Improving Antibiotic Availability by Restructuring the Supply Chain

A Case Study Within Sweden

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Abstract

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Shailesh Garlapati and Vinana Sewoyo

Rising Antimicrobial Resistance is a threat faced all over the world. Bacterial infections that were treatable with antibiotics only a few years ago can now lead to life-threatening conditions. This thesis is part of the work of a large platform, PLATINEA, trying to reduce the rate of new resistances occurring in Sweden by preventing non-optimal treatment. Due to shortages of the right antibiotics, suboptimal antibiotics are prescribed, which has shown to be accelerating the resistances among the bacterial populations. This study proposes an information exchange database and a central storage model for critical antibiotics to circumvent stockouts and inconveniences resulting from shortages of medically valuable antibiotics.

Through interviewing prominent actors in the Swedish pharmaceutical supply chain an inside into the procurement of antibiotic in Sweden and what concerns are faced by the organs involved was created. Literature studies on occurred shortages of antibiotics in Sweden and the world were examined and possible reasons for these were identified. Examination of governmental efforts and assignments created the context in which gaps were identified that this thesis work could fill. A focus on Benzylpenicillin and Rifampicin were kept throughout the study.

The collected data led to the implementation recommendation of two models by this study. An information platform suggested to allow better, faster and more accurate information exchange between all involved actors of the supply chain as well as a centralized storage model for the storage of antibiotics with medically high value in Sweden.

Through the implementation of the model systems shortages of critical antibiotics can be circumvented and better availability of information leads to quicker reactions ability to stock outs of other antibiotics.

Keywords: Pharmaceutical supply chain, Antibiotics, PLATINEA, Benzylpenicillin, Rifampicin, Antibiotic procurement, Antibiotics supply chain, Antimicrobial Resistance, AMR, Antibiotic Shortages
POPULAR SCIENTIFIC SUMMARY

The topic of antimicrobial resistances is unknown to many. We hear that infections cannot be treated anymore or that more people die as a consequence of severe pneumonia, but do we really think about why? Small “germs” make us sick, but we expect that the doctor we go to see can fix it. But what if even they cannot help us anymore? The threat of resistances against commonly used medications is higher than ever. Bacterial infections, such as pneumonia, urinary tract infection or tuberculosis, are treated with antibiotics. Mistreatment and the overuse of antibiotics have led to the bacteria developing systems of resistance. When on top of that the wrong antibiotic against an infection is used, the rise of resistance is accelerated.

Many people rely and depend on antibiotics. But their supply is fragile and shortages, stock outs and deficiencies often are faced in the pharmaceutical supply chain. The threat of a disruption in the antibiotic supply chain is being paid increasing attention to in the past years. A sustainable and reliable supply of antibiotics is a priority for many countries around the world. PLATINEA, a platform for innovation of existing antibiotics, is a Swedish initiative that aims to create exchange and collaboration between different actors involved in the pharmaceutical supply chain, the health care sector and academic research institutions. This thesis is part of this initiative and focuses on examining the existing supply chains and the establishment of incentive models to circumvent stock outs and shortages of existing, medically highly valuable antibiotics in Sweden.

The focus of this work is placed on Benzylpenicillin and Rifampicin, two critical antibiotics. Their supply to and in Sweden is examined, the actors involved are identified and mapped, and problems are recognized. The objective is to suggest how the current system of delivery and accessibility can be improved. Assessing and understanding the complex and multifaceted pharmaceutical supply chain of these antibiotics is needed and highly important in order to take measures countering possible supply chain problems. With this thesis, the vulnerabilities of the pharmaceutical supply chain are highlighted.

Two models are proposed in order to establish an efficient information exchange between all involved actors and be better prepared for occurring shortages. Preparedness and awareness are the tools chosen in this work to fight against the threat of rising antimicrobial resistances. We need to continue our efforts to further investigate the antibiotic shortages and their reasons and collaborate for a better and more sustainable availability of antibiotics in Sweden.

Bacteria could also infect you. Hopefully our research and efforts can make sure that your “germs” are not resistant and that you can get the antibiotics you need on time.
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Finally, a special thank you to my girlfriend for listening to my nonstop rumbling about the thesis ideas, for motivating me when I felt tired and for her rocksteady support throughout this work. Thank you for not losing motivation helping me to translate Swedish health care documents and never getting tired of analyzing the interviews with me and preparing me for the next ones.

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### ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AB, A/B</td>
<td>Aktiebolag roughly equivalent to the abbreviations Ltd and PLC.</td>
</tr>
<tr>
<td>AMR</td>
<td>Antimicrobial resistance</td>
</tr>
<tr>
<td>API</td>
<td>Active Pharmaceutical Ingredient</td>
</tr>
<tr>
<td>DDD</td>
<td>Defined Daily Dose</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>EEA</td>
<td>European Economic Area</td>
</tr>
<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
</tr>
<tr>
<td>FoHM</td>
<td>Folkhälsmyndigheten</td>
</tr>
<tr>
<td>GPP</td>
<td>Good Procurement Process</td>
</tr>
<tr>
<td>LV</td>
<td>Läkemedelsverket</td>
</tr>
<tr>
<td>MAH</td>
<td>Marketing Authorization Holder</td>
</tr>
<tr>
<td>MPA</td>
<td>Swedish Medical Products Agency</td>
</tr>
<tr>
<td>OECD</td>
<td>Organization for Economic Co-operation and Development</td>
</tr>
<tr>
<td>PI</td>
<td>Parallel importer</td>
</tr>
<tr>
<td>PSCI</td>
<td>Pharmaceutical Supply Chain Initiative</td>
</tr>
<tr>
<td>RDT</td>
<td>Resource Dependency Theory</td>
</tr>
<tr>
<td>SALAR</td>
<td>The Swedish Association of Local Authorities and Regions</td>
</tr>
<tr>
<td>SCM</td>
<td>Supply Chain Management</td>
</tr>
<tr>
<td>SKL</td>
<td>Sveriges Kommuner och Landsting</td>
</tr>
<tr>
<td>SoS</td>
<td>Socialstyrelsen</td>
</tr>
<tr>
<td>STRAMA</td>
<td>Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance</td>
</tr>
<tr>
<td>SVARM</td>
<td>Swedish Veterinary Antibiotic Resistance Monitoring</td>
</tr>
<tr>
<td>SWERDES</td>
<td>Swedish Antibiotic Utilisation and Resistance in Human Medicine</td>
</tr>
<tr>
<td>TLV</td>
<td>Tandvårds- och läkemedelsföranksverket</td>
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1. **INTRODUCTION**

The introduction will primarily present the background to the research area and its context followed by a presentation of the Swedish health care system. The purpose of the conducted research will be introduced after which the research questions will be defined.

1.1. **BACKGROUND**

Antibiotics have played a huge role curing a lot of infectious diseases and saving a lot of human life since being discovered. Even today infectious diseases affect human populations on large scale in both developed and particularly in developing countries in resource poor settings. A privileged minority of the world’s population has great access to treatment and medical resources, including antibiotic supply which is often taken for granted (Smolinski et al., 2003). Only a very few people understand the enormous impact the discovery of antibiotics has had on treatment of infectious diseases. About 70 years ago, many of today’s easily treatable bacterial infections were still deadly (Davies and Davies, 2010).

Antibiotics are chemical compounds that kill or inhibit the growth of bacteria (Ventola, 2015). There are multiple different mechanisms of action in which the drug can work. Some antibiotics work by breaking down or interfering with the bacterial cell wall or cytoplasmic membrane, some inhibit the protein synthesis whereas others work by obstructing bacterial replication, interfering with the integrity of the DNA or preventing the folic acid metabolism (Dugassa et al., 2017).

One of the most significant accomplishments in the history of medicine is the control and treatment of infectious diseases by the use of antibiotics (Davies and Davies, 2010). Antibiotics are a huge advantage in healthcare treating infected patients. To ensure successful treatment in the future, the rise of resistant bacteria needs to be controlled. Through controlling the use of antibiotics and preventing excess and unwanted treatment resistance can be limited (Ventola, 2015). Patients should only be able to access antibiotics upon a doctor’s prescription. Such regulations are set in a few countries around the world, whereas antibiotics are ‘over the counter’ drugs in the majority of nations. Norway and Sweden are few countries closely regulating the use of antibiotics (Paget et al., 2017), whereas in Italy, Spain and Greece the drugs are sold over the counter without any prescription (Paget et al., 2017). In countries with no governmental limitations the patients lack of financial means or the shortage of the drug itself are the only regulatory factors of usage. To ensure the successful and sustainable use of antibiotics even in the future, stricter regulations need to be implemented in more countries around the world.

When there are shortages of antibiotics to treat an infectious disease, people get prescribed antibiotics which are less effective and less optimal as treatment which can lead to higher chances of antimicrobial resistances (AMR’s). Every time we consume an antibiotic that is sub optimal in fighting the bacterial infection, we give the bacteria a chance to slowly adapt and over time develop a resistance against it. This resistance can be passed on to other bacteria and into the environment leading to a rising burden of existing antimicrobial resistance. In order to decrease the threat of AMR doctors need to be able to prescribe the right antibiotics against the right bacterial organisms (Cogan et al., 2018).

Alexander Fleming, the discoverer of Penicillin, foresaw in an interview for the New York times in 1945 that redundant usage of antibiotics would lead to a resistance problem (Fleming, 1945). In the interview he predicted that, when the population starts to request Penicillin treatment “then will begin an era […] of abuses”. Upon excessive use, microbes
that are resistant to Penicillin will get a selective advantage and can be passed on from one infected individual to another until they reach someone who gets a sepsis or a pneumonia where the antibiotic Penicillin will have lost its effect to. In the unfortunate event of a patient surrendering to an infection with resistant bacteria, Fleming positions, that the moral responsibility for the death lies on the person “thoughtlessly […] playing with Penicillin treatment”. He hoped that “the evil” could be prevented. Unfortunately, his foreseeing became reality and his hopes would have been shattered. Due to uncontrolled and excessive usage of antibiotics, people succumb in previously treatable bacterial infections.

The growing problem of antibiotic resistance in Sweden and globally is driving researchers and pharmaceutical companies into finding new strategies and new chemicals to treat infections caused by resistant bacteria. With antibiotics being less and less effective it is an important task for humanities to make the process of treating patients with resistant pathogens as efficient as possible. Sweden is good in preserving the use of antibiotics, but with other countries being less protective about the use and distribution of these antimicrobials, resistance will increase globally. One way to combat the mounting threat of ineffective antibiotics is by developing new technologies of producing antimicrobial chemicals (Nwokoro et al., 2016). Another approach is ensuring the supply of already existing antibiotics to enable appropriate treatment of patients and thereby lowering the selective pressure of establishing resistances in the bacterial populations. To allow this, it is important to establish a communication platform for the antibiotic pipeline coordinators such as the industry, health care providers, research institutions and public authorities and to strengthen the antibiotic supply chain (Baraldi et al., 2018, Koffmar, 2017). To ensure appropriate treatment of patients the supply of antibiotics need to be ensured in all parts of the health care structure additionally. Suitable purchasing strategies and logistical models need to be proposed in order to succeed to improve the accessibility of antibiotics throughout Sweden.

1.2. STATE OF RESEARCH ON ANTIBIOTIC SHORTAGES

The shortage of antibiotics is a major problem when treating bacterial infections in Sweden. The reasons for these shortages of antibiotics are many and complicated. Some of the reasons include fragmented supply chains and inconsistent antibiotic supply (Access to Medicine Foundation, 2018). Some stages of the global antibiotic supply chains consist of many actors whereas other important stages are supplied by only very few (Cogan et al., 2018). This can cause bottlenecks and interruptions in the flow of production leading to antibiotic shortages.

The Public Health Agency of Sweden (FoHM), investigated the reasons for the lack of accessibility of antibiotics in Sweden in a report published in 2017. In the report they identified three indicators the FoHM classified as major contributors to this problem. They investigated the problem based on the limited number of suppliers of Active Pharmaceutical Ingredients (API) to Sweden, low number of annual sales in Sweden and additionally looked into documented cases of antibiotic shortages in Sweden (The Public Health Agency of Sweden, 2017). The FoHM report exhibits a limited perspective by analyzing only three indicators. The accessibility problem can depend on more than these three variables and should therefore be investigated in more detail.

In order to obtain more detailed information on possible problems in the production and distribution of pharmaceutical agents, the FoHM has appointed The Medical Products Agency (LV) to collect detailed information on medicine shortages in Sweden (Folkhälsomyndigheten, 2017). According to FoHMs report “Modeller för lagerhållning och distributionsvägar - Delrapport 3 i regeringsuppdrag om Tillgänglighet till antibiotika” The
Medical Products Agency (LV) has identified two causes for shortages through their investigations. They state that production problems and logistic problems are the major contributors to the lack of accessibility of antibiotics in Sweden. There can be a lack of active substances, quality defects, changed production processes, unexpectedly high demand of antibiotics, errors in planning and transportation damages effecting accessibility.

The overall accessibility problem of antibiotics in Sweden cannot be generalized. Each shortage of a particular antibiotic needs to be investigated in the individual supply chain. In comparison to the existing literature this research will explore the current risks to the supply chains and suggest improvements. Besides purely logistical and production planning problems, it is important to also consider the environmental impact, the political risk, the regulatory framework, the climate vulnerability and the social sustainability (increased requirements for producing according to ethical conditions).

A fragmentation of the supply chain carries both benefits and dangers. Fragmentation enables cost-effective and efficient production of medicines, but the production chain also needs to be well balanced and planned in detail to facilitate a steady production flow. At every fragmentation point, there are production pathways merging. The amount of these nodes at any stage varies with every antibiotic production chain. The less nodes there are at any step of the supply chain the more vulnerable it gets to the above-mentioned risks. Therefore, it is essential to investigate each possible risk and establish strategies to prevent them from effecting the supply of antibiotics to Sweden.

1.3. Overview of the Swedish Health Care System

The Swedish word for healthcare *folkhälsa* was defined as “an expression of the health status of the population, which considers both level and the distribution of health” by Urban Janlert and expresses the fundamentals of an equal treatment system regarding health care in Sweden (Janlert, 2000). The access of health care and medicinal products is aimed to be evenly distributed in the country. To facilitate good regional providence and control of the health care

![Figure 1: Overview of the Swedish Healthcare System](image-url)
facilities, the responsibility is divided between three governmental administration levels: National, County Councils and Municipal Regions as illustrated in Figure 1. Even if different organs act on different levels there is no hierarchical relationship in between the actors. All organizational levels are self-governing local authorities (Anell et al., 2012).

At the national level The Ministry of Health and Social Affairs (Socialdepartamentet) is responsible for the overall health and health care of the Swedish population. There are multiple other agencies at the national level, The Public Health Agency of Sweden (Folkhälsoomydigheten: FoHM) being the most important one, which collaborate with the Ministry to issue laws, policies and regulations which provide directions for the county councils and regions. Other agencies involved at the national level are The Swedish Dental and Pharmaceutical Benefits Agency (Tandvårds- och läkemedelsförmånsverket: TLV), the Swedish Medical Products Agency (Läkemedelsverket: LV), The National Board of Health and Welfare (Socialstyrelsen: SoS) and the Swedish National Food Agency (Livsmedelsverket: SLV) among others (Rechel et al., 2018). On the regional level, The Swedish Association of Local Authorities and Regions SALAR (Sveriges Kommuner och Landsting: SKL) is the employer and a member organization for all the Swedish 290 municipalities and 21 county councils. The association acts on behalf of its members and especially influences local and regional politics. Additionally, it operates a procurement company, SKL Kommentus AB which is the legal organ that can procure medicines for county councils. However, except vaccines for national vaccine programs, the company is rarely used by the county authorities.

The Health and Medical Services Act of 1982 specifies that the task of providing “good health care on equal terms for the entire population” falls on the county councils, municipalities and regions (Affairs, 1982). The county councils or regions own most of the public health facilities (hospitals, primary care units) in Sweden but are also responsible for the economical funding and the provision of services in all facilities (Anell et al., 2012). The funding for the health sector in each county is imposed on the inhabitants through the county tax (Pontén Johan 2017). There are 21 county councils in Sweden which get guidance and directions from the national level, but are relatively free and independent on making decisions regarding the county’s regional health care needs and facilities (Pontén et al., 2017, Rechel et al., 2018).

1.4. Purpose

The proposed research will focus on the aspect of improving the general availability of antibiotics to Sweden. Specifically, we will conduct research to circumvent shortages and stock outs of medications in Sweden.

The problems of the Swedish pharmaceutical and antibiotic supply chain processes are the limited information, high complexity and lack of transparency of the supply chain and the buying process. A complicated procurement process can lead to shortages in availability of antibiotics, which can cause problems of access to antimicrobial medicines in case of disease.

Usage of the wrong or non-optimal treatment in case of an infection can lead to the establishment of resistances in the bacterial population. Since antimicrobial resistance (AMR) is an emerging threat even in Sweden, authorities should pay more attention to this issue.

In this thesis, there are three objectives. Firstly, we aim to map and understand the antibiotic supply chains to and inside Sweden. Second, we want to generally identify the stages of antibiotic procurement in Sweden and focus on the supply of Benzylpenicillin and Rifampicin. To understand how the antibiotic distribution looks in Sweden and what the needs for the specific antibiotics are is another essential part we aim to understand. Benzylpenicillin
can be seen as a representative for hospital administered antibiotics whereas Rifampicin is a
typical prescription antibiotic. The result can therefore be utilized to analyze similar antibi-
otics and their supply chains. Lastly, we hope to be able to establish suggestions on how the
antibiotic supply chain in Sweden could be improved and how procurement can be made
more efficient, based on our obtained data and conclusions.

1.5. RESEARCH QUESTIONS

This thesis will focus on examining the structure of the Swedish pharmaceutical supply chain
and its flaws and problems leading to shortages of antibiotic supply in the country. The first
question addresses the lack of knowledge of the general structure of the supply chain. Liter-
ature research and interviews on the overall flow of resources will be utilized to answer this
question. The second question is relating to the first one and will focus on exploring the
details of the supply chains for the two antibiotics Benzylpenicillin and Rifampicin. Experts
in the supply of these antibiotics as well as manufacturers will be tried to be contacted to
gather this information. Online databases and articles will be used to complement the data.
The last two questions will focus on examining the collected data and finding problems and
flaws and proposing possible solutions to circumvent the issues of antibiotic shortages in
Sweden.

The design of the study goes from general investigations over more detailed examinations to
solution proposals. The chosen case study format of research combined with intense literature
studies and interviews helps to gather the required information to answer the questions. The
first two questions were developed before the start of the study whereas the third and fourth
questions evolved during the analysis of the gathered results. The main question for the anal-
ysis of the latter two questions was how shortages in the antibiotic supply chain could be
circumvented.

Below are the exact research questions that have been formulated and answered in the anal-
ysis chapter of the thesis (6).

Research Question One

What is the structure of the pharmaceutical supply chain as seen from the Swedish
market at present?

Research Question Two

How are drugs procured into the Swedish market? An explanation of the drug delivery
pipeline for Benzylpenicillin and Rifampicin.

Research Question Three

How can information sharing and collaboration between the different stakeholders
in the pharmaceutical supply chain help to endure drug shortages in Sweden?

Research Question Four

How can combined stock reserves of drugs in Sweden be an alternative to circumvent
drug shortages in countries health care systems?
2. LITERATURE REVIEW

This section examines the literature in the related fields of the supply chain, supply chain management, strategies and networks, supply chain risks and the agility of the supply chain. Additionally, a focus is set on how information sharing, and a good procurement process can help to create a well working supply chain.

2.1. SUPPLY CHAIN AND SUPPLY CHAIN MANAGEMENT

The system of activities, people and resources involved in the production and supply of a product starting from the raw materials leading to the end product is referred to as the supply chain. The logistical flow of goods, information, materials, money and man-power across the supply chain and the satisfaction of the customer needs and demands is required to be effective and organized to comprise a successful supply chain (Forrester, 1958). It is however not the responsibility of one person or one company to regulate these activities. Multiple people from multiple companies at different stages need to be actively involved in making sure the processes flow efficiently and sustainably (Anderson et al., 2007). The main activities of this supply chain management (SCM) group are setting up strategies for the production, the procurement of raw materials, the actual production of the product which can consist of manufacturing, conversion or assembly, the products distribution and the company’s customer interface (Mentzer et al., 2001).

Supply chain management is a distribution management. To direct the flow of information, materials, money, man-power and capital equipment throughout the entire supply chain, so that every single station in the production chain runs smoothly, is what the supply chain managers are in charge of (Forrester, 1958). It is the management of interrelationships between separate company functions, between the company and its market and industry and the respective nation’s economy (Forrester, 1958).

The overall objective of the supply chain is to fulfil the consumer demands and the supply chain management helps to make it profitable for the company (Chopra and Meindl, 2007).

2.2. SUPPLY CHAIN STRATEGIES AND NETWORK

Several authors described that Supply Chain Strategies are related to cost, adaptability and speed responsiveness (Tarafdar and Qrunfleh, 2017, Fisher, 1997, Qi et al., 2011). In order to have an efficient Supply Chain Strategy, several things such as the life cycle of the product, forecast of the demand, product types and the lead times for market condition should be considered (Fisher, 1997).

In order to have a suitable strategy, the pharmaceutical company should understand the supply chain flow process and network as well. For some companies, mapping supply chains is one of the strategies to track all the suppliers for the specific production process. It is vital because normally, the company can only control the production from their first-tier suppliers. Having a large extent of the supply chain tier when mapping the supply chain, helps to avoid the failure which is caused by the supply chain disruptions (Christopher et al., 2018a).

Moreover, to have a resilient supply network, it is important to map the supply chain network. There are several purposes of mapping the supply chain network, for example to identify the bottleneck in the process and to improve the unnecessary process (Christopher et al., 2018a). Through the supply chain mapping, some strategies could be used to have a resilient supply
chain network, specifically in pharmaceutical industry for example to source the active ingredients from the low-cost country, lean management or having the centralized distribution (Christopher et al., 2018a).

Further, to be able to create a resilient supply, a continuous planning is needed. We must be able to identify all the stakeholders, especially the ones from the procurement process until the delivery process and then evaluate which process can caused the bottlenecks (Christopher et al., 2018a).

2.3. SUPPLY CHAIN RISKS

Organizations, information, resources, people, transportation logistics and products are involved in the manufacturing of medical goods and devices. There are multiple opportunities along the supply chain were disruptions can occur leading to the risk of shortages in supply to the consumers.

Leading pharmaceutical companies can make business decisions that increase the risk of disruption in the supply chain. Over the past decade globalization of manufacturing processes has increased steadily (Chan et al., 2004). The use of overseas suppliers and factories has shown to be much less expensive than domestic production but entails the higher possibility of disruptions to the supply at every stage that is facilitated outside of the home country. Currency, fluctuating rates, interest rates, cash flow and changes in the political situations of the respective countries are another factor creating instabilities and possible dangers for the supply chain (Enyinda et al., 2010, Breen, 2008, Mehralian et al., 2012).

Natural disasters, sovereign debts and political strife are often not controllable and can cause vast shortages and disruptions of the supply. The tsunami and earthquake in Japan destroying production facilities and the volcano outbreaks on Iceland effecting air transport are recent examples of natural catastrophes that disrupted the pharmaceutical supply chains.

The risk of a lack of supply of raw materials to the primary manufacturing facilities or of the finished product to the wholesalers and distributors is the most important risk in the supply chain (Jaberidoost et al., 2013). The quality of the raw materials (Mehralian et al., 2012, Blos et al., 2010) relationships and contacts with the suppliers (Breen, 2008, Shah, 2004, Enyinda et al., 2010), the heavy fragmentation (Breen, 2008) and the nature risk factors are mayor factors contributing to disruption of supply at early stages of production. To give a real-life example, in 2017 an explosion in a Chinese API production factory led to a Europe wide shortage of the antibiotic Piperacillin, since this company was used as a primary manufacturing site by multiple downstream pharma companies (Cogan et al., 2018).

Regulation of the different stages in the supply chain constitute another risk for the pharmaceutical supply chain. Monitoring the inventory, organizing the research and development of new drugs and the overall company strategy remain threats to the stability of the stream (Jaberidoost et al., 2013).

To control and foresee the demand for a drug or an API is one of the biggest challenges in the pharmaceutical industry. Fluctuating demands can lead to shortages of medicines or to the over production and subsequent halt in production of drugs in primary or secondary manufacturing sites (Shah, 2004, Breen, 2008). Without careful monitoring and control of demand, usage and stocks of important medicines the supply in case of need is not secured.
2.4. AGILITY AND FLEXIBILITY IN THE SUPPLY CHAIN

Besides having the proper strategy in the supply chain process, it is also important to pay attention to the agility of the supply chain. Agility in supply chain focuses on how flexible, quick and effective the supply chain responds to the customer’s needs and alteration in the market. (Tarafdar and Qrunfleh, 2017, Lin et al., 2006, Christopher et al., 2018a, Christopher, 2000, Yusuf et al., 2004).

In this era, agility is needed so that the company can survive and compete with others. In pharmaceutical companies, where the strong focus is on the interdependency between the chain such as suppliers, manufacturers, governmental agencies, distributors and customers, the agility is very much needed. The pharmaceutical business is fragile which means shortages of drugs or antibiotics can happen anytime, but these shortages might take a while to be solved. New suppliers need to be identified and these might not have the requested drugs ready on stock (Kacik, 2019). Therefore, pharmaceutical business having to deal with the uncertainty of the demand and the business market, is an example for where an implementation of the agile supply chain having the market sensitivity so that the company can take proper action to the changes is recommended (Lin et al., 2006, Christopher, 2000).

Nowadays, many companies that are involved in the manufacturing business have several common characteristics, for example they are more up to date and have more advanced customers, meaning that products must be personalized in a short period of time. Therefore, in order to compete in a new era, companies must be able to be more flexible in their production (Stevenson and Spring, 2007). According to Upton 1995, flexibility specifically in manufacturing can be related to the product range, mobility and uniformity to perform (Upton, 1995). In the beginning, flexibility only applied in manufacturing, specifically through automation in relation with set up times, volume and products. However, by the time the concept got broader and transformed the organizational business as well (Christopher, 2000).

One way to tackle the disruptions in a supply chain is to implement a flexible supply chain. Flexible supply chains are easier to adjust to temporary disruptions in an efficient way, for example an alteration in demand. But at the same time still preserve the same level of service to the consumers (Stevenson and Spring, 2007).

Gerwin 2005 found seven classifications for flexibility which are mix, changeover, modification, rerouting, volume, material and sequencing (Gerwin, 2005). While (Vokurka and O'Leary-Kelly, 2000), expand it to fifteen classifications which are “machine, material handling, operations, automation, labor, process, routing, product, new design, delivery, volume, expansion, program, production and market”. Based on their founding, there are three main foundations which can be applied to supply chain which are “flexibility is multi-dimensional, different elements of flexibility are more important in certain environments than in others and flexibility is a capability that does not have to be demonstrated” (Stevenson and Spring, 2007, p. 689).

The flexibility in supply chain should be applied in volume wise, sourcing in short and long-term period, strategy and procurement agreement. Further, the volume flexibility is related with the way company acts with the sourcing partners in terms of outsourcing, planning and create the strategy to source and partnership, both internally and externally (Stevenson and Spring, 2007). Additionally, doing flexible agreement for long-term procurement also contributes to give the supplier more balance and at the same time the buyer can answer the instability of the demand (Stevenson and Spring, 2007).
2.5. **Information Sharing**

Several authors are devoted to do research on information sharing and how the suppliers’ respond to make the decision and create policy with the demand (Du et al., 2012, Bourland et al., 1996, Chen, 1998). Demand information sharing is very important for the supply chain management to take further steps with their business whether to make the right and efficient coordination and to manage the inventory and the vendor as well (Chen et al., 2006, Arshinder and Deshmukh, 2008); (Arshinder et al., 2008).

Moreover, there are four types of information sharing according to (Du et al., 2012), p. 90), namely “order exchange, operational information sharing, strategic information sharing and strategic and competitive information sharing”. Likewise, there are several points that must be involved in order to have a successful cooperation to share the information such as “partnership coordination, commitment, trust, high communication quality, participation and joint problem solving” (Du et al., 2012), p.89).

To improve the performance during the partnership between actors, specifically while exchanging the information, the strategy in which for being competitive and the efficient operational in the company are needed (Sodhi and Son, 2009); (Du et al., 2012). In addition, when it comes to data information sharing, the actors that involve in such process normally have different intentions (Du et al., 2012), in which several points that we mentioned above play an important role to ensure the continuity of flow process. It is also necessary for all the actors involve having the compliance to share the data between each other in a truthful manner.

There is one common finding from all the papers about information sharing, which is with the correct and sufficient information, then follow with the suitable process, the management can predict the demand more accurate and then take a correct respond/policy accordingly.

2.6. **Inventory Management**

In relation with inventory management, information sharing in the partnership performance should be in line with the supplier’s capacity to catch the information about the demand and allocate it accordingly. Further, the global sourcing in pharmaceutical industry makes the supply chain, specifically regarding the inventory management is hard to manage. Global sourcing is difficult to manage compare to the local sourcing because of the distance and geographic location which affects the lead times during the process and lead to another problem such as increasing of the inventory stock amount and cost (Golini and Kalchschmidt, 2011).

Companies usually manage their own stock by themselves and rely on their vendors to control the inventory strategy during the supply chain process (Dai et al., 2017). However, this is not the case (relying only on vendor) in pharmaceutical industry because pharmaceutical supply chain has a great duty for the society, in terms of ensuring the drugs reach the customers in the appropriate time and condition Therefore, some of pharmaceutical industries have vast inventory as a solution (Uthayakumar and Priyan, 2013). Further, due to the complex pharmaceutical supply chain - in terms of dependency between actors and various business processes-, special drugs treatment and to prevent the drugs shortages in the hospital, the accurate inventory management, strategy, coordination and decision should be applied. Another reason to have the correct inventory management and strategy is to prevent/reduce unplanned inventory costs (Uthayakumar and Priyan, 2013).
2.7. **GOOD PROCUREMENT PROCESS**

Moreover, to do a responsible purchasing in pharmaceutical, it is vital for the companies to follow the instruction from World Health Organization (WHO). The guidelines from WHO has four primary aims to do the strategic procurement method or is also known as Good Procurement Process (GPP), which are (World Health Organization, 1999):

- Purchase the cost-effective medicines in the correct amount
- Choose the vendors who have the good reputation and produce high quality products
- Guarantee the on-time delivery
- Acquire the cost to be as low as possible

In addition, besides the strategic procurement, GPP is also plays an important role in operational principles. Since the procurement process involves in different drugs options, drugs productions and drugs documentations. Therefore, the processes and activities which related to procurement should be transparent, planned and monitored well (World Health Organization, 1999).

2.8. **ANTIBIOTICS SHORTAGES AND PHARMACEUTICAL POLICY**

As antibiotics concern the interface between public and private actors, different interests inevitably collide. While public actors need to satisfy the demand for antibiotics within a country and ensure that its citizens have access to these drugs, companies work from a profit-oriented perspective and try to earn money. Based on these resulting conflicts, this chapter provides an overview of how much antibiotics are being used in Sweden, Scandinavia and worldwide, how the pharmaceutical and antibiotics policy looks like in Sweden, and what impacts antibiotics supply chains and consequently lead to shortages.

2.9. **ANTIBIOTICS SHORTAGES AND PHARMACEUTICAL POLICY**

After entering the European Union (EU) in 1994, Sweden promoted the introduction of so-called parallel imports of pharmaceuticals in 1996, which proposed to have both pharmaceuticals and generic substitutes, and later in 2002 agreed to choose the cheapest supplier for delivery of pharmaceuticals. Hence, this competition-based policy and parallel merchants competing with each other lowered the cost of pharmaceuticals, letting customers and patients benefit the most throughout entire Europe. Moreover, there is evidence that through the competition of also using generic pharmaceuticals, manufacturers of branded pharmaceuticals lower the prices as well. Overall, Sweden's approach of parallel imports of pharmaceuticals has resulted in a medium price advantage of 14.9% and a 1.6% lower drug bill between 2002 and mid-2004. Per capita, savings of EUR 5 in 2003 in Sweden are twelve times higher than the results of parallel trade in Norway (Poget, 2008).

2.10. **GAP IN THE CURRENT RESEARCH FIELD**

Even though the availability and accessibility to pharmaceuticals and antibiotics is essential for a functioning health care system, supply chain management and procurement research has been focusing on other industries. Studies from the US revealed, that certain supply chain issues were related to higher likelihood of shortages occurring, however no clear connection was drawn on which solutions could help circumvent these shortages from happening. This thesis therefore aims to close the gap between the recognition of a shortage happening in the
downstream supply and the upstream supply chain issues responsible. It shall be understood why shortages happen at the customer stage in the Swedish antibiotic supply, why these shortages happen and the what the opinion of the involved actors in the supply chain regarding these stock outs is.
3. THEORETICAL FRAMEWORK

This section explores theoretical framework in the related field of this study. The section provides analysis of published sources on the topics related to the fields of purchasing over the past two centuries, the procurement process and the purchasing of pharmaceuticals. Additionally, two theories are introduced that will be utilized to analyze the collected data.

3.1. THE VIEW ON PURCHASING OVER THE PAST TWO CENTURIES

Purchasing was already recognized as an important function of general management in the second half of the 19th century (Leenders and Fearon, 2008). In 1896 it was recognized that alignment of the purchasing function with other important management roles was essential for the company’s success. At the starting of the 20th century material management, centralization of processes and outsourcing of the purchasing function were introduced as new company concepts (Leenders and Fearon, 2008). Large companies can stay more competitive when the purchasing function is outsourced. Outsourcing can leverage the company’s economies of scale and have the experience and trained staff that cut costs and enhance efficiencies.

The World War I, greatly impacted purchasing practices all over the world and made a cut into most business strategies. Price escalations and shortages of materials and workforce lowered the purchasing at this time (Leenders and Fearon, 2008). When the economy started to work again and before the next world war started the public sector became more aware of the importance of purchasing. This led to development of procurement legislations in the 1920s to 1930, to ensure ethically correct procedures during purchasing (Leenders and Fearon, 2008). After the second world war, when peace had advanced, the importance of purchasing as a strategic interchange for the company was increasingly considered (Cavinato, 1992). Starting in the 70s purchasing was considered critical in making profit, and high importance was given to it in the companies and literatures (Henderson, 1975, Kiser, 1976, Farmer, 1978). In the 80ies and 90ies global sourcing as a concept came up as global efficiency exploitation (Monczka et al., 2014). A global market over geopolitical boundaries led to cost reduction of labor, raw materials and production and taxation alternatives in other countries were examined and companies moved their headquarters into more tax beneficial countries (Cavinato, 1992).

In the early 2000s strategic factors of purchasing decisions were established and defined (S.M., 2009, Ting and Cho, 2008, Joyce, 2006). Purchasing became more and more complex and important for the companies’ competitive strength in the market. Today globalization, electronic purchasing, sustainability and collaboration aspects are highly discussed concepts in the field of supply chain management (e.g. suggestions by (Walker et al., 2012, Zheng et al., 2007)). Strategic purchasing has been, is and will always be one of the most important supply chain management functions.

3.2. THE IMPORTANCE OF STRATEGIC PURCHASING AS A SUPPLY CHAIN MANAGEMENT FUNCTION

Purchasing is one of the most important and highly crucial steps of all supply chains. Purchasing is the sum of all operational and strategic activities of a private or public company carried out as part of the procurement of materials, goods, equipment and services. This includes the identification and specification of needs, the identification of decision criteria, the
initial screening of preferred suppliers, the selecting suppliers, and the monitoring performance (Van Weele, 2010, Kakouris et al., 2006). Procurement refers to all processes for supplying the users with input factors that are not created by the company (Figure 2). The most important procurement processes are demand determination, make or buy decision (own or external sourcing), supplier management, order / notification / order processing and delivery schedule. Therefore, the purchasing process is part of the procurement process and a clear line is often hard to be defined between purchasing and procurement. According to the definition, procurement serves to maintain supply of those input factors required for operating processes, which cannot be or are not provided by the company itself. The term "procurement management" on the other hand covers the decisions that go beyond the individual requirements of the supply of goods and services at the production sites. These include for example the procurement of labor, information, capital, rights, goods and services.

Traditionally purchasing was not considered as a frontier to achieve competitive advantage nor as a strategy to achieve the strategic goals of the company (Van Weele, 2010, Lawson et al., 2009). Purchasing was understood as an isolated function not included in the organization’s success strategy. It was a note of buying instructions from the internal company, listing what needed to be purchased according to the company requirements (Lawson et al., 2009).

In the past years this view has changed. Companies understood that to keep their competitive advantage on the market the view on purchasing as a strategic function needed to be established. Leenders and Fearon stated in the early 21st century that purchasing is never just about buying resources (Leenders and Fearon, 2008). Integration of the purchasing function into the general management is good and needed for accomplishment of the companies’ goals and the achievement of profits.

Figure 2: Definition of the supply functions in the supply chain management in terms of scope of activity.
3.3. **THE PROCUREMENT PROCESS**

The procurement process can be divided into five different phases (de Boer et al., 2001, Christopher et al., 2018b). It is self-evident that the better a company or organ plans and coordinates the purchasing process the more competitive and efficient it becomes in the market. Each organ decides based on the situational demands and circumstances the amount of effort that is spent on each step. The purchasing aspect is nowadays recognized as a strategic function for the organization and has a profound influence on the overall performance and success of the process.

![Figure 3: Reference process for purchasing.](image)

The responsibilities of the purchasing units can be operative or strategic (Figure 3). Operative purchasing includes order processing, reclamation handling, schedule coordination, invoice verification and the processing of order confirmations among others. Strategic purchasing on the other hand deals with procurement market research, supplier management (research, selection, evaluation), negotiation of the general agreements and implementation of the selected purchasing strategy.

Purchasing is currently experiencing a shift from mainly operational towards strategic purchasing. Organizations think more value-based, implicating that purchasing is no longer seen as a cost factor, but as a success factor with a focus on strategic activities. Accordingly, the "new purchasing" combines different abilities: it is strategic, innovative and quality-, customer- as well as future-oriented.

Cooperative purchasing also known as group purchasing, collaborative purchasing, collective purchasing or shared purchasing can be used in pharmaceutical supply chains as a way to tackle the shortages experienced (Schotanus and Telgen, 2007, Rego et al., 2014). Cooperative purchasing is involving more than one organization in the horizontal collaboration with several purchasing steps such as sharing the information, the volumes or risk in the market, material and demand (Schotanus and Telgen, 2007, Schotanus et al., 2010, Rego et al., 2014).
3.3.1. **The Initiation Phase**

The fundamental step of the purchasing process is the identification of needs for products or services (Van Weele, 2010). Good internal communication and an intensive interchange of information are required for an efficient planning process. The purchasing strategy which is to be chosen initially sets the general guidelines for the complete purchasing process. The purchasing strategy is among others derived by the counties consumption estimations, from discussions with internal actors, the management and the product sector. Considerations about the feasibility of plans and the analysis of anticipated benefits have to be cautiously conducted. Costs and risk consequences have to be weighed against each other and the possible outcomes have to be managed. When developing the purchasing strategy, it is important to have a good degree of flexibility in order to adapt quickly to internal and external changes.

3.3.2. **The Planning Phase**

This phase is central to the entire purchasing circle and needs to be well established for a functioning process. In this step various criteria for suppliers, bids, customer needs, and delivery are set and discussed. All process requirements are defined, standardized and set in

![Figure 4: The purchasing matrix adjusted after Kraljic. Supplies such as pharmaceuticals can be categorized into four different categories depending on their importance for the customer and difficulty of procurement (Caniëls and Gelderman 2005).](image-url)
detail. In the material group management, all articles in an organ’s procurement portfolio are grouped together using common characteristics. The grouping features should be chosen in such a way as to maximize the value of purchasing, which can be recognized both internally (within the organ) and externally (outside the organ). The focus lies here on ensuring the effective communication and accurate fulfilment of the customer needs by the suppliers. Meeting the customer requirements directs the performance characteristics towards fulfilling the customer desires rather than optimizing and setting precise configurations. Both qualitative and quantitative criteria are established to ensure a balance between the tangibles and intangibles factors. The most relevant criteria to be considered here are quality, on-time delivery, cost (Verma and Pullman, 1998, Karpak et al., 2001) environmental issues (Handfield and Nichols, 1999), and manufacturing costs, technology and services (Bhutta Khurrum, 2002).

Different products and services have varying value to the services and products offered by the purchasing company. Depending on the value, supplies can be categorized into four different categories as seen in Figure 4. The illustration is based on previous literature (Caniëls and Gelderman, 2005).

1. **Leverage materials** are usually easy to obtain, meaning the procurement risk is low. However, they have a high impact on the operational result - their value share in the procurement sum is high. Leverage materials are usually relatively simple items which should be standardized as far as possible in order to ensure the best possible staking of quantities.

2. **Strategic materials** are difficult to obtain and their value share in the procurement volume is high. Therefore, for these materials it should be aimed to have suppliers in a close and long-term partnerships and this relation should be deeply integrated into the purchasing processes.

3. **Standard materials** are easy to procure and do not represent a largely to the purchasing volume. The procurement of these products should be as easy as possible or ideally standardized. The procurement of these materials could be made by a service provider who e.g. self-fills these materials of the company.

4. Although the share of **bottleneck material** in terms of the purchasing volume is low, it still is difficult to obtain these due to only a few suppliers or rare materials. If possible, bottleneck materials should be replaced by standard materials to ensure the supply. It is also plausible to cooperate with a service provider who has very good knowledge of the procurement markets to provide better and more sustainable access to these materials.

Which products and which materials the purchaser focuses on fluctuates between organs and markets, and services or products produced. Nevertheless, a uniform opinion to focus on price, quality, delivery and services can be seen in different markets respectively. Common subjects discussed and analyzed are the relative weights of each factor against the others and decisions concerning the factors critical, objective and subjective status (Houshyar and Lyth, 1992). Additionally, the identification of the true decision maker in the process is an essential part of the planning phase. Decision makers can be single individuals, groups within an organ or in certain cases even a region or company as a whole.
3.3.3. **The Qualification Phase**

The result of the procurement market research is the potential supplier identification. Request and verification of certificates, dispatch of preliminary questionnaires to suppliers / self-disclosure containing questions about the suppliers’ basic data, the development capacities and the quality of methods are used in practice for supplier limitation and selection. The pool of potential suppliers is evaluated against the established criteria from the planning phases and a list of supplier candidates is generated. All suppliers are reduced to a set of acceptable suppliers (de Boer et al., 2001). For existing suppliers, the current delivery behavior is established as a selection criterion. When new suppliers are advertised or identified, the added value that the inclusion of this supplier into the suppliers’ pool would have is assessed.

The suppliers are sorted according to the purchasers’ criteria not ranked. Factors that qualify the suppliers are not necessarily major determinants of success for the suppliers in general (Slack, 2005). The suppliers’ performance has to match the purchasers’ requirements and be above a particular level. Performances below that level are not considered whereas performances above do not automatically give the supplier a competitive advantage.

Depending on the pharmaceutical there will be more or less available suppliers. Especially for bottleneck or strategic antibiotics the variety of suppliers might be highly limited.

The qualification phase ends with a request. The request is an invitation by the county to the qualified suppliers to submit a binding offer, with the aim concluding the contract by simply accepting the offer. For the purchaser the request is a survey of potential suppliers, regarding whether these can provide certain supplies and/or services at competitive prices with the desired quality and timing.

3.3.4. **The Winning Phase**

The first choice that the purchaser has to make before accepting an offer is the sourcing choice (Table 1). The choice of a sourcing method depends on the product group. In practice tenders or bids are often carried out (especially for services) or individual queries are sent to the supplier. Within the framework of the quotation management, an evaluation of the offers received and a bid comparison (e.g. by comparison in a decision matrix) is made resulting in the award decision. Principles that are taken into consideration by the management are often manufacturing-related criteria such as the price, delivery reliability, delivery speed, quality, demand increases, product range, design and distribution and non-manufacturing criteria such as design leadership, marketing, sales, capabilities, band name, technical liaison support and after-sales support (Hill and Hoskisson, 1987). When commissioning new suppliers, samples of the products or services are often requested before the final order is made. For existing suppliers, this step is omitted. If the framework for a supply contract already exists, it can be extended or can be renegotiated. Alternatively, an individual contract for specific suppliers are negotiated. But as Corbett and Van Wassenhove concluded in 1993, winners of bids or tenders in one year undergo competitive pressure which might make them a looser in the next round or in the future.
The incoming products or services are inspected by the incoming goods department. At this point a review of the performance is made and compared against the initial agreement between the purchaser and the supplier. In the event of a defect or shortage, reclamation information is provided by the incoming goods department and forwarded directly to the operational purchasing department, which then establishes communication with the supplier. When major problems are encountered the strategic purchasing department will be involved. If no complaints are found and the supply is according to the purchasers’ criteria a long-term relationship between the supplier and the purchaser can be established. Suppliers are continuously managed, purchasing is controlled, and risks are evaluated and managed over time.

### Theories

Theories are a useful tool in order to get a better understanding of the environment in which organizations are operating (Radnor et al., 2012) and the relationships and dependencies among all parties involved.

#### 3.4.1. Network Theory

Thorelli defined the term network in 1986 as a system of two or more organizations that are involved in a long-term relationship with each other (Thorelli, 1986). Harland added in 1996 that a network is “a specific type of relation linking a defined set of persons, objects or

<table>
<thead>
<tr>
<th>Sourcing Concept</th>
<th>Description</th>
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<tbody>
<tr>
<td>Modular Sourcing</td>
<td>Prefabricated modules are predominantly purchased. In most cases, one main supplier takes over the pre-assembly and the coordination of the subcontractors.</td>
</tr>
<tr>
<td>Single Sourcing</td>
<td>Single sourcing refers to the procurement of a defined range of goods/services from a single supplier.</td>
</tr>
<tr>
<td>Multiple Sourcing</td>
<td>Multiple sourcing means having multiple to many suppliers for a product. The quotas for the production share of individual suppliers can be kept stable over a longer period of time (quota reference), or change in situ. Here, the use of short-term favorable market conditions in the focus.</td>
</tr>
<tr>
<td>Local Sourcing</td>
<td>The suppliers are situated close to the purchasing company.</td>
</tr>
<tr>
<td>Global Sourcing</td>
<td>The term is not clearly defined in the literature. Often, global sourcing is defined as sourcing the cheapest product on the world market. In the sense of the procurement strategy this means the efficient use of worldwide resources/international sources of supply. International procurement is thus a strategic element for generating competitive advantages. In practice, global sourcing often goes hand in hand with multiple sourcing. The customer has a cheap supplier on the world market for every product. However, it is also common in global sourcing strategies to maintain the relationship with a few key suppliers.</td>
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</table>
events” (Harland, 1996) explaining that networks not only can be composed of companies but can also refer to individuals or activities. Today all processes and systems around us are complex networks that form a sophisticated and multifaceted web. Supply chains are no exception. The more global trade and business got, the more wide-spread and international the supply chain networks became. As the result of profound research in the topic the definition of the network in the supply chain became further complex and diverse. In 2012 Chang, et. al concluded that the “specific context [of the network] depends on the relationships among the network members” (Chang et al., 2012).

To examine and understand the complexity and relationships in the purchasing function of the antibiotic supply chain in Sweden, fundamentals of the network theory will be used. Utilizing the Network Theory dynamics of inter-organizational relationships between different actors in the same network can be explained and the theoretical evaluation of reciprocity can be demonstrated (Kotzab et al., 2007, Oliver, 1990). An organizations constant interaction with other actors in the supply chain plays a very vital role in achieving the objectives of developing new resources, forming strategic alliances, sharing crucial information and risks and outsourcing of value-chain stages and organizational functions (Snehota, 1995, Little, 1987, Gulati et al., 2000). The network theory emphasizes the importance of ‘personal chemistry’ between the actors to achieve the objectives effectively and efficiently through trust and reliability. The associations between firms can be achieved by exchange practices such as the trade of information, goods and services, and by adjustment processes such as personal, technical, legal, logistical and administrative adaptation (Johanson and Mattsson, 1987).

Sharing resources available in a supply chain always benefits all organizations involved. Acting alone in a complex web like the supply chain can be challenging and puts reliable supply at risk (Kotzab et al., 2007). Moreover, strong ties between companies build reliability and dependencies ensuring security of the connection (Gadde et al., 2010). Weak ties are less reliable but maintain the company’s individual flexibilities (Gadde et al., 2010). The theory can further help to identify and map different activities, actors and resources in a supply chain. The sole focus of the network theory is to foster lasting, trusting connections among the supply chain associates (Kotzab et al., 2007). A well working network provides all participating actors access to information, resources, markets and technologies and creates a platform with the advantages of learning, scaling and scoping economies together (Gulati et al., 2000).

The Pharmaceutical supply chains are long and complex. Products often need to travel around the globe to get from the manufacturer to the end-user. The functioning of all organizations in the pharmaceutical supply chain are dependent upon 1) How efficiently they can cooperate with their direct partners and 2) How well these partners cooperate with their own business associates. Especially in the field of antibiotic production where there are multiple stages and multiple actors that can outsource or produce products in house a good understanding and overview of the network is essential.

The purchasing of antibiotics into Sweden was equally complex and blurred at the beginning of this work. There are multiple actors involved and the antibiotics go through various stages when entering the country until reaching the end-user, but the specifics need to be further examined to get the complete picture. One goal of this work is to use the Network theory to help identify the distributors, the purchasing organs and the end users in the continuous supply of antibiotics in Sweden and to identify and characterize the relationships and dependencies in-between these actors as described by Miles and Snow in 2007.
3.4.2. Resource Dependency Theory

The Resource Dependency Theory (RDT) examines how the reliance on certain, essential resources affects the operations of the company and how this influences the behavior of an organization (Pfeffer and R. Salancik, 1979). As a response to external factors the resource dependency theory claims that the internal behavior of an organization has to be validated and potentially changes have to be issued to cope with the external system (Kash et al., 2014). The Fundamental assumption in the resource dependency theory is that organizations have the capability to actively lower unnecessary dependencies by strategic considerations leading to an elevated ability to survive and succeed in their market (Johnson, 2009). The theory argues the goal of an organization has to be to minimize its dependency on other organizations for the supply of scarce resources in its environment. It examines the relationship between organizations and the resources they need. Resources not only comprise raw materials but also include the accessibility or purchasing of skilled personnel, machinery and the availability of funding. If one company for example maintains the majority of a resource which two companies need, the other company will become dependent towards the supplier and the first company, creating a conditional relationship.

Too much dependency creates uncertainty for one side, which leaves the organization in subject to risks of external control. External control is then imposed by the dominating side of the relationship onto the weaker edge.

Literature research conducted as part of this work has led to the assumption that the antibiotic supply chain at many stages has actors being dependent on other members of the production line. Even in Sweden the purchasing part of the antibiotic supply chain is assumed to be a construct of dependencies between the different actors involved. The resource dependency theory therefore is a useful tool to investigate the current state of Sweden’s antibiotic supply to examine if changes in dependencies could lead to a more stable and secure supply of crucial antibiotics in Sweden. In this case the focus will be given to analyze the situation with regard to the purchasing of Rifampicin and Benzylpenicillin.

The crucial variables to be examined according to the resource dependency theory are the availability and accessibility of resources (munificence), the uncertainty of the system (dynamism), and the complexity of the environment (complexity) (Yeager et al., 2014).

To analyze the dependency with respect to the above-mentioned antibiotics the first consideration should be to analyze how vital the resource is for the Swedish market. The second step is to determine the extent to which other actors control the resource. With respect to the availability of the antibiotics to the end user the extent of control inside Sweden should additionally be investigated.
4. **Methodology**

The methodology chapter describes the research methodology, the chosen design, the research approach and discusses the collection of the data. Considerations on the limitations and the ethical aspects in the thesis conduction follow. This section will describe how the aimed for knowledge about the Swedish pharmaceutical supply chain and its flaws and problems is generated and analyzed.

4.1. **Research Methodology**

This thesis combines qualitative analysis and literature studies in order to obtain as accurate and detailed results as possible. According to Bryman and Bell (2011) combining different methods of data collection and information generation leads to the best quality results (Bryman and Bell, 2011). The literature study in this thesis focused on reviewing literature connected to the Swedish pharmaceutical supply chain, the medical procurement process and the Swedish health care system structure. Scientific articles, reports and governmental documents were studied and analyzed for information on the desired topics. The Qualitative data for this thesis was generated through interviews. Various semi-structured interviews were conducted, transcribed and analyzed to generate a more detailed understanding of the Swedish pharmaceutical supply chain, the involved stakeholders and the problems and flaws seen by the involved actors.

4.2. **Research Design**

There are five types of research designs according to Bryman and Bell (2011), `experimental design`, `social survey design`, `longitudinal design`, `case study design` and `comparative design`. The process flow as conducted in the thesis is illustrated in this graph.

*Figure 5: Research design illustration. The process flow as conducted in the thesis is illustrated in this graph.*
design’ (Bryman and Bell, 2011). Since the topic of antibiotic shortages due to supply chain issues is very complex, a case study design was chosen to get in-depth information and narrow down the broad field of the antibiotics supply chains (Jónasdóttir et al., 2018). In Figure 5 the research design used in this thesis is illustrated.

The first research question regarding the general structure of the Swedish pharmaceutical supply chain is analyzed through interpretation of data collected in several interviews, found in scientific articles and organization reports. Data for the analysis of research question two, concerning the detailed delivery pipeline of the two chosen antibiotics is gathered from interviews, reports and online database information. Research question three and four highly rely on the information gathered and analyzed from the conducted interviews combined with scientific articles and the authors ideas and possible solutions.

The conducted research is designed in the chosen way to give the best possible base to answer the research questions. Information on the Swedish pharmaceutical supply chain was scattered and distributed into multiple literature resources before this study. The establishment of a general understanding of the pharmaceutical supply chain system was therefore required before more detailed examinations could be taken into consideration. The focus on the two selected antibiotics and their supply pipelines was given by our supervisor. During the interviews it became evident that focusing all research just on these two antibiotics would be impossible due to confidentiality issues. Therefore, research questions three and four were developed in a broader sense, not only focusing on the two chosen cases but on drugs with high medical value in general. The developed models in the result section are therefore generally valid for the Swedish pharmaceutical supply chain and based on a combination of information of the two selected case antibiotics and the general supply chain information that could be obtained.

4.3. RESEARCH APPROACH

A deductive research approach was used to analyze already existing literature and reports. An inductive research approach was utilized to analyze data from interviews with the Swedish governmental organizations, the pharmacy association and the county council representatives, all working actively with the pharmaceutical supply chain. Combining a deductive and inductive research approach enabled the analysis of existing patterns and systems and create new models to enhance and innovate existing processes (Bryman and Bell, 2011).

Detailed observations of the general procurement processes in Sweden were used to develop generalizations and identify preliminary associations and connections between different outcomes and their reasons (Bryman and Bell, 2011). The observed patterns were used to create two models as suggestions to solve the examined problem.

A qualitative approach was chosen in connection with data collection through interviews in this thesis. The relation between different actors and the process of antibiotics supply chains with a special focus on the procurement process in Sweden were aimed to be understood. Therefore, the gaining of an understanding of the underlying reasons and motivations of the procurement system were valued as more important than the collection of numerical data or the utilization of a larger sample size. Trends and insides into the general process of procurement were the aimed outcome of the data collection process which could be achieved through interviewing a small number of experts rather than a larger number of subjects randomly selected from the population of interest. The subjects in this study were selected through convenience sampling. According to Barrett and Twycross, (2018), a qualitative approach is helpful to develop a deep understanding of the selected topic and analyze on what bases actors make their decisions and which factors affected these (Barrett and Twycross, 2018b).
Moreover, the theoretical framework study was created in order to investigate the procurement strategy concepts in relationship with antibiotics supply chain processes in Sweden. This research aims to apply the Network and the Resource Dependency Theory to optimize the purchasing of antibiotics in Sweden to circumvent antibiotic shortages and its consequences.

Firstly, the Network Theory is used to examine and understand the complexity and relationships in the purchasing function of the antibiotic supply chain in Sweden as well as to identify the distributors. Since the pharmaceutical supply chains are long and complex, the Network Theory is needed to identify the relations between actors and map their activities and responsibilities.

In order to investigate the dependency between actors to manage secure supply of pharmaceuticals in Sweden, specifically in relation to Benzylpenicillin and Rifampicin, the Resource Dependency Theory is used. The scope of this theory includes raw material purchasing, skilled personnel purchasing and funding availability.

Furthermore, the Marketing Authorization Holder (MAH) and API companies involved in the Benzylpenicillin and Rifampicin purchasing process were traced and identified.

4.4. DATA COLLECTION

The first step in research is to gather information on the studied topic, to analyse what has been done, results of previous research, analyse existing data for validity and identify research gaps and possible new areas of research. After setting the research design, a thorough literature study characterised the research topic and created the base for the formulation of the research questions. A case study on the selected antibiotics in Sweden provided the detail information required to select interview participants for generating even deeper knowledge of the supply chain processes involved in the delivery pipeline of antibiotics to Sweden. The conducted interviews were transcribed and analysed and yielded information that led to a slight modification of research question three and four.

In order to have in depth knowledge and data for this thesis, interviews were conducted for primary data collection. According to Barrett and Twycross, (2018), interviews shall be utilized to obtain valid and reliable data on a particular subject (Barrett and Twycross, 2018a). Semi-structured interviews were conducted with conveniently sampled participants. An advantage of semi-structured interviews is that the interview questions and the preferred approach to the interviewees can be adjusted during the conversation (Barrett and Twycross, 2018a, Bryman and Bell, 2011). This allowed for a flexible approach and an adjustable interview guide. The basic interview guide can be found in the chapter Appendices.

4.4.1. LITERATURE STUDY

Secondary data sources were utilized to create a better understanding of the general Swedish healthcare system, the pharmaceutical company organization and processes, the purchasing processes and the procurement strategies applied in the pharmaceutical supply chain process in Sweden. Several scientific journals, annual reports and websites were used for secondary data collection. Secondary data was additionally useful while preparing the interview guide and its questions and follow the gathered information and arguments during the interview.

Relevant literature was found mainly using the online services of Uppsala University Library, the PubMed database and Google Scholar. The following search terms and combinations

4.4.2. Case study

Case studies can be seen in four different categories which are a single organization, a single location, a person and a single event (Bryman and Bell, 2011). For this thesis, the case study category of a single location, Sweden, applies and a single event which is to study the procurement process for Benzylpenicillin and Rifampicin within the country and its problems leading to shortages.

According to Flyvbjerg (2006), case studies have the aim to catch the different experience and understanding from various people. There are two points that must be considered to relate a case study to the actual problem in detail. Firstly, to relate the research with reality and several theories during the activities. Secondly, the researchers could learn something from the case that they focus with and eventually establish the ability to be better while doing the study (Flyvbjerg, 2006). Further, it is important to choose the method based on the issue and the condition in the field. In this thesis, we gathered the data by structuring several interviews from several people which are the experts on the antibiotics and pharmaceutical field.

Such a case study together with an analysis can be an exemplary case that helps all stakeholders to identify reasons for vulnerable supply chains for these two antibiotics. This could also then be important to investigate the supply chains of other drugs and antibiotics in other scientific research projects. However, a case study investigating a single country and event can raise doubts to which degree such a case can be generalized or be valid. However, an increasing number of researchers realized the potential and value of such case studies to obtain knowledge (Flyvbjerg, 2006). Flyvbjerg (2006) set up five ‘misunderstandings’ about case studies to dismantle the generalizability accusations which are summarized in Table 2.

Table 2: The five misunderstandings about case studies adapted from Flyvbjerg (2006) (Flyvbjerg, 2006, p. 219-245)

<table>
<thead>
<tr>
<th>Misunderstanding</th>
<th>Restatement</th>
</tr>
</thead>
<tbody>
<tr>
<td>General knowledge is more valuable than context-specific knowledge</td>
<td>Universals can't be found in the study of human affairs. Context-dependent knowledge is more valuable.</td>
</tr>
<tr>
<td>One can't generalize from a single case so a single case doesn't add to scientific development.</td>
<td>Formal generalization is overvalued as a source of scientific development; the force of a single example is underestimated.</td>
</tr>
<tr>
<td>The case study is more useful in the first phase of a research process; used for generating hypotheses</td>
<td>The case study is useful for both generating and testing of hypothesis but is not limited to these activities.</td>
</tr>
<tr>
<td>The case study confirms the researcher’s preconceived notions.</td>
<td>There is no greater bias in case study towards confirming preconceived notions than in other forms of research.</td>
</tr>
<tr>
<td>It is difficult to summarize case studies into general propositions and theories</td>
<td>Difficulty in summarizing case studies is due to properties of the reality studies, not the research method.</td>
</tr>
</tbody>
</table>
To “One cannot generalize on the basis of a single case is usually considered to be devastating to the case study as a scientific method” (p.224) for example Flyvbjerg argues that, citing single cases might yield very powerful and valid data. With giving the experiences of Galileo, Newton, Einstein, Bohr, Darwin, Marx, and Freud as examples for researchers that based fundamental advances in research on single event observations, Flyvbjerg makes the point that both human and natural sciences can be advanced by a single case.

Therefore, the aim of this master thesis to contributing to the understanding of the general Swedish pharmaceutical supply chain by analyzing the case of Benzylpenicillin and Rifampicin fall into this misunderstanding category. Generalizations can be considered through the generated results of the case studies.

According to Bryman and Bell (2011), a case study can be utilized for both quantitative and qualitative methods (Bryman and Bell, 2011). This thesis follows a qualitative approach as the authors identified a lack of previous research concerning the two addressed antibiotics in the Swedish market. With the help of semi-structured interviews, qualitative data could be obtained and compared to other conducted interviews. Moreover, this interview style inherits a flexible nature, questions could be adapted within the ongoing interview.

### 4.4.3. Interviews

The first step in primary data collection was to interview the selected experts in the field of the pharmaceutical supply chain in Sweden.

According to Chadwick et. al (2008), the best way to conduct an interview starts with general question which can easily be answered by the interviewees and break the tension. Then, one can move on to more specific and detailed questions. During the interview, we introduced ourselves, explained what kind of topic we focus on in our thesis and asked the interviewees to introduce themselves. Subsequently questions relate to the study were asked. The interview guide was utilized as a basic structure. Since the different interviewees were experts in slightly different fields however, an individual focus was laid during each interview. Extra questions and detail enquiries were noted in the transcripts. All the sessions were recorded and subsequently transcribed.

The interview questions focused on the general pharmaceutical supply chain, procurement, antibiotic purchasing, drug availability and medicines storage in Sweden with a special focus on Benzylpenicillin and Rifampicin. Investigations of the supply chain process of antibiotics in Sweden with the focus of purchasing process optimization from a public buyer’s perspective were additionally conducted. The detailed structure and the flow of the interview can be seen in the appendix chapter 10.

In total we had twelve interviews with participants from Sweden. Three with employees from a governmental organization, two with county council personnel, two with employees in a county council hospital, two with distributors, two with the pharmacy association and one with a private pharmacy. We selected the interviewees through convenience and purposive sampling receiving contact information from our supervisor and additionally contact to selected actors was established through online research. Convenience sampling refers to individuals that were easy to reach, such as through receiving of contact information from the supervisor or simply getting a reply from the selected people. Purposive sampling means choosing individuals to include in the study that are thought to have the required knowledge needed for the research purpose. The interviewees can be seen in Table 3.

Three responsible persons from the Swedish county councils were interviewed, specifically from Kronoberg, Jönköping, and Östergötland. They provided information on the shortage
situation of the selected antibiotics Benzylpenicillin and Rifampicin. In addition, information about internal communication and collaboration between county councils could be obtained. During the interview with the Public Health Agency of Sweden (FoHM), the responsible persons provided information on a pilot model of reimbursement. Also, they explained their responsibility in the health care system and their noninvolvement in local antibiotic purchasing processes of the county councils. Information about changes in the availability of pharmaceuticals before and after the decentralization in Sweden could also be obtained.

*Table 3: Interviewees organized in descending order according to the time of the interview*

<table>
<thead>
<tr>
<th>Company/Organization/County Council</th>
<th>Interviewee</th>
<th>Title</th>
<th>Mode of Interview</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kronoberg Region</td>
<td>Magnus Munge</td>
<td>Unit Head of the Pharmaceutical Unit</td>
<td>Video</td>
</tr>
<tr>
<td>Östergötland Region</td>
<td>Johanna Orraryd</td>
<td>Chief pharmacist</td>
<td>Video</td>
</tr>
<tr>
<td>The Public Health Agency of Sweden (FoHM)</td>
<td>Charlotte Edlund</td>
<td>Analyst, Expert in antibiotics and antibiotic resistance, professor at FoHM</td>
<td>Video</td>
</tr>
<tr>
<td>The Public Health Agency of Sweden (FoHM)</td>
<td>Salumeh Bastami</td>
<td>Program Officer</td>
<td>Video</td>
</tr>
<tr>
<td>The Public Health Agency of Sweden (FoHM)</td>
<td>Moa Grahm</td>
<td>Analyst, Emergency Preparedness and Crisis Management Unit</td>
<td>Video</td>
</tr>
<tr>
<td>Jönköping County Council Hospital</td>
<td>Thomas Axelsson</td>
<td>Purchasing, Business support and service</td>
<td>Phone</td>
</tr>
<tr>
<td>Jönköping County Council Hospital</td>
<td>Sofia Tidstrand</td>
<td>Pharmacist</td>
<td>Phone</td>
</tr>
<tr>
<td>Tamro</td>
<td>Peter Danberg</td>
<td>Executive Assistant</td>
<td>Phone</td>
</tr>
<tr>
<td>Oriola Oy</td>
<td>Nicklas Widding</td>
<td>Site manager</td>
<td>Phone</td>
</tr>
<tr>
<td>Apoteksföreningen</td>
<td>Johan Wallér</td>
<td>Chief executive officer</td>
<td>Phone</td>
</tr>
<tr>
<td>Apoteksföreningen</td>
<td>Fredrik Boström</td>
<td>Head pharmacist</td>
<td>Phone</td>
</tr>
<tr>
<td>Apoteket Hjärtat</td>
<td>Ali Manar¹</td>
<td>Category Manager RX</td>
<td>-</td>
</tr>
</tbody>
</table>

During the interview with responsible personnel from the hospital questions regarding the procurement procedures of the Jönköping hospital were answered. Additionally, differences between their hospital in particular compared to other hospitals and county councils in Sweden were explained. Information about the Jönköping usage and availability of the two antibiotics in focus were given.

¹ This interview was conducted by Gabriel Chivi as part of his master thesis project.
Interview with two big distributors in Sweden, Oriola and Tamro yielded information on the distributor’s role and responsibilities in the supply chain. Large amounts of information could not be shared by the interviewed employees due to confidentiality.

The two spate interviews with representative from the Swedish pharmacy association generated information about the pharmacy system in Sweden, problems seen in the supply chain from the pharmacy perspective and what improvement the interviewees would wish for to make the pharmaceutical supply chain more efficient and fluent. The data from Apoteket Hjärtat yielded information on a private pharmacies point of view and what challenges are faced by them. Additionally, information on what the Swedish government should do to help the shortages of antibiotics was expressed.

4.5. DATA ANALYSIS

Data from the literature study was characterised according to information on the pharmaceutical supply chain with a special focus on Sweden. All information gathered was compared and sources with differing information were analysed more thoroughly to yield a consensus on the processes and actors in the Swedish pharmaceutical supply chain.

Interview data was transcribed and coded. Code themes were selected and all experts were organised into these themes. Selected themes included ‘Supply chain’, ‘Hospitals’, ‘FoHM’, ‘Pharmacies’, ‘Collaboration between county councils’, ‘Procurement’, ‘Storage/stocks’, ‘Availability’, ‘Shortages/problems’, and ‘Improvements’. All interviews were analyzed with respect to these themes and quotes and information were chosen that were relevant to these themes. The themes were further merged into categories to be able to answer the research questions. ‘Supply chain’, ‘Hospitals’, ‘FoHM’, ‘Pharmacies’ and ‘Collaboration between county councils’ were merged to the supply chain actor’s category. ‘Storage/stocks’, ‘Availability’ and ‘Shortages/problems’ were merged to the problems and solutions category whereas ‘Procurement’ and ‘Improvements’ were awarded their own category respectively.

4.6. QUALITY OF RESULTS

According to Bryman and Bell, (2011), four several criteria must be fulfilled in order to have a good result and ensure trustworthiness of the qualitative study: ‘credibility’, ‘transferability’, ‘dependability’ and ‘conformability’ (Bryman and Bell, 2011, Laprie, 1992, Mills et al., 2010).

Credibility is an action to ensure that the research is made based on the correct approach. As a result, the research can be presented to the society as a valid one (Bryman and Bell, 2011, Mills et al., 2010). Primary data was collected by interviewing three employees from a governmental organization, two county council personnel, two employees in a county council hospital, two distributors, two pharmacy association employees and one private pharmacy representative. Before the interview, the questions were approved by the thesis supervisor. All the interviews were recorded to avoid the missing or overhearing important details and for better subsequent transcribing. To validate the primary data, it was compared to the gathered secondary data and in case of contradictions additional data was utilized and additional interviews conducted.

Transferability is an action in which results of one research are applied to other similar situations (Bryman and Bell, 2011). The findings from a research can, if a transfer is possible, be considered as general findings of an area. The gathered data on the antibiotic supply chain and the procurement process of pharmaceuticals from the experts that were interviewed were
compared to existing literature and combined, these can be applied onto the whole Swedish pharmaceutical market. Therefore, transferability is given in this context.

Dependability is given when stability of data over time and over conditions can be assured. The interviews have been transcribed and the contact details of each interviewee have been stored. Record of all used data have been (Laprie, 1992). All interviews conducted were recorded and transcribed. The traceability and stability of data can therefore be ensured in the future. Conformability is when we make sure that during the data collection, our personal thoughts are not involved and the objectivity is not influenced by that (Bryman and Bell, 2011). Hence, we conducted the interviews via phone or video calls to eliminate confusion and misunderstanding.

4.7. LIMITATIONS AND ETHICAL CONSIDERATIONS

All research designs can be discussed in terms of their relative strengths and limitations. The advantages of a particular design are fundamentally related to the motivation for selecting it as the most appropriate strategy for addressing the research problem. The case study design is selected because of the nature of the research problem and the questions being asked in this thesis. The case study approach offers the possibility of investigating complex situations consisting of multiple variables. The issue of generalizability is often discussed in relation to case studies. Since information in case studies focuses on a single unit or a single instance it might not be true or valid in another situation. However, much can be learned even from investigations of just a specific scenario (Stake, 2005). Even Erickson (1986) argued that the general patterns are found from single observations (Erickson, 1986). Utilizing the case study format to conduct our thesis is limiting us to not directly generalize the findings but utilize them as possible concepts for generalizability upon further investigation of similar scenarios. This thesis is a qualitative case studies which might be limited by the sensitivity and integrity of the investigator. We as the researchers are the primary instrument for collection of data and analyzing it. This is both an advantage of the method, since all kind of information can be gathered, but also a limitation since observation and interviewing can have a bias. The instincts and abilities of the researcher are what case studies rely on.

Ethical consideration play an important role in the procurement process in Sweden since it is involving several actors in the supply chain and procurement process. They are especially important to consider when different individuals are involved in the setup of a study. The ethical implications can be seen during the interview sessions, as well as in the relation with the involved actors in Sweden.

During the interview session, there are several ethical implications that must be considered. According to Bryman and Bell (2011), there are four different ethical guidelines that need to be followed when interviewing which are harm to participants, informed consent, invasion of privacy and deception (Bryman and Bell, 2011).

It is important to follow a good practice when working with the intellectual property of involved participants, their thoughts, information and personal data (Kvale, 2007). Procedures of the interview as well as expected outcomes and purpose for the interview were stated at the beginning of each conversation. Participants could choose which channel of communication was preferred to their comfortability, hence some interviews are conducted through video whereas others are conducted with voice calls only. The platform for communication also changed since each interviewee was able to choose here the interview would be conducted. Confidentiality and permission of data usage are important concerns while conducting interviews especially for sensitive data collection. In all interviewees it was highlighted that the interviewees can decide if permission for usage of their personal details was given
or if they chose to stay anonymous. Additionally, confidentiality issues were taken very se-
riously especially when interviewees were concerned about not crossing any boundaries with
their respective clients. For all data and names used in the empirical part, a permission of
usage has been given by the respective persons.

Therefore, informed consent has been secured, and harm to participants and invasion of pri-
vacy countered. By conducting several interviews and crosschecking with the subject reader
of this master thesis and the existing literature, deception is prevented.
5. **Empirics**

In the empirics the data finding based on literature research and interviews conducted in this study will be stated. This section describes the procurement process in the Swedish pharmaceutical supply chain, the delivery pipelines of two important antibiotics and highlights problems and improvements suggested by the interviewees. For the following research two essential antibiotics have been chosen to be investigated, Benzylpenicillin and Rifampicin.

5.1. **The Pharmaceutical Supply Chain**

When a doctor prescribes or administers a medicine to a patient at a hospital or clinic in Sweden, we as receivers of the treatment rarely think about the complex web of events and processes that lie behind being able to provide us with this drug in case of disease. The worldwide network of actors involved in the pharmaceutical supply chain can be a life saver for many patients in need. Getting the drug to the end users in Sweden however involves a multistage procedure. Various activities and processes need to be highly coordinated and monitored all over the world to successfully deliver medicines to the patients (Committee on Assuring the Health of the Public in the 21st Century, 2003).

Handfield and Nichols defined pharmaceutical supply chains in 1999 as “the integration of all activities associated with the flow of and transformation of raw materials through to the end-user, as well as associated information flows, through improved supply chain relationships to achieve a sustainable competitive advantage” (Handfield and Nichols, 1999).

A typical pharmaceutical supply chain flow is shown in Figure 6 as seen below and is comprised of the primary manufacturers, the secondary manufacturers, the wholesalers and distributors, the health care providers and the final customers (Shah, 2004). All logistical flow needs to be highly regulated between all actors to comprise a well-functioning and effective drug supply to the customers.

In some cases, pharmaceuticals can additionally to the delivery through the normal supply chain also be parallel imported. In a normal supply chain, the product is passed on from the Marketing Authorization Holder (MAH) for Sweden to the distributors followed by the delivery to the pharmacies. Parallel imported pharmaceuticals in contrast enter the country without a MAH in Sweden. The parallel import of pharmaceuticals is based on the agreements of free movement of goods within the European Economic Area (EEA) and implicates the sale of drugs in EEA-member countries different from the country of drug origin and licensing. The drug is repackaged or re-labelled with a Swedish label and is provided with a Swedish package leaflet by an approved packer. Before the parallel importer can market a parallel imported drug, a sale authorization is required, which is granted by the Swedish Medical Products Agency (Läkemedelsverket, 2019b, European Patients Academy, 2016).

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2 Marketing Authorization Holder is a drug manufacturer who has applied and received the permission to market and sell a product to the requested market (European Patients Academy, 2016).
5.1.1. PRIMARY MANUFACTURING SITES

The main responsibility of the primary manufacturers\(^3\) is the production of the APIs. The production of APIs involves several chemical and biochemical processes and separation stages to form the complex pharmaceutical molecule (Mousazadeh et al., 2015). The often-multistage production of APIs involves very lengthy processing times often requiring multiple shifts. Due to the multistage procedures there is a requirement for storage of intermediate products between the different production stages. Furthermore, substrates from intermediate stages have to pass a regulatory quality check to be certified for usage in the downstream processes. This can lead to delays in the production system due to the unavailability of certain substrates at different time points of the production process (Shah, 2004). Nilay Shah (2004) predicts that this mode of production might not react well to a state of unplanned demand for the produced APIs or in a state of emergency with unexpected extremely high demands.

The involvement of contract manufacturers by the primary manufacturers causes another complexity in the primary manufacturing sites. These external manufacturers are involved to develop or to produce some or all active ingredient stages additionally to or instead of the primary manufacturers. The primary organizations benefit of this in terms of being able to concentrate on development of new competences instead. This external participation can cause further coordination problems in the supply chain (Shah, 2004).

For rifampicin there are a total of seven API manufacturers that export to the European Union and to the United States of America. Three of the API manufacturers are located in Europe, namely two in Italy and one in the Ukraine. The remaining four are located in Asia; two in India, and one each in China and the Republic of Korea (Cicek et al., 2019).

There are only three API manufacturer for Benzylpenicillin in the European Union, one of which is Sandoz GmbH, an Austrian company and two manufacturers located in Italy of which the name could not be discovered (Cicek et al., 2019). Other API manufacturers around the world could not be identified but are most likely existing.

5.1.2. SECONDARY MANUFACTURING SITES

The secondary manufacturing sites, often outnumbered by the primary manufacturing sites, are responsible for the production of the final drug. Their first duty is verifying the identity of the substances, then moving on to the next stages of production which involve blending ingredients, sieving, granulation and drying of substrates. Furthermore, secondary manufacturers are responsible for packaging of the final drug product (Mousazadeh et al., 2015).

The secondary manufacturing sites are often located in different geographical sites compared to the corresponding primary manufacturing situates. Strategically this is an advantage since manufacturing of APIs at locations with tax benefits and lower wages save manufacturing costs optimizing the production price (Shah, 2004). One API producer might be used by many secondary manufacturers. The APIs received are here combined with supplementary ingredients according to different country regulations and company guidelines.

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\(^3\) Primary manufacturers process raw materials to produce active pharmaceutical ingredients and supplementary substances which will be used to develop the complete drugs, Mousazadeh et al., (2015), *A robust possibilistic programming approach for pharmaceutical supply chain network design.*
5.1.3. Distribution

After the drug has been assembled to its final form, it is distributed to healthcare providers (hospitals, physicians and pharmacies) through wholesalers or distributors. In some cases, the manufacturers can directly provide the final product to the customers (government, employers, and individuals) bypassing the route through wholesalers or distributors (Kritchanchai, 2012).

5.2. Antibiotics selected for our research

The two antibiotics were selected on the base of their inclusion in the World Health Organization’s (WHO’s) Essential Medicines List (EML) (World Health Organization, 2017) and due to their importance for the Swedish medical care. The WHO’s Essential Medicine List was established in 1977 and has been updated every two years since. The purpose of the list is to categorize and catalogue medicines essential to the world’s health care needs based on previous epidemics. According to the WHO the most important and vital medicines must be available in adequate quantities and good quality at affordable prices in each health care system (World Health Organization, 2017). The list was formed to act as a guide for the development of national and sub-national EML’s. Many countries have created a national EML specified to the health care needs of their population (World Health Organization, 2017).

The antibiotics selected are also included in the Public Health Agency of Sweden’s (FoHM) list of antibiotics of special medical value with risk of accessibility. The list includes 34-37 antibiotics approved in Sweden. FoHM have rated the identified antibiotics depending upon the degree of medical value with a maximum of 20 for high importance and a minimum of 1. All of the antibiotics mentioned in the list by FoHM have only one or a maximum of 2 MAHs in Sweden. Additionally, some of the identified antibiotics have a sales value of less than 4 million SEK per year, which is a low revenue for a drug on the Swedish market. The identified antibiotics are further divided into new antibiotics with market protection; requisition antibiotics without market protection; prescription antibiotics without market protection; and tuberculosis antibiotics. Rifampicin and Benzylpenicillin fall under the above described categories being a tuberculosis antibiotic and requisition antibiotics without market protection respectively. Benzylpenicillin can be seen as a representative for hospital administered antibiotics whereas Rifampicin is a typical prescription antibiotic. The result can therefore be utilized to analyze similar antibiotics and their supply chains.

Antibiotics are chemical compounds that kill or inhibit the growth of bacteria (Ventola, 2015). Antibiotics are classified after their mechanism of action and all antibiotics known today can be categorized into six groups based on their site of antibiotic activity. Antibiotics can inhibit cell wall synthesis, protein synthesis at the 30S or 50S ribosomal subunit, RNA or DNA synthesis or can be an antimetabolite in important cellular pathways (Murray et al., 2016).

Benzylpenicillin is a revolutionary, natural, narrow spectrum antibiotic in the family of beta-lactams (Murray et al., 2016). According to the Public Health Agency of Sweden (FoHM) Beta-lactamase sensitive penicillins, to which Benzylpenicillin belongs, are one of the most

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4 Narrow spectrum antibiotics are substances that selectively act on specific bacteria. They do not affect the majority of microbes present in the body ACAR, J. 1997. Broad- and narrow-spectrum antibiotics: an unhelpful categorization. Clinical Microbiology and Infection, 3, 395-396.
sold antibiotic classes for outpatient care within Sweden and the most intensively used anti-
biotic types throughout all age groups (Swedres-Svarm, 2017). The bacterial cell wall is as-
sembled of building blocks synthesized by the bacteria and transported out to its surface. At
the surface they are cross linked to form a protective layer. Beta-lactams work by inhibiting
the cross linkage of the building blocks by binding to the bacterial enzyme that facilitates
this process. Inhibiting cell wall synthesis weakens the bacteria and leads to their death. Ben-
zylpenicillin was one of the first antimicrobial agents discovered. The basic compound of all
Penicillin, the beta-lactam ring is synthesized by the mold Penicillium chrysogenum (Murray
et al., 2016). Benzylpenicillin is a biochemical modification of the basic structure and is used
against susceptible strains of Gram-positive and Gram-negative bacteria, spirochaetes, and
actinomycetes as a first line treatment for severe septicemia, meningitis, pericarditis, endo-
carditis severe pneumonia, syphilis and rheumatic heart diseases (DrugBank, 2005, Stuart et
al., 2009, Cogan et al., 2018). It is administered intravenously or intramuscularly due to a
poor oral absorption. This particular antibiotic has been of limited supply in 39 countries due
to unstable supply chains, since Benzylpenicillin is dependent on four API producers globally
(Nurse-Findlay et al., 2017). Benzylpenicillin generally provides very little economic incen-
tives or profits to the manufacturer and the demand for Benzylpenicillin is higher in poorer
countries with a very low economic status so the manufacturers do not produce enough prod-
uct due to low economic profitability (Cogan et al., 2018). The active ingredient Benzylpen-
icillin is sold in the salt form of Benzylpenicillin sodium in Sweden under the name of Ben-
zylpenicillin Panpharma and Bensylpenicillin® Meda (FASS, 2019).

Rifampicin is a semisynthetic, broad spectrum antibiotic. It was first extracted from the soil
colonizer Amycolatopsis rifamycinica and is now synthesized commercially (Boeree, 2013).
It was first introduced into the market in 1966 as a first line medication against tuberculosis
and tuberculosis-related mycobacterial infections (DrugBank, 2005b). It is administered in
form of a capsule with good oral absorption. Rifampicin works as a protein synthesis inhibi-
tor by binding to the beta subunit of the DNA-dependent RNA polymerase of the bacteria
(Goodman et al., 1996). The process of protein synthesis is essential and by blocking this,
the antibiotic kills the bacteria. The active ingredient rifampicin is sold in the forms of an
oral suspension or as a capsule under the brand names of Rifadin®, Rimactan®, Rimactazid®,
Rimstar®, Rifampicin Ebb and Rifampicin Orifarm. There have been two reported shortages
of rifampicin containing drugs on the Swedish pharmaceutical market in the past year
(Läkemedelsverket, 2019a). The Rifadin® oral suspension from Sanofi AB was noted to be
short on the 28th February 2019 and the shortage lasted until the 1st March 2019. Sandoz A/S
Rimactazid® tablets containing isoniazid and rifampicin have been in shortages since the 1st
of June 2019 and the shortage has not been resolved as of today (August 2019). A warning
was given out two months in advance that a shortage is likely to be encountered. An alterna-
tive repackaged drug which has not been licensed for sale in Sweden has been imported as
an alternative to the Swedish market (Läkemedelsverket, 2019a).

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5 A first line treatment is the first choice of medication against a specific disease. It often has proven to
be the treatment with highest efficacy and safety profile for the lowest cost. There might be alternative
treatments that can be applied if the first line treatment fails or is not available. These options can be
costlier as well as less effective and safe NCI Dictionary of Cancer Terms, First line treatment (2019).

6 Broad spectrum antibiotics work on a variety of bacteria. They do not selectively act only on a specific
bacterium. They can even affect nonpathogenic bacteria in the human body ACAR J., Broad- and narrow-
spectrum antibiotics(1997).
5.3. THE USAGE OF AND PER CAPITA SPENDING ON ANTIBIOTICS IN SWEDEN

While drug shortages, and specifically antibiotics shortages and limited supplies, have been a big problem in the last century, taking a look on the consumption patterns of Swedes and an international comparison helps to understand in which quantities antibiotics are used.

Scandinavian countries, encompassing Sweden, Denmark, Norway, Finland and Iceland, have a comparatively low antibiotics consumption overall, while the US is leading the ranking by having the highest pharmaceutical consumption per capita, followed by Japan, France and Belgium (Swedres-Svarm, 2017). Sweden however is the leading Scandinavian pharmaceutical consumer. Public spending for healthcare in Sweden is lower, which is partly due to comparatively lower distribution costs as Sweden has a higher number of inhabitants per pharmacy (Bergan, 2001). Moreover, the growth rates of benefit levels between 1970 and 2002 were only 2.35 percent in average in Sweden, which is considerably lower than the growth rates of up to 5 percent in countries of the Organization for Economic Co-operation and Development (OECD) such as Norway, Spain and the US. While Sweden’s healthcare spending was the highest per capita throughout OECD countries in 1970, a third more than what Norway spent, Norway healthcare spending was already 60% higher than Sweden’s in 2002 (Hagist and Kotlikoff, 2005). Sweden’s policy of limiting spending levels has therefore been a success.

5.4. SHORTAGES OF DRUGS DUE TO SUPPLY CHAIN ISSUES

Traditionally the health care providers have been focusing solely on the cost of specific drugs or medical devices in the supply chain aspect. But disruptions in availability has forced health care providers to take a broader view on the reasons behind the shortages. Supply chain managers are considering more long-term approaches to prevent shortages by controlling what medicines or devices are inevitable, determining the risks in case of supply chain disruption and by setting up guidelines, emergency reservoirs and alternative treatment plans (Jensen, 2013). Continuous monitoring of shortages and stock outs is essential to create attentiveness and prevention plans.

Over the past decade the incidences of drug shortages have increased threefold (EAHP, 2018). In 2013 the FDA (U.S. Food & Drug Administration) released information about what reasons for the shortages of 117 drugs had been reported (Figure 7). Lack of or problems with the raw materials constituted for 27% of the shortages, the quality of the manufacturing created 37%, delays and capacity issues 27%, the loss of manufacturing sites 2%, an increased demand for particular drugs 5% and discontinuation of production contributed with 2% to the shortages (Jensen, 2013).

The shortages challenge the hospitals and practicing physicians. Not only is a tremendous amount of time and money invested into looking for alternatives, but treatment cannot be facilitated to an ideal level due to the non-optimal drug options and schedules for treatments can get disorganized. Identifying the root cause of the shortages, the relative risks and uncertainties and assessing how these relate to the total value of the medicine investigated is an important task to sustainably reduce and prevent drug shortages for the future.
5.5. **THE ANTIBIOTICS POLICY IN NORWAY: A SUCCESSFUL CASE**

Norway can be seen as a successful case of how to handle antibiotics supply chain issues, minimize AMRs and ensure constant supply of needed antibiotics and other drugs to an affordable price for its citizens. The so-called Norwegian marketing authorization and reimbursement systems for medicinal products is a governmental effort to ensure just this. By introducing stringent guidelines that support proof-based prescribing of antibiotics, AMRs declined steadily. Moreover, the use of new antibiotics could be minimized in case of an emergency. While these policies are highly favorable to its citizens, they have more negative effects on companies operating in the private sector, indicating that there are only low margins and profits possible within the antibiotics business (Årdal et al., 2017).

As a member of the European Economic Area, Norway is part of the marketing authorization procedure of medicinal products. These are taken care of by the European Medicines Agency EMA. Norway and its Norwegian Medicines Agency take care of the marketing authorization, costs setting, reimbursement of antibiotics and other medications within the country. Once a medication receives marketing authorization, it can be sold in community and hospital pharmacies, but does not guarantee that these buy or use the medication. The Norwegian national insurance schemes reimburse private spending on prescription medicines to assure...
that Norwegians are able to obtain urgently important medicines. However, not every antibiotic or medication is reimbursed. Usually, antibiotics are not reimbursed as many infectious diseases are only short-term. In 2014, the number of reimbursed antibiotics prescriptions amounted to just 13% (Årdal et al., 2017). Compared to Sweden, Norway is able to follow a more organized path and channel its efforts with the help of its governmental authority Norwegian Medicines Agency.

5.6. Case Study: The Procurement Process of Drugs Today in Sweden

It is self-evident that the better the county councils and hospitals plan and coordinate the purchasing process the more competitive and efficient it becomes in the market. Each council drug unit or hospital decides based on the situational demands and circumstances the amount of effort that is spent on each step of the procurement process.

Before the decentralization of the pharmaceutical system in Sweden in 2009 the Swedish state was the organ controlling the procurement of all pharmaceuticals to the country. Salumeh Bastami, Program Officer at The Public Health Agency of Sweden (FoHM), adds that when it was state controlled, the state also had something called Sammhällsansvar (community responsibility) which now has disappeared (Bastami, 2019). This meant that the state was responsible to have access to all medications when they were needed. Since the decentralization there is no organ or body that has inherited this responsibility.

In the Swedish pharmaceutical procurement now, all responsibilities of the purchasing planning lay in the county councils. All the big business and the deals are made up and settled between the Swedish county councils and the pharmaceutical companies or manufacturers, says Fredrik Boström, head pharmacist at the Swedish Pharmacy Association (Sveriges Apoteksförening) (Boström, 2019). “Everyone besides the manufacturers or pharmaceutical companies and the county council’s supply’s important services to the supply chain but have no significant deciding power”. The actors in-between the county councils and the manufacturers are executive organs but have no power of deciding about processes in the supply chain. They have no right to comment on the amount of storage that should be kept, or which medications are especially important, explains Boström. The regions decide which preparation and to what price they shall be bought and ask the pharmacies to procure the decided quantities. Boström says it is an easy "If we order you will deliver within this time, to this location, in this way" system.

5.6.1. Initiation of Pharmaceutical Procurement

The fundamental step of the purchasing process is the identification of needs for products or services. To allow good internal communication and an intensive interchange of information in all regions of Sweden collaborations between counties have been established, says Thomas Axelsson, working with Purchasing, Business support and service for the Jönköping County council. This is highly important so that planning of needed quantities and products can be as efficient as possible. A procurement body manages the legal and administrative aspects of the procurement process and decides which tenders to accept, at county council level (PHIS, 2009). The twenty-one Swedish counties are organized into six healthcare regions as seen in Figure 8 (Sjukvårdsregioner) which act as closed procurement systems to coordinate purchasing to an increasing degree among the regions of Sweden (Axelsson, 2019). In some instances, other informal assemblages of county councils and regions can make joint procurements (Pontén et al., 2017). The collaboration enables joint utilization of the region's healthcare resources and mutual responsibility in relation to pharmaceutical procurement.
According to Axelsson, the South eastern healthcare region consisting of Östergötland, Jönköping and Kalmar county, for example divides part of the procurement responsibilities between the members. Information is collected from all member counties but then Jönköping is responsible for the antibiotics, Östergötland for the cytostatics and Kalmar for the procurement of liquids. The collaboration network allows each region to adjust their procurement according to the population structure and healthcare needs in each geographical location.

Figure 8: Division of the Swedish counties into six different healthcare regions. The twenty-one Swedish councils are divided into six healthcare regions which represent individual purchasing units. Table illustrates information collected from the Swedish Association of Local Authorities and Regions (Sveriges Kommuner och Landsting) (SKL, 2017).
5.6.2. Planning of what should be procured and when

This phase is central to the entire purchasing circle and needs to be well established for a functioning procurement process. In this step various criteria for suppliers, bids, customer needs, and delivery details are set and discussed. All process requirements are defined, standardized and set in detail. Which products to procure and which materials the county councils and hospitals focus on fluctuates among the health care regions. Nevertheless, a uniform opinion to focus on price, quality, delivery and services can be seen in different markets respectively. The frequency of procuring medicines varies between the county councils, but it is usually performed once a year for all medicines, no matter if these are strategic, leverage, standard or bottleneck pharmaceuticals (Pontén et al., 2017).

5.6.3. Qualification of suppliers for the pharmaceuticals

The result of the procurement market research is the potential supplier identification. Depending on the pharmaceutical there will be more or less available suppliers. Especially for bottleneck or strategic antibiotics the variety of suppliers might be highly limited.

The Swedish Public Procurement Act regulates the procedure of procurement of pharmaceuticals and applies to the procurement of medicines for in-patient use. Since the year of 2008 the processes of public procurement are monitored by the Swedish Competition Authority. The Authority monitors that all purchases with a value above a certain threshold must be publicly procured, and that all contracting actors shall treat suppliers in an equal and non-discriminatory manner and shall conduct procurements in a transparent manner. Suppliers of pharmaceuticals shall not be evaluated, just ranked based on criteria set by the procuring authority (PHIS, 2009). The qualification phase ends with a request of the county councils or hospitals towards the suppliers to make an offer or tender for procurement of selected drugs.

The procuring authority might ask the supplier to include proof of economic standing and proof of technical and professional ability in the tender. The county councils can additionally request medical information about the product or information on fulfilling of environmental standards if such are set and determined in the procurement guidelines of the purchasing authority (PHIS, 2009).

5.6.4. Winning phase

The first choice that the purchaser has to make before accepting an offer is the sourcing choice. The choice of a sourcing method depends on the product group. The county councils lay down a set of criteria that need to be fulfilled in order to take the decision to accept a tender sent by a supplier. In the collaboration areas, where multiple county councils procure medicines together the set of criteria tend to be uniform. Each tender is judged on how medically and pharmaceutically it is suitable for the counties and how secure and stable the delivery of the drug will be to Sweden. The pricing of the product is an important factor, but the suitability and medical aspects of the product for the Swedish market and health care system are prioritized criteria (PHIS, 2009).

The sourcing options for Benzylpenicillin and Rifampicin for Sweden that the counties have decided on are summarized in Figure 9. The situation behind the MAH can be a bit unclear for some medications explains Fredrik Boström, the MAH in Sweden might just be a juridical person and the actual holder of the license is in a different country. This makes it hard to always get a clear picture of the whole supply chain (Boström, 2019).
5.6.5. MONITORING, REVIEW PHASE AND SHORTAGE REPORTING

Especially in the pharmaceutical supply chain shortages or an impossibility of delivery can occasionally occur. Reports and statistics on previous and current shortage situations are incomplete. Fredrik Boström agrees that the Medical Products Agency's (LV) list is not a complete picture. It is based on the facts and information that the pharmaceutical companies report to the LV. And the pharmaceutical companies do not always report. The LV can urge manufacturer for information when a shortage is seen on the market. The LV is however not scanning the market for the present situation. For their list only reported and delivered information is used (Boström, 2019).

Additionally, Johan Wallér, Chief executive officer at the Apoteksföreningen reports, that the Apoteksföreningen monitors when situations of shortage occur but does not actively influence any of these. Their goal is to assist the pharmacists to solely get the information of a shortage as quickly as possible (Wallér, 2019). Shortage information at the Apoteksföreningen is gathered from the LV and the pharmaceutical industry and manufacturers.

Johan Wallér and Thomas Axelsson agree that shortages are quite common on the drug market and that the shortcomings occur at the pharmaceutical manufactures and their manufacturing sites. Both do not think that the fault is at the distributors, in Sweden that refers to Tamro and Oriola. The problems arise before this step in the supply chain (Wallér, 2019, Axelsson, 2019).

Vaccines are a typical products that experience shortages, whereas stock outs in case of antibiotics are more rarely seen according to Nicklas Widding, Site manager at Oriola Oy, Sweden (Widding, 2019). And even Sofia Tidstrand, Pharmacist at The County Council of Jönköping tells that no shortages of Rifampicin and Benzylpenicillin were experienced at the Jönköping hospital (Tidstrand, 2019). Charlotta Edlund, Analyst, Expert in antibiotics and antibiotic resistance and professor at The Public Health Agency of Sweden (FoHM), Department of Communicable Disease Control and Health Protection however says, that some tuberculosis expert considered that there are specific procurement problems related to Rifampicin. “According to him it is not so seldom that we cannot get it when we want it” says Edlund (Edlund, 2019).
5.7. WHAT HAPPENS IN BETWEEN?

The previous description focused on the relationship between the suppliers, the manufacturers or pharmaceutical companies and the purchaser, the county councils. But the procurement of antibiotics in Sweden involves multiple intermediary actors. The antibiotic supply chain in Sweden follows in principal the setting of the traditional pharmaceutical supply chain (Figure 6). Each antibiotic however has modifications to who the supplier is, if the drug is parallel imported additionally to the normal supply and who the selected distributors and customers are.

5.7.1. THE DISTRIBUTORS

The first intermediary station are the distributors (Danberg, 2019). There are two big distributors in Sweden, Tamro and Oriola. Magnus Munge, Unit Head of the Pharmaceutical Unit in the Kronoberg Region explains, Tamro and Oriola are two wholesalers and have approximately half of the market shares each. In Sweden a one channel distribution system is followed meaning one product for the Swedish market is only distributed via one wholesaler. E.g. Pfizer can have their product at Oriola and MSE can have a similar product at Tamro (Munge, 2019). Nicklas Widding, Site manager at Oriola Oy, Sweden however adds, that one manufacturer can have contracts with multiple distributors for different products (Widding, 2019). “Normally we have one contract for one product with one supplier. If we have more than one contract it creates a problem for the supplier. How much will they buy from me? How much will they buy from another [supplier]. And that way will not bring more security in deliveries. I think it is better we have one contract and that [contractor] has to deliver when we ask them. If they don't, they have to pay us and we buy it from someone else. And because they have to pay, we think that they take care for not being in that situation” says Thomas Axelsson, responsible for purchasing, business support and service at Jönköping Region (Axelsson, 2019).

Most drugs are delivered to the Swedish market via one of the big distributors. “We can buy drugs from other smaller distribution companies, but most of the drugs come via Tamro or Oriola. The manufactures have chosen that way for delivering” says Sofia Tidstrand, pharmacist at The County Council of Jönköping (Tidstrand, 2019).

The distributors are however no deciding actors in the Swedish antibiotic supply. They are executers of orders. “We don’t order drugs; we simply store the medications for the manufacturers at the right storage conditions” says Nicklas Widding. The pharmacies can then place orders every day and the distributors deliver, if the drug is available, as fast as possible five days a week. Normally when an order is placed in the morning the delivery happens in the afternoon says Peter Danberg, Executive Assistant at Tamro, Sweden (Danberg, 2019).

5.7.2. THE PHARMACIES

The pharmacies are the second intermediary organ in the antibiotic supply in Sweden. After the decentralization there is only one fully state-owned pharmacy left, Apoteket AB whereas all other pharmacies in Sweden are privately owned (Wallér, 2019). Nevertheless all pharmacies must sell all medicines approved in Sweden emphasizes Johan Wallér, Chief executive officer at Apoteksföreningen (Wallér, 2019). They cannot choose to only sell medications that are economically beneficial for the pharmacy. The pharmaceutical industry supplies both state and private pharmacies with pharmaceuticals (Wallér, 2019) but the pharmacies have to get their pharmaceuticals through the wholesalers says Johanna Orraryd, chief pharmacist at the Östergötland Region (Orraryd, 2019). Apoteket AB, Kronans Apotek and
Apoteket Hjärtat have small storages of their own at Tamro, Oriola and another distributor respectively, but no other pharmacy has a warehouse or grater stocks. Normally pharmacies have in their storage what the regions/county councils have ordered them to have in stock for a specific period of time explains Fredrik Boström, head pharmacist at Apoteksföreningen (Boström, 2019). Apoteket Hjärtat however has their own storage or distribution warehouse. Sometimes Hjärtat’s contracts are made directly with the pharmaceutical companies, but for some medicines Tamro and/or Oriola have to be involved because the pharmaceutical companies do not want to make separate contracts says Manar Ali, category Manager RX at Apoteket Hjärtat (Ali, 2019).

ApoEx and Apoteket AB as well as some county councils by themselves (Jönköping, Kalmar, Östergötland, Blekinge and Dalarna which circumvent the pharmacies) are responsible for drug procurement to the hospitals (Wallér, 2019). ApoEx and Apoteket AB are the only hospital pharmacies. ApoEx works with hospitals, institutions such as veterinarians, and dentists but holds no private stores. Apoteket AB works in the same way but has additional stores for outpatients and nonprescription drugs (Wallér, 2019).

5.7.3. The Hospitals

The clinics, wards or hospital collaborations are responsible for ordering the needed medications to the hospitals. They either order from the hospital pharmacies (ApoEx or Apoteket AB) or directly from the suppliers in the case of Jönköping, Blekinge, Dalarna, Kalmar, and Östergötland county hospitals (Wallér, 2019, Tidstrand, 2019, Orraryd, 2019). “In the Jönköping hospital in-house pharmacy, we run the whole procurement process by ourselves unlike other hospital pharmacies. Some differences when compared to other hospital in-house pharmacies are, that the others don't have the stocks of all the drugs in-house, they sort of order them when they want it” says Sofia Tidstrand pharmacist at the Jönköping county council (Tidstrand, 2019). The Jönköping hospital keeps small quantities of drugs often used in this hospital in stock.

5.8. The Delivery Pipeline of Benzylpenicillin and Rifampicin in Sweden

According to information gathered in interviews and through literature research illustrations of the delivery pipelines for the selected antibiotics have been constructed. The delivery pipeline for Benzylpenicillin and Rifampicin in Sweden are illustrated in Figure 10 and Figure 11 respectively.
Figure 10: The delivery pipeline for Benzylpenicillin in Sweden. The antibiotic is brought to Sweden via two Marketing Authorization Holders (MAHs), Meda Ab and Panpharma SA. These store their medication at the warehouses of Oriola and/or Tamro which are the two biggest distributors in Sweden. These in turn deliver the antibiotics to ApoEx and Apoteket AB, the two Swedish pharmacies that deliver pharmaceuticals to hospital pharmacies. The hospitals in Jönköping, Kalmar, Östergötland, Dalarna and Blekinge counties make up an exception. The hospital pharmacies here are delivered by the distributors directly without an involvement of an intermediate pharmacy. The customers are only hospitals since the formulation of Benzylpenicillin is an infusion solution which can only be given to the patients in the hospital. The illustration is constructed according to information gathered in interviews and through literature research. Reservations for inaccuracy might prevail.
Figure 11: Delivery pipeline for Rifampicin in Sweden. In the case of Rifampicin, the drugs are brought to Sweden in two ways. Firstly, two MAHs import Rifampicin containing drugs to Sweden, Sanofi AB and Sandoz. Additionally, there are six companies that parallel import Rifampicin containing drugs to Sweden. These Parallel Importers (PI) are located in France (FR), Spain (ES), The Netherlands (NL), and Austria (AT). The MAHs store their drugs at the distributors Oriola and or Tamro and additionally they might have a separate contract with the Apoteket Hjärtat warehouse to store drugs that are meant for Apoteket Hjärtat pharmacies in their own distribution center. The PIs do not use the services of the distributors located in Sweden but supply to the pharmacies directly. An exception again is Apoteket Hjärtat’s warehouse. The drugs from the MAHs are then delivered to the pharmacies by the distributors upon request. The customers for the Rifampicin containing drugs are the patients with prescriptions for the medication by their doctors. The illustration is constructed according to information gathered in interviews and through literature research. Reservations for inaccuracy might prevail.
The Swedish pharmaceutical market does not comprise a particularly big portion on the global market. And that, of course, is not specific for Sweden but for any small country. So if one has a specific antibiotic that is used mainly in Sweden, or the Nordic countries, it could be a problem (Orraryd, 2019). The sales of the drug might be too low to establish an economically beneficial deal with the manufacturers. This can lead to shortages and stock outs in the Swedish market. If one has an antibiotic that is used all over Europe for example and shortages in manufacturing occur the pharma companies cut the supply to smaller countries like Sweden because they do not want shortages to occur in bigger markets like the United Kingdom or Germany, says Manar Ali from Apoteket Hjärtat (Ali, 2019). These shortages can be caused by bankruptcies of actors involved in the supply chain, accidents or natural disasters. Ali concludes that shortages are a result of the demand and supply being out of balance. Magnus Munge, Unit Head of the Pharmaceutical Unit in the Kronoberg Region says, that the information from the pharmaceutical companies when it comes to shortages is very often very poor. The information on shortages and stock outs come from the wholesaler or from the hospital pharmacies. “But then when the product is back on the market, then the pharma company sends out an email to us saying, well, now the product is back on the market again” (Munge, 2019). But no information is provided by the manufacturers when the drug disappears from the market. Manar Ali continues saying, that more resistance against antibiotics arise due to shortages and resulting mistreatments (Ali, 2019). Pharma companies invest more in research and development of cancer drugs than into antibiotics. Sometimes, he says, a shortage problem can be solved by prescribing a drug that is not licensed in Sweden but can help treating the patient. It is not easy to do it this way, but it is done for the patient (Ali, 2019). Manar Ali adds, that antibiotics for less severe infections are easier to access and less shortages occur. Antibiotics like Benzylpenicillin and Rifampicin are for severer infections (often only used or prescribed in hospitals) and are harder to procure and more often show shortages in supply.

Johanna Orraryd thinks, that larger stocks could help prevent shortages if there is a problem at the manufacturing end (Orraryd, 2019). But Moa Grahm, Analyst at the Emergency Preparedness and Crisis Management Unit of The Public Health Agency of Sweden (FoHM), thinks that it is a general problem that no one wants to keep a stock of rare medicines (Grahm, 2019). Charlotta Edlund, Analyst, Expert in antibiotics and antibiotic resistance and Professor at The Public Health Agency of Sweden (FoHM), Department of Communicable Disease Control and Health Protection agrees and adds that the reason is that it takes money to keep them in stock (Edlund, 2019). Rifampicin is not a regular product, so the normal pharmacies do not want to have large stocks of the medicine either. So sometimes they wait until a patient comes with a prescription before they try to order it from the distributor, says Charlotta Edlund. And even the hospital pharmacies do not have large stocks that could cover up for longer interruptions of supply by the distributors and suppliers, says Fredrik Boström from Apoteksföreningen. They have in their storage what the regions or county councils have ordered them to have in stock for a specific period of time according to the previously documented needs of the counties (Boström, 2019).

The lack of information seems to be an important factor worsening the shortage situation. Johan Wallér thinks, that a better and faster flow of information about occurring or predicted shortages to all involved actors of the supply chain, especially to the care givers, would lower the frustration of everyone involved and help to prepare alternative treatment plans (Wallér, 2019). Johanna Orraryd as the chief pharmacist of the Östergötland Region and Ali Manar
from Apoteket Hjärtat agree, that better and quicker information is needed to deal with shortages better and circumvent treatment impairment (Orraryd, 2019, Ali, 2019). Ali Manar continues by explaining that he wishes the Swedish government would issue more penalties or withdraws additional benefits from pharma companies that show shortages in their supply. He states, that as of now, only The Swedish Dental and Pharmaceutical Benefits Agency (TLV) uses these options for short term shortages (Ali, 2019).

The distributors Oriola and Tamro similarly do not have contracts or arrangements for larger stocks. “We are not in charge of any stocks. It is a very transparent process. The manufactures can see for themselves how high the demand is and what size of the stock at ours is. Based on this they can decide what they want to do. We are just the distributors”, says Nicklas Widding, Site manager at Oriola Oy, Sweden (Widding, 2019). And Peter Danberg, Executive Assistant at Tamro, Sweden adds “We have in stock what the manufacturers decides” (Danberg, 2019). The distributors rent out space with the right conditions for short term storage of the medicines to the manufacturers.

The Jönköping county council has a in house stock for the three hospitals in Jönköping, Eksjö (Höglandssjukhuset) and Värnamo in case of short term lack of deliveries (Tidstrand, 2019). According to Sofia Tidstrand, Pharmacist at The County Council of Jönköping, the stocks are adjusted for all drugs and medicines depending on how much they are used and how much is needed for the hospitals if there is a high demand. If it is a drug used in critical health situations the stocks are slightly bigger (Tidstrand, 2019).

Charlotta Edlund remembers that shortages were much less of a problem before the decentralization of the pharmacy system in Sweden. Before, when there was a state-owned system, one could transfer drugs from everywhere to everywhere. Now hospitals and pharmacies are prohibited by law to send drugs from one to another (Edlund, 2019). Even if there is a shortage in one region but not in another, collaboration regarding the supply is prohibited, says Thomas Axelsson, working with purchasing, Business support and service at the Jönköping Region (Axelsson, 2019). Sofia Tidstrand adds, that only in highly special scenarios there might be assistance from other counties when there is shortage of drugs. But it is not a normal situation. Normally all drugs have to be obtained from the pharmacies or the distributors (Tidstrand, 2019). “This is why they want to keep some important drugs at the pharmacies because then they are available for everyone” says Moa Grahm (Grahm, 2019).

The Public Health Agency of Sweden (FoHM) has a mission to make sure that pharmaceuticals are available to procure by the county councils. They have obtained a governmental assignment to suggest models to creating better availability of antibiotics in Sweden (Edlund, 2019). Critical drugs that do not sell above a threshold of 4 million SEK a year or only have 1 or 2 MAHs in Sweden are defined to be problematic antibiotics and are included in the assignment (Edlund, 2019). Charlotta Edlund adds both Rifampicin and other antibiotics are on suspension of different cancer treatments.

Johan Wallér, Chief executive officer at Apoteksföreningen, concludes that the problem with deficiencies is very multifaceted. It is not that there is one error or fault that lies with one operator or actor. There are many different things that need to work together to solve the problem with the shortcomings. One of the simplest and perhaps most important factors is information he says. Everyone who is concerned with one particular drug and its accessibility needs to get information about its availability in advance. Often it is known in advance that there will be a shortage of this drug. And that information has to come out especially to the caregivers that prescribes this drug to patients he suggests. A doctor needs to get information that now you are about to prescribe a drug that does not exist. If the doctor does not get this information, it is not good. In this situation it would be better to know about the shortage and
prescribe another drug if there is an alternative he stresses. If information would be available in time, everyone in the supply chain would not be frustrated by finding out too late that the drug was not available. This needs to be available before the prescription moment, says Johan Wallér.

He continues explaining that the production of drugs is done by global companies with production sites everywhere around the world. And then they will supply the whole world with drugs in some way. “Some way” in this context is an expression of the lack of knowledge about the supply chains and the significant variation between companies. This leads the production to be a very complicated chain with many involved actors he reveals. The chain can easily fail somewhere and then suddenly a shortage of a drug in a country or on a whole continent is obtained. Even if one asks the pharmaceutical industry themselves what the reasons for specific shortages are, no one really knows, he states. Sometimes there is an obvious reason, a fire in a factory or something that has happened, which leads to an understandable situation that might cause shortages in manufacturing. But sometimes one does not really know why shortages arise, he explains. He implies, shortages might arise due to there being different price levels in different countries, different distribution of the drugs to different countries or that the reason might simply be a distribution problem. All sorts of things can affect the availability in the end and can lead to shortage situations that end up being visible at the pharmacies, he concludes.

It is a very difficult and complex system. And when one has a difficult and complex systems, a small error somewhere can cause a domino effect all the way through the supply chain ending up at the patients.
6. ANALYSIS

In the analysis, the results and the findings are examined in accordance with the research questions. This section summarizes results relevant to each of the research questions focused on in this study.

6.1. RESEARCH QUESTION ONE

What is the structure of the pharmaceutical supply chain as seen from the Swedish market at present?

Through the utilization of the network theory, the stakeholders of the pharmaceutical supply chain were identified. The mapping of the different sources led to the discovery of the general flow through the different actors in the chain. A typical pharmaceutical supply chain consists of the manufacturers, the suppliers, the distributors, the pharmacies and the customers (5.1). In some cases, pharmaceuticals can also be parallel imported from outside Sweden directly to the pharmacies without involvement of a local MAH. The other processes are similar even for these pharmaceuticals. Since no contact or connection could be established to the MAHs or the suppliers to investigate these and their primary and secondary manufacturers, the following analysis of the pharmaceutical supply chain will focus on the events and actors following the point of entry into Sweden.

The involvement of the Swedish health care system in the pharmaceutical supply chain starts with the procurement process. All responsibilities of procurement of pharmaceuticals lay in the county councils (5.6). All orders and agreements of purchasing and delivery of pharmaceuticals are made up between the manufacturers or suppliers and the county councils (5.6). All in between actors, the distributors, the pharmacies and the health care facilities are executive in their functions. They follow what they are told but do not have real deciding power regarding what, when and in which quantities pharmaceuticals should be procured.

To combine responsibility and to order in slightly higher quantities, making a more reliable buying source for the manufacturers, the twenty-one Swedish counties are organized into six healthcare regions. These act as procurement systems to coordinate purchasing to an increasing degree among the regions of Sweden (5.6.1) Such kind of cooperative purchasing can be used in pharmaceutical supply chains as a way to tackle the shortages experienced since the volumes or risk in the market, material and demand decreases when higher volumes can be ordered at once. The collaboration likewise enables joint utilization of the region's healthcare resources and mutual responsibility in relation to pharmaceutical procurement.

The, by the health care regions ordered quantities are provided to the chosen distributors, mainly Oriola and Tamro in Sweden, and stored at their warehouses at the right conditions. One manufacturer could have different contracts with several distributors for different products (5.7.1). Upon receiving an order from the healthcare providers for the need of a medicine, the pharmacies contact the distributors and ask for the delivery. The manufacturers can choose how the distributors deliver the products (5.7.1).

If, however, the quantities that have been preordered are utilized, the distributor solely pass the information to the pharmacies which forward it to the health care providers. These have to contact the respective county councils and ask for the procurement of more medicine. In the event of a stockout happening at the health care providers, no storage or central warehouse exists that could be contacted for the particular medicine.
Orders from health care providers usually pass through the pharmacies which contact the distributors in case they do not have the medicines available in house. In rare cases, for the five county councils of Jönköping, Kalmar, Östergötland, Dalarna and Blekinge the procurement process circumvents the pharmacies and medicines are delivered from the distributors to the respective health care facilities in the county directly (5.7.3).

ApoEx and Apoteket AB pharmacies are responsible to supply to the hospitals. All other pharmacies are responsible for supplying outpatients and the primary health care related drug needs.

The Swedish pharmaceutical system does not include a central storage for medicines with high medical value. A few stakeholders have however created their own small-scale storages to be able to react to minor stockouts of drugs largely used. Jönköping hospital has a small stock in their in-house pharmacy (5.7.3). Apoteket Hjärtat is the only pharmacy with a small-scale storage facility in Sweden (5.7.2).

6.2. RESEARCH QUESTION TWO

How are drugs procured into the Swedish market? An explanation of the drug delivery pipeline for Benzylpenicillin and Rifampicin.

Benzylpenicillin and Rifampicin are two antibiotics with high medical value for the Swedish society. Benzylpenicillin is widely utilized whereas Rifampicin is used to a lesser extent but in more severe cases of illness. The supply chain for both antibiotics respectively follow the general pipeline for pharmaceuticals, but they show some differences among each other.

In the case of Benzylpenicillin, the antibiotic is brought to Sweden via two Marketing Authorization Holders (MAHs), Meda Ab and Panpharma SA. These store their medication at the warehouses of Oriola and/or Tamro which are the two biggest distributors in Sweden. These in turn deliver the antibiotics to ApoEx and Apoteket AB, the two Swedish pharmacies that deliver pharmaceuticals to hospital pharmacies. The hospitals in Jönköping, Kalmar, Östergötland, Dalarna and Blekinge counties make up an exception. The hospital pharmacies here are delivered by the distributors directly without an involvement of an intermediate pharmacy. The customers are only hospitals since the formulation of Benzylpenicillin is an infusion solution which can only be given to the patients in the hospital (0). For Benzylpenicillin, there are a total of eight API manufacturers, but only three are situated within the EU, making import distances rather long and potentially vulnerable in case of a disruption within the supply chain (Figure 10).

In the case of Rifampicin, the drugs are brought to Sweden in two ways. Firstly, two MAHs import Rifampicin containing drugs to Sweden, Sanofi AB and Sandoz. Additionally, there are six companies that parallel import Rifampicin containing drugs to Sweden. These Parallel Importers (PI) are located in France (FR), Spain (ES), The Netherlands (NL), and Austria (AT). The MAHs store their drugs at the distributors Oriola and or Tamro and additionally they might have a separate contract with the Apoteket Hjärtat warehouse to store drugs that are meant for Apoteket Hjärtat pharmacies in their own distribution center. The PIs do not use the services of the distributors located in Sweden but supply to the pharmacies directly. An exception again is Apoteket Hjärtat’s warehouse. The drugs from the MAHs are then delivered to the pharmacies by the distributors upon request. The customers for the Rifampicin containing drugs are the patients with prescriptions for the medication by their doctors. For Rifampicin, there are seven API manufacturers exporting to the EU and USA, and three
even located within the EU securing short supply distances, giving importers more choices for supplying this drug (Figure 11).

6.3. RESEARCH QUESTION THREE

How can information sharing and collaboration between the different stakeholders in the pharmaceutical supply chain help to endure drug shortages in Sweden?

The importance of successful, quick and uninterrupted flow of information between all actors of a supply chain for a successful production has been stressed since the early definitions of the supply chain (5.1). As multiple previously conducted studies highlighted the horizontal collaboration between buying organs in several purchasing steps such as sharing the information, the volumes or risk in the market, material and demand can support tackling shortages (3.3).

The information flow in the pharmaceutical supply chain is not highly established. There are smaller clusters in which information is forwarded and collaboration is established but the complete picture shows multiple interruptions of the flow of information in the supply chain. Shortages are an important and sometimes life-threatening fact in the pharmaceutical supply chains. And especially in these pharmaceutical supply chain shortages or an impossibility of delivery can occasionally occur (5.6.5). Since the supply chain is so multifaceted and complicated, these shortages are hard to circumvent completely, but with fast, efficient and complete information flow, life-threatening situations due to inappropriate treatment or impossibility of treatment can be prevented by alternative treatment plans.

Improved supply chain relationships are significant to achieve a sustainable success. In the US more than a third of shortages in drug supply originate in delays or capacity issues. These delays or capacity issues are communicable and with an intensive interchange of information efficient problem solving and on time alternatives can be established to circumvent treatment difficulties in the case of shortages (5.6.1).

In Sweden the information about previous and current shortages situations are incomplete. Shortages information is based on the reports and facts that the LV receives from the pharmaceutical companies. These are the manufacturers of the medicines and they might not want to report all shortages. This leads to interruptions of information availability and unexpected shortages at the consumer end (5.6.5). Often information from the manufacturers is given out after the shortage is over, but not prior to or during the situation (5.9). At this stage information flow could be a crucial step in better preparedness for shortages and stock outs of important medicines.

The Apoteksföreningen watches the market situation and gets information regarding noticeable shortages of specific drugs to the pharmacies as fast as possible (5.6.5). Information that the Apoteksföreningen uses is however also gathered from the LV and sometimes additionally from the manufacturers and the pharmaceutical industry directly (5.6.5). Information flow from the pharmacies to the end consumers however does not seem to be regulated.

To allow for good communication and an intensive interchange of information in all regions of Sweden, collaboration between the counties has been established. All Swedish counties have been divided into six health care regions in which information exchange and collaboration is highly advanced (Figure 8). The counties receive information about shortages from the wholesalers or the pharmacies when orders are placed but not before hand.

In conclusion there is no central organ or platform for information exchange that all actors of the supply chain can access and also no obligations of transferring shortage or problem
information is established. As of now, information is exchanged and transferred on a more voluntary basis.

All interviewees in this study however expressed the wish and the need for the exchange and availability of information. A better and faster flow of information about occurring or predicted shortages to all involved actors of the supply chain, especially to the care givers, would lower the frustration of everyone involved and help to prepare alternative treatment plans (5.9). The information collected in the interviews made it clear that everyone concerned with one particular drug needs to get information about its availability and its accessibility in advance. Often it is known in advance that there will be a shortage of this drug, but the information is not passed on. This information has to be available especially to the caregivers prescribing the drug to patients (5.9). If information would be available on time, no one in the supply chain would get frustrated by unexpected shortages and alternative treatments could be prepared.

Another issue critically discussed in the interviews is the prohibition of collaboration between any actors in the supply chain when shortages have occurred (5.9). Even if a drug is available in one county, it is prohibited to send this to another even if they are in need of this drug. Only in highly exceptional scenarios such collaboration can be specially permitted (5.9). It is only permitted to buy the needed drugs from the wholesalers or pharmacies. If they are not available at these stages, access to the drugs is not obtainable in normal situations.

Since all pharmacies must sell all medicines approved in Sweden and cannot choose to only to sell medications that are economically beneficial for the pharmacy a collaboration on the pharmacy level could make it possible to establish better availability to all county councils in Sweden (5.7.2). Models on how such collaboration could look like are addressed in the discussion chapter.

In conclusion, an information exchange platform as well as regulations and rules on which information needs to be made public by each supply chain actor together with better and more widespread collaboration could help to be better prepared for shortages and have alternative, effective treatment plans ready.

6.4. RESEARCH QUESTION FOUR

How can combined stock reserves of drugs in Sweden be an alternative to circumvent drug shortages in the countries health care systems?

Examining the information collected in the empirics, it becomes clear, that shortages were much less of a problem before the decentralization of the pharmacy system in Sweden. When there was a state-owned system, even drugs could be transferred between different stakeholders in the Swedish part of the pharmaceutical supply chain (5.9). In the interview with representatives from The Public Health Agency of Sweden (FoHM), information about a liability of the government towards the people to take care of the public health was described. It was called Sammhällsansvar (community responsibility) and meant that the government was responsible to make sure that enough drugs were available to keep the population healthy. This responsibility disappeared during the decentralization and no organ or body inherited a similar liability (5.9). As of now, there are no centralized stocks of drugs in Sweden.

A dependency of the Swedish pharmaceutical market towards foreign manufacturers has arisen. Additionally, dependencies can also be identified between different actors in the supply chain. Data collection has shown that the pharmaceutical supply chain at many stages has
actors being dependent on other members of the production line. Even in Sweden the purchasing part of the antibiotic supply chain is a construct of dependencies between the different actors involved. The resource dependency theory therefore was a useful tool to investigate the current state of Sweden’s antibiotic supply to examine if changes in dependencies could lead to a more stable and secure supply of crucial antibiotics in Sweden.

The distributors, as the first stakeholders in the Swedish part of the pharmaceutical supply chain, argue that they only store what the manufacturers or pharma companies ask them to store (5.7.1). They do not have any responsibility of monitoring the demand and the production and check for the availability (5.9).

According to Apoteket Hjärtat, none of the other Swedish pharmacies has a warehouse or greater stocks available. According to them, they are the only pharmacy in Sweden that has its own storage or distribution warehouse. But Fredrik Boström corrects and adds that Apoteket Ab and Kronans Apotek likewise possess smaller warehouses for their respective supplies. But since this is limited to only serve the chains own pharmacies in Sweden, their stock capacity is also limited (5.7.2). The other pharmacies normally just keep what the regions ordered over a short period of time. For everything else an order is placed to the next stakeholder in the supply chain (5.7.2).

On the level of the county councils or hospitals likewise almost no storages are found. An exception is the Jönköping county council which has a in house stock for the three hospitals in the area Jönköping, Eksjö (Höglandssjukhuset) and Värnamo in case of short-term lack of deliveries (5.9). However, these stocks are only calculated to fulfil the three hospitals demands and are also based on what usually is needed and used in these. No general storage of important medicines is found here.

All interviewees in this study however expressed the need for larger collaboration stocks at least for rare but highly important medicines. If there would be problems at the manufacturing end, larger stocks could ensure the access to these vital medicines for everyone (5.9). The problem however is, that no one of the stakeholders wants to keep a stock of rare medicines since it takes money to keep them in stock and the possibility of non-usage is given (5.9). An example is given with Rifampicin, one of the selected antibiotics for this study. Rifampicin is a rarely used drug consequently single pharmacies do not want to have large stocks of the medicine in case it will not be used. Pharmacies instead wait until Rifampicin is needed and then try to order it from the distributor (5.9). In case there is a shortage at the manufacturer, the pharmacies will not be able to provide the medication to the patients in need. The wish to keep highly important drugs at the pharmacies for them to be available for every stakeholder is therefore largely expressed in the conducted interviews (5.9).

Not all shortages are predictable. Therefore, stocks of important medicines are advisable. Even the pharmaceutical industry themselves does not necessarily know the reasons for specific shortages. Obvious reasons such as fires in a factory or other natural disasters that have occurred, can lead to predictable and understandable situations of shortages in manufacturing. But sometimes reasons for arisen shortages are not known and therefore can be very unexpected. In the second scenario, shortages can only be circumvented if stock reserves are available (5.9).

In conclusion combined stock reserves of drugs in Sweden can be an alternative to circumvent drug shortages in the countries health care system if a regulated centralized system of collaboration is established. Models how such combined stock reserves could be managed and implemented are illustrated in the discussions chapter.
7. DISCUSSION

In the discussion, the analysis and the findings of the study are considered and critically acclaimed. The conducted research will be evaluated and the proposed improvements and suggestions for the Swedish pharmaceutical supply chain are in cooperated in two models. This will be followed by a suggestion of potential future research aspects.

7.1. DISCUSSION ON THE CONDUCTED RESEARCH

Our investigations confirm, that the problems of the Swedish antibiotic and pharmaceutical supply chains are the limited information, high complexity and lack of transparency. Not only are all involved actors spread all around the country and in case of the manufacturers even around the world, but also is the information within the supply chain scattered and not consistent. The pharmaceutical supply chain turned out to be a complex web of actors, processes, information flows, data gaps and products that are passed around and shipped to finally end up at the hospitals and patients. If something goes wrong in the whole process, the ones who suffer are the patients in need of treatment.

The establishment of resistances in the bacterial population can partly be traced back to the usage of the wrong or non-optimal treatment in case of an infection. Since antimicrobial resistance (AMR) is an emerging threat even in Sweden, authorities should pay more attention to the prevention and circumvention of drug shortages.

In this thesis, we mapped the antibiotic supply chains for Rifampicin and Benzylpenicillin from the Swedish perspective (Figure 10 and Figure 11), we investigated the drug distribution in Sweden and identified what improvements could be made to support a better and more sustainable access of drugs and a better response to stock outs (Chapter 6.3). In the discussion we want to establish suggestions on how the antibiotic supply chain process in Sweden could be upgraded and developed according to the information we have collected.

Firstly, we found that it was very hard to get information on the Swedish pharmaceutical supply chain. Some actors we contacted did not want to share information due to confidentiality issues, others maybe did not want to share information since it might not have been the correct one, others again maybe did not want the supply chain flows to get uncovered. Anyhow, the actors affected by shortages and stock out expressed the need and wish for better information exchange to cope with shortage situations better and more rapidly and constantly. Therefore, we propose a data collaboration system, Medirest, which can help to collect the scope of information needed to circumvent treatment complications due to shortages of drugs.

A second often mentioned subject was the absence of storages for drugs in Sweden. Each customer only orders and stores what is needed individually, but no collaboration or communication is established between the customers. In a small country like Sweden, we believe that the lack of such collaboration exposes the country to a high risk to experience critical health situations in which shortages and non-availability of drugs can be fatal for the patients. We therefore have created a model for a centralized storage for critical drugs in Sweden. This storage will also circumvent the issue of counties not being able to assist each other in case of shortages or stock outs due to the issued laws which prohibit the sending of drugs to other health facilities.
7.2. Medirest: A Platform for Monitoring Drug Shortages

Unlike in other European countries Sweden does not possess a centralized system for monitoring shortages on the drug market (Pharmaceutical Group of European Union, 2017). In Sweden, the information is distributed and centered around each supply chain actor individually. The flow and exchange of information is not fluent which leads to data gaps and problems at the customer end.

While interviewing different actors of the Swedish pharmaceutical supply chain it became evident that most participants were lacking the extensive scope of information that would be needed to be prepared for and react arranged to shortages occurring on the drug market. The need for an information exchange platform was hinted and understood which concluded in us proposing the below illustrated data network (Figure 12).

To monitor the availability of drugs on the market a semi-automated system is proposed: Medirest. A combination of systematized collection of data and obligation to report is what we believe could eradicate frustration of all actors involved in the supply chain and help prevent treatment failures due to unpreparedness for shortages.
Medirest is the central database in which all information is collected and stored. We suggest that the responsibility of the database is given to the Medical Products Agency (LV), as an already central involved information collector in the pharmaceutical supply chain. Information should nevertheless be available for other actors in the network as well.

To make the report system work, the MAHs and Parallel Importers (PI) should be obligated to report the status of production and availability to the system. Therefore, the Ministry of Health and Social Affairs is asked to issue laws obligating the MAHs and PIs to notify shortages lasting for at least two weeks at the starting of the shortage and register foreseen shortages at least one month in advance. Additionally, regular monthly reporting of the status of production should be carried out by logging in to Medirest and filling out standardized forms on drug availability and stability of production.

When hospitals or the county councils drug units place orders at the pharmacies these orders should be automatically registered in Medirest. Moreover, information on if the order was rejected due to shortages or accepted and the drug sent to the customer from the pharmacies shall be added automatically. The orders placed by the customers are summarized in Medirest and compared to the expected demands, set up by the county councils yearly before drug procurement. If the ordered quantities bypass or exceed the calculated available amounts, a warning is issued to the effected county council or hospital. After investigation a warning to all other county councils might be given, if a shortage is expected to arise due to miscalculations of the demands.

Hospitals which circumvent the pharmacies by ordering from the distributors directly also need to be included into the database. Since here no information on orders rejected or received is available from the pharmacies, this information should be automatically collected from the hospitals that order. In this case information on orders and status of orders are received directly.

Patients and doctors as the consumers of the drugs can also be a highly important source of information. Therefore, these should be able to manually report information about shortages to Medirest on a voluntary basis. The voluntary information has to be verified by comparing the data to the automatically generated data and in case of inconsistencies investigations have to be established.

Information in the Medirest shall be monitored and verified by a three-step procedure. If the MAHs and PIs report no problems and no shortages, then automatic information from the pharmacies and customers should support the data by also not showing any stock outs. If, however, inconsistencies are shown, investigations on where the problems arise shall be prepared. If the pharmacies and customers report shortages and the MAH or PI have not reported a problem that has been arising causing the shortages, The Swedish Dental and Pharmaceutical Benefits Agency (TLV) who receives information inconsistencies of reporting, should have the power to issue penalties to the affected MAHs or PIs.

The MPA and FoHM receive information on drugs that often show shortages or where demands fluctuate greatly to evaluate the medicines and determine which medicines are critical and highly important drugs and should therefore be included into the central storage system proposed in the next chapter.
7.3. MODEL FOR CENTRAL STORAGE OF CRITICAL DRUGS IN SWEDEN

Shortages in the Swedish drug market often occur due to problems at the manufacturing end of the pharmaceutical supply chain. As discussed in the analysis, a combined Swedish storage could be one option to circumvent the problems of stock outs of critical medication such as Rifampicin and Benzylpenicillin which have been discussed in earlier chapters.

Each county council has the responsibility to order and procure the drugs that are needed for the county’s population. Since some of the drugs assessed as critically important for Sweden but are not utilized in all counties a storage on regional level would not be financially manageable. In addition, the regulation, we view critically, on how medicines may or may not be shared within Sweden would cause problems for regional storages. Since no drug is allowed to be sent to another county, every small county would have to have all the important medications in their own storage. This neither sustainable nor logistically or financially realizable. A centralized storage could in hold critical drugs with high importance in quantities big enough either to circumvent devastating medical situations or to bridge times until alternative treatment plans or subsidiary medications have been placed.

Since the decentralization, the responsibility for the health care has been divided into all counties themselves rather than integrating it into the Swedish government. So how can a centralized storage work when this again would be based on larger collaboration not only within the logistical realization but also financially? Below we describe and illustrate a model for a centralized storage of critical drugs in Sweden (Figure 13).

One of the main and most impacting considerations is how to finance a system build for emergency situations. The usage of the drugs stored would stay low in situations where no shortages occur. If the drugs are stored but not needed during their validity time, these need to be discarded and the capital invested is gone. It is difficult and unusual that individuals, organizations or administrations can be persuaded to pay for something they may not use, let alone invest in something that eventually might only be specially destroyed. Therefore, we suggest that the financial planning and investment need to be taken to the national level. The storage and associated costs need to be included into the Swedish Governmental Budget Bill. In expenditure area 9, concerning health care, medical care and social services (Ministry of Finance, 2018) the central storage needs to be added as a vital financial opportunity to ensure more sustainable availability of critical drugs in Sweden. The government needs to provide access to special funds designated for the storage to the Ministry of Health and Social Affairs.

The Ministry of Health and Social Affairs is responsible for all governmental agencies concerned with the health care and social well-being of the Swedish population. Also, they have the power to set policies regarding the health sector. All regulatory policies regarding essential drugs need to be issues and decided in the Ministry before actions can be passed on downwards in the Swedish governmental hierarchy. The Ministry must not only forward the designated governmental funds to the Swedish Medical Products Agency (LV) so that the Agency can procure the drugs, but also is obligated to direct the other governmental health agencies in their actions.

The Swedish Medical Products agency (LV) together with The Public Health Agency of Sweden (FoHM) could be responsible for classification and evaluation of which drugs should get the rank of being critical and therefore included in the central storage. The LV currently collects data on shortages occurring on the Swedish pharmaceutical market through voluntarily submitted data from manufacturers, suppliers or health care providers. Consequently, the LV has, even if not complete since only voluntarily reported, data on which drugs are
often in shortage. The FoHM is not directly connected to any manufacturers or suppliers and could therefore assist the evaluation with independent assessments and value calculations.

The Swedish Dental and Pharmaceutical Benefits Agency (TLV) has a supervisory function on the current pharmaceutical market in Sweden and could assist in monitoring the stock situation of drugs. The previously described information system, Medirest, needs to be monitored to ensure accuracy and completeness (Figure 12). The Swedish Dental and Pharmaceutical Benefits Agency (TLV) furthermore has the authority to issue penalties to manufacturers and suppliers that do not fulfill their delivery contracts. In the case that information on shortages is not provided in the regulated time frame set by the Ministry of Health in the

Figure 13: Our Model for the central storage of drugs in Sweden.
policies for essential drugs, the TLV should be entitled to cut benefits and release penalties to the affected suppliers.

The Swedish eHealth Agency collects statistics on drug sales from pharmacies, retailers and distributors. These statistics can be highly important when quantities of drugs that shall be stored are calculated and decided. Quantities need to be large enough to fulfill their purpose in critical situations (E.g. be enough for full treatments of sickened patients or bridge time until an alternative treatment plans are set) but not too large to produce excessive surplus. Careful considerations need to be combined with financial and logistical considerations to establish a well-organized and effective drug security system.

Tamro and Oriola, the two big Swedish distributors, have storage warehouses in which conditions for medications are optimized and adjustable. The financial burden that the construction of a new warehouse would lay on the government can be circumvented by renting space at the two distributors. The storage space should be rented including important inventory management functions. Temperature control and security of the drugs should be provided by the distributors as part of the renting agreement. Other important management functions such as utilization patterns of the drugs in storage as well as a regulated rotation of stock should be governed by the eHealth Agency.

In case of a shortage occurring at the customers which is noted by the pharmacies when orders are placed that cannot be fulfilled, the stock reserves can be requested. In the Policies for essential drugs the Ministry of Health and Social Affairs should define the criteria that shall be given for a request of storage usage to be granted. The evaluation of the request needs to be immediate to ensure quick and effective action in critical health situations. The evaluation function could be taken by the FoHM, as the agency bridges knowledge between the health sector and the pharmaceutical industry. Competencies from both the hospital and the industry come together in FoHM for a good evaluation of the need for quick treatment in situations where patients’ health is in danger.

When a request is granted it might be the lifesaving treatment that a patient needed that would not have been available without the central storage. After the shortage situation is over the storage should be stocked up again and meanwhile alternative treatment plans for future shortages of the drug in question should be discussed.

**7.4. Evaluation of the Proposed Models and Thoughts on their Implementation**

The proposed models should be considered as ideas or bases for similar implementations into the Swedish health care system. We have to our understanding and knowledge analyzed and evaluated the different governmental organs and agencies and divided the tasks according to what we believe would be a plausible and respectable solution. However, we agree that the details would have to be confirmed with specialists of each area to evaluate each step of the networks.

We nevertheless strongly believe that the proposed models should be implemented as solution for the problems in patient treatment due to stock outs and shortages of drugs. With a special focus on antibiotics the arising threat of antimicrobial resistance shall also not be underestimated. Our models can help to avoid non-optimal treatment of bacterial infections which has proven to be a driving force behind new resistances arising.
7.5. **Societal, Ethical and Policy Implications of the Conducted Study**

The benefit of our analysis for the society will be immense, especially in the face of the fact that the big pharma companies like Johnson & Johnson, Novartis, Sanofi and AstraZeneca withdraw financial supports for the discovery and development of new antibiotics (Baars and Lambrecht, 2019). Antibiotics are not profitable enough for the companies to focus on their research and development (Langreth, 2019). The society will have to survive with the already existing antibiotics. Therefore, initiatives like PLATINEA which focus their efforts on innovation and enhanced usage of already existing antibiotics will gain even more attention and value in the near future. This project supports the initiatives of PLATINEA with the creation of models to innovate and improve the supply and availability of antibiotic in Sweden. The biggest societal implementation of our central storage and data sharing models is that they save lives. Life is saved both directly through providing the right medication at the right time and indirectly by lowering the rate of new AMRs arising due to miss treatment of bacterial infections. The importance of hospital facility design has been recognized by Reiling et al. (2008). They emphasize that, fundamental changes of health care processes and the physical environment are necessary and need to be aligned, in order to address the problems of errors in health care and circumvent serious medical safety issues so that the caregivers and the resources that support them are set up for enabling safe patient care (Reiling et al., 2008).

Our central storage model and data sharing model will create work. Even if parts of the systems will be automated, educated personal will be needed to maintain and supervise the systems. In the time of automation innovations and changes often replace manpower with autonomous work. Our systems however will create work opportunities. Validity of data in Medirest is an important ethical issue. There will always be an opportunity to falsify data if data is gathered manually from individuals. Therefore, we suggest an automated system for most of the processes to be implemented to higher reliability of stored data to be correct. Data from pharmacies, hospitals and county council drug units shall be automatically registered in the system. Data manually added by doctors and especially patients’ needs to be distinguished from automatically added information. Collecting medical data always imposes a risk. In our models no individual patient data will be stored, but information on usage of drugs. In case this information is leaked to the wrong receivers, it could be used as weak point to attack the society. Information on usage of medications needs to be encrypted and protected to make storing of this data ethically justifiable.

Policy implications shall all be directed towards promoting patient safety and lowering the rise of new AMRs. The resources to finance the systems of storage of critical drugs and information sharing shall be included in the governmental budget bill. We believe that the systems are of national interest and should therefore be financed by the population in total. We highly recommend to not withdraw the money from other health benefits which ethically might lead to a disadvantage of parts of the population. Policies directing the responsibilities and monitoring of both proposed models between different governmental organization shall be implemented. These obligations are recommended to be divided amongst governmental institutions only to lower the risk of self-interest a private stakeholder might develop. Additionally, policies authorizing the TLV to issue penalties towards suppliers and manufacturers upon lack of or falsification of information need to be implemented.

The drivers and resolutions of AMR are interlinked. To reach high impact, interventions must be coordinated and combined. Political implementations and strong leadership are required to reach changes in policies, the organisation of the Swedish health care system, the information sharing and the legislative structure. The implementations can then be translated into recommendations and knowledge that can be shared and spread to develop a new and better
structure of the pharmaceutical supply in Sweden. With new multidrug-resistant bacteria rapidly evolving being beside well-known older pathogens, the opportunity for prevention of medical disasters is rapidly diminishing: no action today, no cure tomorrow.

7.6. **ACADEMIC CONTRIBUTION**

The results from case studies cannot be generalized directly onto a whole system. The method section of the thesis describes the process flows as comprehensively as possible to allow replication of the study on other similar supply chains. The addition of details from other antibiotic pipelines will higher the value of the concluded results. Since the conclusions on the Swedish part of the supply chain, however, are drawn from interviews with actors involved in not only the Rifampicin and Benzylpenicillin supply but medical supply in general, the results can be generalized as being valid for the entire pharmaceutical supply chain. Additionally, literature has added a general understanding of the processes and their issues in the general pharmaceutical supply chain. Therefore, this thesis contributes to the general knowledge of the Swedish pharmaceutical supply chain and its flaws and problems. The proposed models can be seen as generally valid for the pharmaceutical supply chain and can be used as a base for further academic research or theoretical implementations.

The detailed pipelines for Rifampicin and Benzylpenicillin are additionally described. Further details in these as well as the pipelines for other antibiotics and additional medical classes would add further knowledge of the pharmaceutical supply chain. Our study can be used as an academic base to replicate similar studies for different pharmaceuticals.

7.7. **PROPOSED FUTURE RESEARCH**

Unfortunately, we were not able to establish any connection to a manufacturer, supplier, MAH holder or PI. We believe that an inside to how the market looks from their perspective as well as what challenges they face with shortages would be highly valuable to evaluate the situation further. Likewise, it would be interesting to visit the facilities on ground to get a better understanding of the challenges that are faced there.

Since we felt that great amounts of information were not available for us in the relatively short period of our study, we believe that deeper investigations on each and every actor and process of the pharmaceutical supply chain benefit the understanding of the complete procedures. Each actor should be investigated and examined even more thoroughly.
8. **Conclusion**

The aim of this work was to examine strategies to prevent further increase of AMR due to the shortages of antibiotics. Previous work did not identify the reasons and the supply chain steps in which these shortages arise. Through intensive literature studies and data collection the Benzylpenicillin and Rifampicin supply chains in Sweden could be described and conclusions on the general pipeline for the antibiotics could be drawn. Interviews with actors from most stages of the supply chain in Sweden yielded valuable information on problems and bottlenecks experienced by the different stakeholders. Analysis of the empirical data identified the lack of information flow and the absence of a drug storage has major hazards increasing the risks for the antibiotic shortages in Sweden. Therefore, we recommend the implication of an information sharing platform, Medirest and the creation of a central storage for drugs with high medical value in the Swedish pharmaceutical supply chain. We believe that shortages and AMR related to these can be prevented by the usage of the recommended models. AMR is a rising threat not only to Sweden but to the whole world. This study hopes to create better understanding of the antibiotic supply chain and procurement process in Sweden and increase the awareness of AMR. Our findings will contribute to better public health in Sweden and if our concepts are implemented elsewhere, hopefully around the world.
9. REFERENCES

INTERVIEWS

AXELSSON, T. 2019. Purchasing, Business support and service, Jönköping Region In: GARLAPATI, S., KRAMBRICH, J. & SEWOYO, V. (eds.).
MUNGE, M. 2019. Unit Head of the Pharmaceutical Unit, Kronoberg Region. In: GARLAPATI, S. & SEWOYO, V. (eds.).

LITERATURE


FASS. 2019. *FASS Allmännhet* [Online]. Available: [https://www.fass.se/LIF/result?query=&userType=2](https://www.fass.se/LIF/result?query=&userType=2) [Accessed].


10. APPENDICES

APPENDIX I

Interview Guide for the Pharmacies and Hospitals

Apoteksföreningen

- What’s the role of Apoteksföreningen in Sweden?
- How do you assist pharmacies in Sweden?
- Can you tell us about any information on shortages of antibiotics?
- Have come across any shortages of Benzylpenicillin and Rifampicin in particular?
- Do you know the reasons of these shortages?
- Who supplies antibiotics to private pharmacies?
- Who supplies antibiotics to public pharmacies?
- Does your organization work with hospitals or have any connection with the hospitals?
- Do you have any suggestions or recommendations on how the process can be improved?

ApoEX / Apoteket AB

- What’s the role of ApoEX? How is it different form other pharmacies?
- Who does ApoEX buy the antibiotics from and who do they supply to?
- Have you experienced any reports or shortages of antibiotics? In particular Rifampicin and Benzylpenicillin?
- What were the reasons for these shortages?
- Do you have contact or work with the hospitals?
- Do you have any suggestions or recommendations on how the purchasing process can be improved?

Hospitals

- Have you experienced any antibiotic shortages and in particular Rifampicin and Benzylpenicillin?
- How do you buy or procure antibiotics? From which distributors do you get them from?
- How are the orders made and received? What’s the duration of time it takes for the distributors to provide you with the antibiotics?
- What’s the procedure of purchasing antibiotics for your hospital? How are the antibiotics ordered, do the doctors make the list of antibiotics to be purchased?
- What are the measures/ alternative steps taken by the hospital when a particular antibiotic is in shortage?
- Do you have any suggestions or recommendations on how purchasing processes can be improved?
## APPENDIX II

### General interview guide

<table>
<thead>
<tr>
<th>Category</th>
<th>Topic</th>
<th>Questions</th>
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<tbody>
<tr>
<td><strong>Pharmaceutical market in Sweden</strong></td>
<td>Characteristics of Swedish supply chain</td>
<td>- Are there any characteristics in the Swedish pharmaceutical market that differ in comparison to other countries?</td>
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<tr>
<td></td>
<td>Characteristics affecting availability</td>
<td>- How do these characteristics effect the availability of antibiotics (Rifampicin and Benzylpenicillin) in Sweden?</td>
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<td></td>
<td>Most problematic characteristics</td>
<td>- Which of the characteristics are the most problematic ones to the suppliers, doctors and to the purchasers?</td>
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<tr>
<td><strong>Antibiotic shortages in Sweden</strong></td>
<td>Antibiotic shortages in Sweden</td>
<td>- To your knowledge has there been reports about antibiotics listed as out of stock or in shortage for Sweden?</td>
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<td></td>
<td>Global shortages</td>
<td>- Have there been global shortages?</td>
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<td></td>
<td>Rifampicin and Benzylpenicillin shortage</td>
<td>Do you know any case of Rifampicin or Benzylpenicillin?</td>
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<td></td>
<td>Reasons for shortages in Sweden</td>
<td>- What do you think are the most important reasons behind the shortages of antibiotics in Sweden?</td>
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<td></td>
<td>Connection for shortages globally</td>
<td>- How are shortages in Sweden connected to global shortages of Rifampicin and Benzyl Penicillin?</td>
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<td></td>
<td>Suggestions for preventing shortages</td>
<td>- What kind of suggestions/improvements can be made in order to reduce Rifampicin and Benzyl Penicillin shortages?</td>
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<td><strong>Antibiotic purchasing in Sweden</strong></td>
<td>Purchasing of antibiotics in Sweden</td>
<td>- Who is responsible for purchasing of antibiotics in Sweden?</td>
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<td>How does it look like</td>
<td>- How does antibiotic purchasing look like in Sweden?</td>
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<td>National coordination of purchasing</td>
<td>- Is there any national coordination of purchasing in Sweden?</td>
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<td>Differences among the hospitals and county councils</td>
<td>- Are there any differences when it comes to purchasing of antibiotics between county councils or hospitals to one and another?</td>
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<td></td>
<td>Recommendations for improvement</td>
<td>- Is there any way the public purchasing party can improve the supply/purchasing processes of antibiotics in general?</td>
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<tr>
<td>Antibiotic supply chain in Sweden</td>
<td>National storage of antibiotics</td>
<td>Are important antibiotics nationally stored?</td>
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<tr>
<td>Supply chain of in Sweden used antibiotics</td>
<td>-How does the supply chain look like for antibiotics imported to Sweden?</td>
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<td>Antibiotic production in Sweden</td>
<td>-Is there any antibiotic production in Sweden?</td>
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<td>Logistic responsibility in Swedish supply chain</td>
<td>-Who is responsible for the logistics of the supply chains in Sweden?</td>
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<td>What are the lead times</td>
<td>-Are there lead times that the suppliers give to the buyers?</td>
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<tr>
<td>Antibiotic supply chain in Sweden</td>
<td>Supply chain logistics</td>
<td>-Who or which organ is responsible for collecting usage data?</td>
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<tr>
<td>Usage data collection</td>
<td>-How does each hospital and county define and monitors the amount of antibiotics needed and consumed?</td>
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<tr>
<td>Monitoring of need of antibiotics and consumption by hospitals or county councils</td>
<td>-Are there inventories of antibiotics?</td>
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<tr>
<td>Inventories</td>
<td>-Which antibiotics are these? How big are the inventories?</td>
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<td>Which antibiotics and size of storage</td>
<td>-Are there any last resort antibiotics on hold in Sweden?</td>
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<tr>
<td>Resort of last resort antibiotics in Sweden</td>
<td>-How big are the stocks for antibiotics like Rifampicin which are against rare but severe diseases?</td>
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<tr>
<td>stocks for rifampicin</td>
<td>Specific antibiotics</td>
<td>Easy antibiotics with respect to procurement</td>
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<td></td>
<td></td>
<td>-Example of antibiotics where the needed amount and its procurement are easy?</td>
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<tr>
<td>Hard antibiotics with respect to procurement</td>
<td></td>
<td>-Example of antibiotics where the needed amount and its procurement are hard?</td>
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<tr>
<td>Reasons</td>
<td></td>
<td>-Reasons for this difference?</td>
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<tr>
<td>Demand or supply bigger challenge</td>
<td></td>
<td>-Are the reasons arising from the demand side or the supplier side?</td>
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