antibiotics in the market through having constant contact and having stringent regulations with the suppliers. From the findings through our study, it has been observed that less stringent regulation policies and the selection of
suppliers with low reliability can affect the reputation of a particular firm. For instance, if suppliers who manufacture API for a pharmaceutical firm releases industrial water into the natural environment without appropriate water treatment processes, it can lead to ecological issues. There is a possibility that the supplier might violate the environmental rules and regulations of the country. If the suppliers are found guilty of not following the regulations, it can lead to a shutdown of the supplier manufacturing unit. This will lead to a supply disruption for the MAH. Further, it will cause huge problems to the focal firm in meeting the market demand and also it affects the brand name of the focal firm. Therefore, the focal firms (MAH) must have stricter environmental regulations with its suppliers to avoid unavailability of antibiotics in the market.

The pharmaceutical firms in Western European countries outsource most of their API manufacturing services to Asian countries to leverage low-cost manufacturing services. As a result, the API market in Western Europe has very low competitiveness when compared to the API market in Asian countries. Further, there is high dependence on global suppliers for a critical component (API) in the antibiotic supply chain. The strict policies by the governmental regulation agencies in Western countries are one of the major factors which motivate the companies to outsource to countries with relaxed regulations. The regulation agencies could therefore relax these stringent laws. This could lead to an increase in the API manufacturing in Western countries and thus lower the dependence on Asian suppliers.

**Ethical and Societal considerations**

The ethical impact on conducting the interviews on the interviewees in this study has been mentioned in section 3.9 ‘Ethics’, which covers the ethical aspects considered in the research methodology that has been adopted. However, there are some other ethical considerations in the pharmaceutical industry.

During the period of shortages of a particular drug, it has been found that the healthcare facilities place large orders to their suppliers, to ensure that they have enough supply. This practice is called ‘backordering’. Such backordering increases the duration of shortages. When huge quantities are ordered by a healthcare facility than their actual demand for the particular API, other facilities who are in need of the same API face shortages. This practice should be avoided by healthcare facilities at times of shortages. The actors in the pharmaceutical supply chain take up an ‘altruistic’ view, instead of an ‘egoistic’ view. Therefore, the actors involved in the supply chain should avoid ordering excess quantities to maintain stock in their inventory.

Through the study, it was understood that pharmaceutical firms prioritise larger markets over smaller markets. This is one of the reasons which causes shortages in some countries. Antibiotics play a crucial role in the health of patients. The pharmaceutical firms need to reconsider their investment plans and invest in countries where there is a need for the drug, considering the well-being of the society.

**7.2 Future research**

The study involves certain limitations and essential findings. However, further studies can contribute to PLATINEA’s objectives and to the field of research in pharmaceutical supply chains. For instance, the study only deals with upstream supply chain structures, which avoids discussion
about downstream supply chain actors (Distribution part). So there is a possibility of changes in upstream supply chain structures due to the influence of downstream supply chain actors. Moreover, while conceptualizing the supply chain structures, actors involved in the extended supply chain are not included. Future research on this topic could consider these factors and also other factors that could cause variations in the upstream pharmaceutical supply chain structure. Further, some questions on the practices in Western pharmaceutical firms were generated in chapter 6, ‘Discussions’. Future research on pharmaceutical supply chains could address these questions and bring forth possible solutions.
Bibliography


Appendices

Appendix-1
Interviewee X

**Position:** The interviewee has been working mostly in sustainability issues in supply chains for pharmaceuticals for the last 4 years. Currently working at Company C.

**Company:** The interviewee works in a Multinational pharmaceutical company. The company where the interviewee works is one of the largest antibiotic producers in the world.

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<th>No</th>
<th>Desired Outcomes</th>
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| 1. | Important decision making factors while off shoring | What factors the pharmaceutical industry consider during decision making while deciding to offshore the manufacturing process in the chain, other than low cost manufacturing benefits? | 1. if you want to produce your drug that you have a patent for, you keep it in-house because you don't want anybody to steal the ingredients of the particular drug.  
2. If the companies consider about cost and they intend to reduce cost, companies try to offshore its manufacturing process this often happens in generic drug market.  
3. Then they look into supplier where they are located and their ability to supply the drug on time and their quality of the drug.  
4. Technology level of manufacturing the drug also plays an important role in decision making, if the supplier has very high precision machines, the firms do outsource the drug to the supplier. |
<p>| 2. | Rank important factors mentioned before in | On a scale from 1 to 5, with 1 being the least considered factor | Cost is considered as the most important factor with a rating |</p>
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<th>3. Multiple outsourcing possibilities when considering time-to-market</th>
<th>As time-to-market is a critical factor in the pharmaceutical industry, is there a possibility that an MAH will outsource its operations to more than one contract manufacturing organization in order to achieve faster lead-times?</th>
<th>Yes, this phenomenon does occur very often. But when you have a dual source of supply, it becomes complicated with the double inspection and the paperwork. On the other hand, if you have only one source of supply, you are prone to disruptions and other issues in the supply chain. The situation is complex. The actors involved in the supply chain network have different operations. So, in case one firm approaches a supplier for its services for a particular drug (generic), in order to launch it early into the market, there is a possibility that the same supplier is trying to launch the same generic drug into the market. This gives rise to opportunism and competition.</th>
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| generics industry and 5 the most, how would you rate the factors implanted in generic supply chains? | of 5. Quality and reliability of the supplier is the next important factor with a rating of 4. The responsibility of the supplier holds a rating of 3. Pharmaceutical companies are now trying to streamline their portfolio and focus on their core competencies, by shrinking their number of factories internally and increasing their suppliers for other operations. | This strategy is often
### 5. Advantages and risks associated to offshoring operations

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<tr>
<th>Outsourcing possibility exists in both branded and generic supply chains?</th>
<th>Followed in the pharmaceutical supply chain by companies. But when it comes to advanced drugs or sterile drugs, the companies tend to have the technology in-house. The more advanced the drug is, the API production is handled internally by the focal firm.</th>
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#### Advantages:

1. **Knowledge Sharing:** Sometimes suppliers who have a better idea on certain process and also know how to make the particular process more efficient this helps the focal firm to improve. It also fosters innovation where possibility of reduction unwanted manufacturing process can be avoided.

2. **Sharing the same channels for logistics and market access,** its helps the focal firm to tap into the untapped market.

#### Risks:

1. **Reliability of supplier can sometimes be questionable,** which can lead to affect the focal firms name. For instance if the supplier who is manufacturing API can release water in to natural environment without treating, which leads to ecological issues.

2. **Safety is considered as big issues,** because if something
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|   |   |   | goes wrong, it leads to unavailability of particular drugs in market.  
|   |   |   | 3. Also quality of the product must be one of the major risk. If the supplier produce the product with less quality which will also affects the reputation of the focal firm.  
|   |   |   | 4. Delivery of drugs on time, if the supplier fails to deliver on time, it might cause huge problems for the focal firm.  
|   |   |   | 5. Data security is one of the risks  
| 6. | Rate off-shoring risks | Which risks would you rate to be the highest, lowest and moderate? Hard to rate.  
|   |   | Quality of the drug is always considered as the highest risk, followed by commitment of supply of drugs on time. Finally, the environment risk.  
| 7. | Profit distribution at upstream supply chain: generics vs. branded pharmaceuticals | How does profit distribution vary in the upstream supply chain among different operations with regards to branded or generic drugs manufacturers?  
|   |   | In general the branded drug have high profit for the firm. Whereas for the generic drug the profit is much lower. For instance for company X have a profit of 32% in total.  
| 8. | Outsourcing frequency for generics and on-patent pharmaceuticals | So what do you think how often that the API manufacturers and formulation process, outsourced by an on Patent and producer  
|   |   | In the patented or branded market, you still want to keep your (in general) API production under control. But maybe it's only the last step of the synthesis that you make in-house. It could be that there are suppliers all the way unto the last step where you outsource your synthesis steps and the last step you do in-house for the API production. But even in that step, there's more and more movement to actually outsourcing.  

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<td></td>
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<td>Sometimes if the pharma company does not have the technology there is possibility to out-source even it is branded to avoid risks of lacking knowledge.</td>
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<tr>
<td>9.</td>
<td>Core activities’ differences between on-patent and off-patent pharmaceuticals</td>
<td>How do core activities of an innovator company and generic drug company vary?</td>
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<td>A patent drug manufacturer has a set time plan for the drug and there is more time to carry out operations. They invest more time in upfront sales. There is no major need to optimise the process, other than cutting costs. A generic drug manufacturing company has to act very quickly to its opportunities. They follow rapid decision making. The generic drug companies cannot afford to invest longer periods of time into thinking about a project because of the huge competition in the generic market. Facilities and resources, for example, ‘manpower’ are less in generic companies when compared to patented manufacturers.</td>
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<td>10</td>
<td>Optimization of core operations</td>
<td>Are outsourcing or offshoring decisions made by companies to optimize their core operations?</td>
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<td>Yes, these decisions are made by companies to optimise their core operations. Sometimes, there are legal procedures in certain countries which the companies have to follow. For example, In Bangladesh, to release a drug in the country, it is necessary that the company needs to hold production in the country.</td>
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| 11. | What motivates a company to out license? | Out Licensing is more prominent in branded drug market, what are the different factors that motivate the focal firm to brand other manufacturers license to manufacture their product in different countries? | Yeah, when it comes into the different markets. So maybe you have a partner that markets your drug in the US, because you don't have the sales channels. So there is a lot of crossover happening. Here in Basel for example there is a company called Roche and Company C sell their product but in a different market, so we are partners rather than competitors.

So, one reason for out-licensing to happen is that there are no sales channels for the focal firm in a different market, and it out-licenses to another partner to sell their product. |
|---|---|---|---|
| 12. | Vertically integrated supply chain profitability in generic vs. patented pharmaceuticals | Is vertically integrated supply chain profitable in generic drug market when compared to a branded (patented) market? | Well it needs to be profitable otherwise they don’t survive. So if you look at this Chinese suppliers and Indian suppliers for example, they are completely vertically integrated.

These companies have the whole supply chain inhouse |
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<td>13</td>
<td><strong>Why company go for acquisition and merging</strong></td>
<td><strong>What is the rationale behind the mergers and acquisitions practice in pharmaceutical industries and how does it impact the supply chain?</strong></td>
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<td>The rationale behind this practise is to have growth and profit for the company; it is one way to sell the company and reduce the losses. By this practice, there is enhanced R&amp;D for the entire industry. Sometimes, large firms buy smaller companies which come up with new molecules. This happens in the early phase. This is more prominent in the branded drug industry because you have to ensure a big pipeline inorder to find a new drug. In the generic drug industry, this practice happens in order to streamline their portfolio.</td>
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| 14 | **Can you tell us more about captives, in the industry where focal firm buys a contract manufacturer in another location** | **Firms buy an established contract manufacturer, sometimes in different geographical locations, so that they could act as their subsidiary. The main reason for this would be to ensure supply. This has been prominent in Europe for the last two decades.** |
**Appendix-2**
**Interviewee Y**

**Position:** The interviewee has great experience on pharmaceutical supply chain having worked for many years in Purchasing for a Nonprofit organization.

**Company:** Nonprofit organization works in providing healthcare products to the poor children and people all over the world

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<th>No.</th>
<th>Desired outcome</th>
<th>Question</th>
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<tr>
<td>1</td>
<td>Important decision making factors while offshoring</td>
<td>what factors do pharmaceutical industries consider during decision making in offshoring the manufacturing process Other than low cost Manufacturing benefits?</td>
<td>Normally the company do offshore because of the competition. They could try to reduce costs through offshoring their processes and meet the goals of the company. Regulatory issues are less stringent in countries like Latin America or India. So, the processes could be offshored as the barrier for entry into the markets are less. Some companies have vertically integrated all their operations even down to the intermediate, including the API. Now, branded drug manufacturers tend to outsource their operations. The establish contracts for manufacturing the API with a supplier. The nature of the contract would long-term with guaranteed volumes and they work in close relationships with their suppliers where they have a strong say in the production.</td>
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<td>2</td>
<td>Multiple outsourcing possibilities when as time to market is a critical factor in the</td>
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<td>Yes, it happens. A focal firm can own productions in different</td>
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<td>Consider time-to-market pharmaceutical industry, Is there a possibility that one MAH will outsource its operations to more than one CMO in order to achieve faster lead times?</td>
<td>Geographical locations: They can also outsource their operations for the same product to two contract manufacturers. But the security threat for this would be high and also the cost of maintaining two CMOs for the same operation. At the same time, the focal firm has to guarantee the utilisation of capacity of the CMOs, because that is what the CMOs live off. They cannot afford to lose or wait for orders to come from the focal firms. It is too costly for them.</td>
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<td>3. How lead time affects the supply chain network?</td>
<td>It depends upon the nature of the production. For instance, if the contract manufacturer has accepted to produce the product at a volume, then it's all about (time consumption is more at beginning) setting up a contract and then contract manufacturer has the responsibility of manufacturing and delivering the drug to the focal firm on time. If there are interruptions with the particular contract manufacturer then the focal firm has to change its source to meet the market needs.</td>
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<td>4. Advantages and risks associated to off-shoring operations Could you mention some risks that are associated with outsourcing to contract manufacturers,?</td>
<td>A big risk in outsourcing would be the ‘distance’. A focal firm would establish a relationship with a CMO and set the requirements for the quality. But there needs to be regular interaction with the CMO inorder to monitor if they follow the steps for quality mentioned in the contract or whether they are deviating from the standard agreement. This would be risky to carry out when the CMOs are</td>
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<td>5.</td>
<td>Profit distribution at upstream supply chain: generics vs. branded pharmaceuticals</td>
<td>how does profit distribution vary in upstream supply chain among different operations with regards to branded and generic drug?</td>
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<td></td>
<td></td>
<td>In general, MAH holders shares the maximum profit in branded drug market. Whereas, in generic drug market the manufacturer gets the maximum profit, since the competition is high in the market and majority of profit rely on industrial production.</td>
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<td>6.</td>
<td>Influence of volume on revenue</td>
<td>So it means like high volumes ensure high revenue for the API?</td>
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<td>Yes, and you need to maximize the sources and the volume as much as you can. If something goes wrong for instance low demand of certain drugs in the market, then the firm should be fast and ready to move on to other drugs which has good revenue in the market. Else, it will lead to increase in ideal cost of the particular plant.</td>
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<td>7.</td>
<td>Probability of outsourcing</td>
<td>How often is the API manufacturing, which is the primary manufacturing and formulation, the secondary manufacturing! How often are these processes outsourced by a branded drug producer.</td>
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<td>The branded drug manufacturers traditionally used to have the API production in house. But now, the scenario is changing because of the profits. There are some firms which still keep the API production facilities inhouse,(depending on their business model) and if it is economically viable to them. They do this inorder to secure their production. The API industry is changing nowadays. One pharmaceutical company can own an API manufacturing facility which ensures supply of API for its own products and also takes up production for other companies. This forms a market itself. There can be conflicts when</td>
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<td>8.</td>
<td>Core activities’ differences between on-patent and off-patent pharmaceutical</td>
<td>How do the core activities of an innovator company and generic drug company vary?</td>
<td>For an innovator company, the most important part is the marketing which is the biggest differentiation among the two drug industries. But in the generic drug market, since the drug is already well known, the generic drug manufacturers do not compete with each other to make a better drug, but instead, the competition here is with other manufacturers.</td>
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<td>is about licensing more prominent in the branded drug market? And What are the different factors that motivate the focal firm to grant other manufacturers license to manufacture their product in different countries?</td>
<td>This practice is not very common. It mainly happens for legacy products. It could happen when a patented product is in proximity to patent expiration. Generally, when a company wants to enter into other markets, it does it through joint ventures and co-ownerships with partners who work closely. They don’t sell their license often.</td>
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<td>9.</td>
<td>Reasons for merging and acquisition</td>
<td>What is the rationale behind the mergers and acquisitions practice pharmaceutical industries? And how does it impact the supply chain?</td>
<td>This is due to larger companies want to achieve a certain fleet in the financing, that helps the big firms to support huge operations in the stock market. Secondly, if the demand of certain drug is high in the market the focal firms have to produce huge volume to meet the market demand. So, companies do acquire a few companies to meet</td>
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<td><strong>the market demand.</strong> Sometimes Focal firm do go for acquisitions, in order to concentrate on their core operations. For instance if the focal firms core operation is API manufacturing, then they try to acquire the companies who are very good in API manufacturing inorder to utilize the acquired company's sources like work force, machineries etc.</td>
<td><strong>10. Profit distribution</strong></td>
<td>Is a vertically integrated supply chain profitable in the generic market when compared to the branded market? Do most innovative companies operate in a vertically integrated fashion? Most Generic drug manufacturers do not operate in a vertically integrated fashion. Only very few like Sandoz operate with most of their functions in house, but even then, not 100% of the facilities are owned by the companies. Depending upon the products in their portfolio, some firms may have all the facilities required for the drug. You will not find many multinationals (on-patent drug company) owning API facilities. Rather, they have a legacy that they may work with, where they set conditions to maintain a capacity for years. They concentrate more on ‘managing the business’ than ‘managing the profits’, because when focal firms manage on their business, designing the products and going through with the approval process within a minimum time, they can achieve competitive advantage.</td>
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<td><strong>11. Trend that cause shortage</strong></td>
<td>Are there any trends within the pharmaceutical industries as the needs of the</td>
<td>It is very difficult to establish clear trends in pharmaceutical industries as the needs of the</td>
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market which causes a shortage in the supply of antibiotics to Europe? products keep evolving. For example, in the late 1980s and 90s, the Penicillin production shifted towards countries like India and China, which never returned to Europe. Now, Companies in India and China started producing finished products and we have two levels competing with each other causing disruption in the market. Due to the competition, there could be supply shortages when a captive industry in Europe depends on API from China or other Asian countries. This is a huge disruption in the generic market. The model is very different in the generic industry, as their large portfolios are based to serve local national markets. The disruption caused leads to the entry of new entrants into the market with heavy vertical integration without much dependence on third parties.
### Appendix-3

**Interviewee Z:**

**Position:** The interviewee works as a production expert for antibiotics manufacturing and research center for the past seven years, especially in new drug development.

**Company:** The research center works in development of new drug, which has been working towards implementing innovation in manufacturing process.

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| 1.  | To identify the main actors involved in antibiotic supply chains | What are the main actors involved in antibiotics supply chain? | 1. Raw material/basic intermediaries: This are the actors who plays a vital role in the beginning stage of the supply chain, as the API manufacturing needs the raw mater. They are focused on mass production. Raw materials are mostly procured from India and China.  
2. API manufacturers, actors are majorly from China & India, as it cheaper and low labour cost. Also, the advance intermediaries are from China and India.  
Other country’s manufacturers are also supplying the APIs for the antibiotic (e.g. Spain and Italy). However, China and India have the biggest market share.  
3. Company that produces final dosages: they import the API and finishes the product this is known as formulation process in the pharmaceutical industry.  
4. Agents: the main job of the agents is to take the responsibility of providing good communication and connecting between various actors in the supply chain. And |
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<td>getting commission between the two actors. 5. Distributor: he takes the role of buying and selling the product (for example from the focal firm to the pharmacy or the hospitals).</td>
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<td>2. To get a general layout of the upstream supply chain network</td>
<td>Can you outline the structure of antibiotic upstream antibiotic supply chains?</td>
<td>The first step is the research and development for the drug. Most branded drug manufacturers tend to have the R&amp;D in-house, but now there are also scenarios where the R&amp;D is being outsourced to CROs (Contract Research Organizations). Then there is the API production which is largely carried out in countries like India and China. The next step is the formulation to achieve the Finished Dosage Form (FDF) which is either outsourced to other contract manufacturers or carried in house. The final step in the upstream supply chain is the packaging of drugs. The products then reach the MAHs for distribution.</td>
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<td>3 To understand the role of the focal firm in the network</td>
<td>What role does the focal firm play in the supply chain?</td>
<td>The focal firm is the MAH (Market Authorisation Holder) of the drug; and holds the license to manufacture and sell the drug. The MAH acts as an agent between the different actors in the supply network, and can also perform different operations in house, based on their business model.</td>
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<td>4 Important factors considered when choosing suppliers</td>
<td>What are the factors to be considered when choosing an external supplier?</td>
<td>Location, reliability, cost, quality, technology of the supplier and safety are the most important factors considered</td>
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<td>5</td>
<td>Multiple sourcing in pharmaceutical firms</td>
<td>Do firms use multiple suppliers to outsource a particular operation for the same drug?</td>
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<td>6</td>
<td>Offshoring and near shore reasons</td>
<td>When the firms will offshore and nearshore?</td>
</tr>
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