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REASONS FOR SHORTAGES IN FINNISH MEDICINE SUPPLY CHAINS AND MITIGATION STRATEGIES

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ABSTRACT

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The aim of this thesis was to research which supply chain risks contribute to medicine shortages occurring in the Finnish market. In addition, the objective was to find out how medicine shortages could be mitigated or prevented through supply chain risk management practices. Medicine shortages have increased globally during the last decades which is why the issue needs to be researched and sustainable solutions to overcome the issue are needed.

The empirical part of the study was conducted as a qualitative multiple case study by interviewing representatives from pharmaceutical wholesale licence holders and a wholesaler operating in Finland. The empirical findings mainly support previous research findings. The results indicate that the reasons behind medicine shortages are often complex and in most cases there are more than just one reason affecting behind a shortage. Thus, strong political commitment as well as national and multi-national efforts are needed to find solutions for the issue.

TIIVISTELMÄ

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Tämän Pro Gradu -tutkimuksen tarkoituksena oli tutkia, mitkä toimitusketjun riskit aiheuttavat lääkkeiden saatavuusongelmia Suomen markkinalla. Lisäksi tarkoituksena oli selvittää, miten lääkkeiden saatavuusongelmia voitaisiin hallita tai estää toimitusketjun riskienhallinnan keinoin. Lääkkeiden saatavuusongelmat ovat lisääntyneet maailmanlaajuisesti viimeisten vuosikymmenien aikana, minkä takia ongelma vaatii tutkimista, ja ongelman selvittämiseksi on löydettävä kestäviä ratkaisuja.

Tutkimuksen empiirinen osio toteutettiin laadullisena monitapaustutkimuksena haastattelemalla Suomessa toimivien lääkkeiden myyntiluvan haltijoiden sekä tukkumyyjän edustajia. Empiirisen tutkimuksen tulokset tukevat pääosin olemassa olevan tutkimustiedon löydöksiä. Tulokset osoittavat, että lääkkeiden saatavuusongelmien taustalla vaikuttavat syyt ovat usein monimutkaisia ja useimmiten saatavuusongelmien taustalla vaikuttaa useampia tekijöitä. Siksi, poliittista sitoutumista sekä kansallisia ja monikansallisia toimia tarvitaan jotta ongelmaan löydetään ratkaisuja.

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The master's studies at LUT University have been interesting and educational in many ways. I am convinced that this degree opens up new doors career-wise and serves as a valuable reference. Even though this journey ends, I am sure that the things I have learned while studying at LUT will influence my mindset in the future as well.

This master's thesis project has been very interesting but at the same time challenging. I want to thank professor Katrina Lintukangas for first of all suggesting this thesis topic, and also for valuable advice and support during the writing process. Also, I want to express my gratitude to the interviewees that took part in the empirical study. Thank you for the interest towards the study and for the expert comments and insights.

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Laura Anttila

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

1 INRODUCTION

Increasing complexity of products and services as well as trends such as outsourcing, single sourcing and reduction of the supplier base, globalisation and focusing on removing the slack from the supply chain have caused a shift from traditional supply chains to complex and dynamic supply networks (Harland, Brenchley & Walker 2003; Hendricks & Singhal 2012; Jüttner, Peck & Christopher 2003). The above-mentioned strategies have improved organisations' performance, but due to their intricacy, supply chains and networks are more susceptible to risk and disruptions and thus, more vulnerable than before (Hendricks & Singhal 2012; Fang, Zhao, Fransoo & Van Woensel 2013; Teuscher, Grüninger & Ferdinand 2006). To deal with supply chain risks, companies must develop robust capabilities which requires leadership, detailed and careful planning and commitment of resources (Hendricks & Singhal 2012). By deploying reactive and proactive supply chain risk management strategies companies may prevent the negative effects of supply chain risks or control and mitigate them.

The above-mentioned strategies used to strive for economic advantage and efficiency within the pharmaceutical industry have resulted in concentration of medicine manufacturing and distribution which again have contributed to shortages of raw materials and active ingredients used for medicine manufacturing as well as finished medicines. European Association of Hospital Pharmacies' (EAHP) surveys on medicine shortages in Europe have indicated a negative trend in increasing medicine shortages on each survey period from 2013 to 2019 (EAHP 2019). As medicine shortages are a common problem world-wide and hamper healthcare professional's work on a weekly basis, and because the consequences of medicine shortages are threatening patient's health and life, it is important to raise awareness of the problem (Barbosa-Povoa, Jenzer & de Miranda 2019). Furthermore, EAHP's medicine shortages report 2019 suggests that medicine shortages will presumably worsen in the future, especially due to the outburst of COVID-19 pandemic, which is why it is necessary to research the reasons behind medicine shortages and find ways to improve medicine availability on a global scale.

Problems in the availability of raw materials of medicines as well as finished medicines have caused problems increasingly in Finland during the last years as well. Global shortages naturally have the potential to affect availability in the Finnish market as well. In addition, country-specific factors such as dependence on foreign manufacturing, small size of the market and the geographical location of Finland add to the risk regarding the availability of medicines. (Heiskanen, Ahonen, Kanerva, Karttunen & Timonen 2017)

1.1 Background

Scientific research on medicine shortages has increased during the recent years because of the topicality of the issue around the world. However, there is not enough reliable information available to assess the magnitude of medicine shortages and to establish a global coordinated action to tackle the issue. (Besancon & Chaar 2013; Barbosa-Povoa, Jenzer & de Miranda 2019). Furthermore, the characteristics of the problem vary notably between countries. In the USA medicine shortages have been studied and tracked since the early 2000's, however, despite measures taken to tackle medicine shortages, the issue has not disappeared. (Besancon & Chaar 2013; Fox, Sweet & Jensen 2014) Furthermore, medicine shortages in Europe have not been as extensively studied as in the USA (Pauwels, Simoens, Casteels & Huys 2015; Bogaert, Bochenek, Prokop & Pilc 2015).

Shortages in essential medicines have been increasing globally during the recent years (Besancon & Chaar 2013; WHO 2016). EAHP has collected evidence of medicines supply shortages in Europe from 39 countries in the hospital sector since 2013, interviewing pharmacists, physicians, nurses and other health care professionals. Surveys have indicated a negative trend in increasing medicine shortages on each survey period. (EAHP 2019) This development is alarming as medicines have a huge role in protecting, restoring and maintaining people's health and the provision of appropriate medicines is a concern of global and national policy makers as well as agencies implementing health activities and programmes (WHO

2011). Jenzer, Sadeghi, Maag, Scheidegger-Balmer, Uhlmann & Groesser (2019) even argue that if the medicine shortage issue is left alone it threatens to become a crisis in terms of the ability to implement patient care.

In the U.S. there was a significant increase in medicine shortages starting in 2008, at the same time with the economic downturn. Despite the economic recovery, medicine shortages have persisted, albeit declined. (Mazer-Amirshahi, Goyal, Umar, Fox, Zocchi, Hawley & Pines 2017) Aging communities and availability of more effective treatments have caused an ever-growing demand for medicines which, combined with medicine shortages, often results in inability to provide medicines when they are needed where they are needed (Ward & Hargaden 2019; Besancon & Chaar 2013). The demand of medicines generally remains constant over time which makes them a unique commodity. In addition, the consumer of a medicine is not in control of the choice of product. (Fox, Sweet & Jensen 2014)

The European Association of Hospital Pharmacists (EAHP) has conducted surveys on medicine shortages in Europe since 2013. For the first time in their 2019 survey EAHP gathered information on possible reasons for medicine shortages. Top three answers for healthcare professionals and hospital pharmacists were the global shortage of an active pharmaceutical ingredient (API), manufacturing and supply chain problems. for physicians top three answers were prices of medicines, supply chain problems and parallel export related issues. (EAHP 2019) Other studies have also recognized the role of supply chain related issues in inflicting medicine shortages. Heiskanen et al. (2017) found out that reasons for medicine shortages were more often supply than demand related. According to the study of Pauwels et al. (2015) hospital pharmacists stated manufacturing problems as the most important reason for medicine shortages in Europe. The University of Utah estimated that in 2012 36% of medicine shortages in the USA resulted from manufacturing issues, 8,3 % was related to supply/demand reason, 7,8% was due to discontinuation of a product and 3,9% was due to lack of raw material, for 44% of shortages no specific reason was reported (Besancon & Chaar 2013). In addition, a review conducted by the Federal Drug Administration (FDA) in the

USA identified that main causes for medicine shortages were manufacturing problems (43%), delays in manufacturing or shipping (15%) and lack of API (10%) (Fox, Sweet & Jensen 2014). According to WHO's Drug Information quality and raw material issues at the manufacturing level have been increasingly related to medicine shortages e.g., due to increased global competition of API's (WHO 2016).

Heiskanen, Ahonen, Karttunen, Kanerva & Timonen (2015) found out that 80% of the Finnish pharmacies studied, reported encountering medicine shortages daily or almost daily and in every third case the shortage caused problems for the pharmacy as the customer could not receive medicine. The medicines in short supply were commonly used medicines (Heiskanen et al. 2017). Medicine shortages in the Finnish market have not yet been studied extensively and only a few research papers can be found which handle the topic. Authors have suggested similar reasons and characteristics for medicine shortages occurring in the Finnish market (Sarnola & Linnolahti 2019; Heiskanen et al. 2015; Heiskanen et al. 2017). Heiskanen et al. (2017) however point out that based on current research, the reasons behind medicine shortages are often not determined. Authors have also found similarities between the characteristics of medicine shortages occurring in the Finnish market and in other markets. However, there are also country-specific factors related to Finnish pharmaceuticals market that affect the availability of medicines and thus must be taken into consideration when contemplating the issue from Finland's perspective (Junttonen 2017).

1.2 Research objectives, questions and limitations

According to previous research data, supply chain related reasons have a crucial role behind medicine shortages (EAHP 2019; Heiskanen et al. 2017; Besancon & Chaar 2013; Junttonen 2017). Therefore, this thesis will have supply chain risk and supply chain risk management viewpoint. The aim is to study which risks in the global supply chains have the biggest potential to cause medicine shortages and to find out which supply chain risk management strategies are being applied or could be applied to tackle the medicine shortage issue. Thus, the theoretical framework of this thesis is

built on supply chain risk and supply chain risk management theory. The literature on these two topics is rather extensive as they have been studied widely and from diverse perspectives throughout the past decades. Hence, there is a wide range of supply chain risk and SCRM related literature available to support the theoretical framework of this study. However, due to the novelty of the topic of medicine shortages, there is still a limited number of academic literature available in that field, especially regarding medicine shortages in Finland. The situation is similar with the reasons behind medicine shortages, especially with those related to supply chain risks. Hence, there is still gaps in the research and various angles remaining from which the issue could be studied.

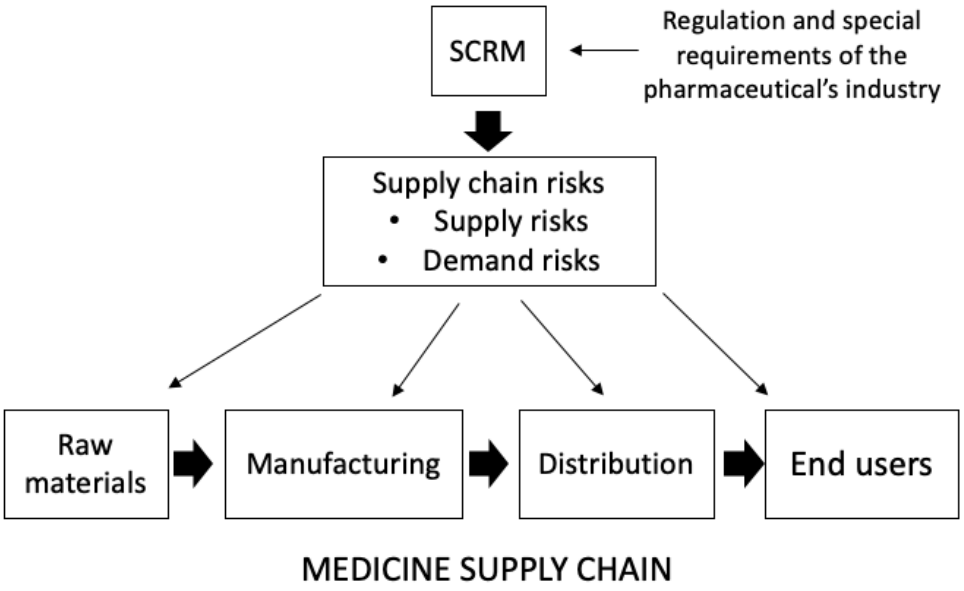

Figure 1 Thesis framework

Figure 1 illustrates the theoretical framework of this thesis i.e., how the key concepts (explained in chapter 1.3) and theory are linked together to form a framework for the study. The thesis is based on theory about supply chain risks and supply chain risk management which are then applied to the medicine supply chain context focusing on the issue of medicine shortages. The special requirements and regulation related to

the pharmaceutical industry are examined to provide an overview on how they affect the supply chain risk management practices.

The objective of this thesis is to study the root causes for medicine shortages from the viewpoint of pharmaceutical wholesale licence holders and wholesalers operating in the Finnish market. The aim is also to find out how medicine shortages could be mitigated or prevented through supply chain risk management practices. Thus, this thesis will consist of a theory chapter about supply chain risks and SCRM, a review on medicine shortages based on literature and an empirical research study on medicine shortages in Finland. The operational environment within the pharmaceutical market differs between countries (Heiskanen et al. 2017). Thus, the characteristics of medicine shortages and the reasons behind them also vary and need to be studied at a country level as practices taken in some other country may not be feasible in the Finnish market environment. Thus, the main research question and two sub-research questions of this thesis study are:

1. ***Why do medicine shortages exist?***
    - ***1.1. Which supply chain risks cause medicine shortages in Finland?***
    - ***1.2. How to mitigate medicine supply chain risks?***

There are some limitations done in the scope of this study. Firstly, the study focuses on medicine shortages in Finland and to some extent also Europe as being part of the EU Finland has to comply with the EU rules and requirements regarding medicine authorisation and monitoring (EMA 2016). Furthermore, according to Heiskanen et al. (2017) European countries mainly share common underlying reasons for medicine shortages. The empirical part is based on pharmaceutical wholesale licence holders' and wholesalers' perceptions on medicine shortages as it was considered that they are well acquainted with the operation and characteristics of the pharmaceutical market and pharmaceutical supply chains. Other countries or markets are excluded from this research to better manage the topic.

1.3 Key concepts

The key concepts of this thesis are presented below. The chosen explanations were considered the most appropriate ones regarding the context of this thesis.

Medicine (pharmaceutical, drug) shortage: "*Shortcoming in the supply of a medicinal product that affects the patient's ability to access the required treatment in due time."* (Pauwels et al. 2015, 1)

Supply chain risk (SCR): "*Supply-chain risks can become full-fledged supply-chain problems, causing unanticipated changes in flow due to disruptions or delays. Disruptions can be frequent or infrequent; short- or long-term; and cause problems for the affected organization(s), ranging from minor to serious."* (Chopra & Sodhi 2004, 54)

Supply risk: "*The probability of an incident associated with inbound supply from individual supplier failures or the supply market occurring, in which its outcomes result in the inability of the purchasing firm to meet customer demand or cause threats to customer life and safety."* (Zsidisin 2003, 222)

Supply chain risk management (SCRM): "*The identification and management of risks for the supply chain, through a co-ordinated approach among supply chain members, to reduce supply chain vulnerability."* (Jüttner, Peck & Christopher 2003, 9)

1.4 Structure of the thesis

This thesis consists of 6 main chapters presented in figure 2. First, in the introduction chapter the background, aims of the research, research questions and key concepts are presented. The second chapter entails theory on supply chain risks and supply chain risk management based on existing literature. In the third chapter, a literature review on medicine shortages is provided as a background information for the empirical findings of the thesis. In the fourth chapter, the research methodology and data collection methods of the empirical study are presented. Fifth chapter covers the

empirical results and findings, and in the sixth chapter these findings are summarized and reflected to the theory presented in chapters two and three.

Figure 2 Thesis structure

2 SUPPLY CHAIN RISKS AND SCRM

Every purchasing organisation is exposed to supply risk which is why it is important for businesses to understand and manage risks, and to include risk management perspective in the implementation of their business strategy (Smallman 1996; Zsidisin 2003). Christopher (2011) argues that the biggest risks to business continuity in the volatile, contemporary business environment lie in the supply chain. A disruption anywhere in the supply chain may result in a supplier's failure to deliver the purchased goods or services and can have detrimental effects for the purchasing firm and further in the downstream supply chain (Zsidisin, Ellram, Carter & Cavinato 2004; Jüttner, Peck & Christopher 2003). Uncertainty causes risks, however, often it is impossible to remove uncertainty from the supply chain in which case the uncertainty must be accepted and a strategy that enables matching supply to demand despite the uncertainty must be developed (Hallikas, Karvonen, Pulkkinen, Virolainen & Tuominen 2004; Christopher & Towill 2001).

Risk has multiple definitions and can be perceived differently depending on the context which means that no single definition of risk will be appropriate in all circumstances (Zsidisin 2003). 'Risk' can refer to either the sources of risk and uncertainty or the consequences of them (Jüttner, Peck & Christopher 2003). Mitchell (1995) defines risk concisely as the probability of loss and the significance of it. According to Harland, Brenchley & Walker (2003, 52), risk is a "chance of danger, damage, loss, injury or any other undesired consequences". Finally, Sitkin and Pablo (1992, 10) define risk as "the extent to which there is uncertainty about whether potentially significant and/or disappointing outcomes of decisions will be realized". The latter definition entails dimensions of the uncertainty, expectations and potential of the outcome which should also be taken into consideration in the context of organisation's supply management (Zsidisin 2003).

In literature, terms 'supply chain risk', 'supply risk' and 'supply (chain) disruption' have similar meanings and are sometimes difficult to distinguish from each other. Chopra &

Sodhi (2004, 54) define supply chain risk as “Supply-chain risks can become full-fledged supply-chain problems, causing unanticipated changes in flow due to disruptions or delays. Disruptions can be frequent or infrequent; short-term or long-term; and cause problems for the affected organization(s), ranging from minor to serious.” Zsidisin (2003, 222) defines supply risk as “The probability of an incident associated with inbound supply from individual supplier failures or the supply market occurring, in which its outcomes result in the inability of the purchasing firm to meet customer demand or cause threats to customer life and safety.” Finally, Bode & Wagner (2015, 216) define supply chain disruption as “the combination of an unintended and unexpected triggering event that occurs somewhere in the upstream supply chain (the supply network), the inbound logistics network, or the purchasing (sourcing) environment, and a consequential situation which presents a serious threat to the normal course of business operations of the focal firm.” A common characteristic for all three definitions presented above is the interruption in material (or service) flows within the supply chain. All these definitions also feature the possibility of a large set of issues such as quality problems with suppliers, delivery outages, supplier defaults or fires (Bode & Wagner 2015).

2.1 Supply chain risks

To be able to respond rapidly to changing market environment, it is inevitable that organisations form networks and collaborate, which makes them more interdependent (Hallikas et al 2004). With increased outsourcing supply chains extend from one side of the world to the other, and confederations of companies are linked together to form ‘network organisations’ that consist of multiple tiers of suppliers (Christopher 2011; Hallikas et al. 2004). Risk related to the operation of supply networks is increasing as networks get wider and risks may occur in different parts and processes of the network (Harland, Brenchley & Walker 2003; Kleindorfer & Saad 2005). Also, whilst companies become more exposed to the risks of other companies as the dependency between them increases, it must be noticed that risks that are not substantial to one organisation, might cause significant consequences elsewhere in the supplier network

(Hallikas et al. 2004). However, technical development including digitalisation, data analysis capabilities as well as connectedness provide organisations operating in the contemporary business environment tools to detect and prevent supply disruptions and other risks within the supply network more efficiently than before (Zsidisin & Henke 2019).

Supply chain risks can be broadly divided into two major categories: demand and supply risks. Demand risks include seasonal imbalances in demand and new product adaption whereas supply risks include manufacturing and logistics capacity risks. (Johnson 2001) Chopra and Sodhi (2004) categorize potential supply chain risks in delays, disruptions, forecast inaccuracies, systems breakdown, intellectual property breaches, procurement failures, receivables problems and inventory or capacity issues. On the other hand, risk sources can result from supply disruptions, caused by major global events or less extreme and more locally appearing events. Such events inflicting supply disruptions may include for example natural disasters or natural phenomena, labor strikes, issues in shipment, machinery breakdowns, financial or political crises or acts of war or terrorism. (Fang et al. 2013; Chopra & Sodhi 2004; Hopp, Irvani & Liu 2012)

Christopher (2011) divides supply chain risks to external risks, arising from e.g. natural disasters or government-imposed legal restrictions, and internal risks arising as a result of how the supply chain is structured and managed. He further proposes that five main sources of risks across the supply network are supply risk, demand risk, process risk, control risk and environmental risk. Process risk refers to the resilience of the processes and the amount of variability in them, as well as locating the bottlenecks and how much additional capacity there is available if needed. Control risk refers to how much do the internal control systems, such as order quantities or safety stock policies of an organisation, contribute to supply disturbances or causing ‘chaos’. Finally, environmental risk refers to locating the points in the supply chain where the organisation is exposed to vulnerabilities.

Zsidisin (2003) found out through his study that risk is defined as a multi-dimensional construct by purchasing organisations. The concept of supply risk includes both sources and outcomes of risks. furthermore, the scope for how supply risk is understood varies according to industry. Supply management professionals must take the time to understand the sources and outcomes of risks as the effects of a harmful supply event may cause consequences throughout the organisation's supply network. Supply risk is often determined by the negative outcome, especially by the inability to meet customer requirements or even threats to customer life and safety. The inability to meet customer requirements may result in loss of customer business and negative impact in revenues and profits. Also, issues with product integrity, reliability or durability may result in endangering customer life and safety. (Zsidisin 2003) Hendricks & Singhal (2012) argue that supply disruptions indicate that a firm's supply chain is not robust and reliable. If such disruptions are ignored, they may lead to shipment disruptions of finished products to the customer. Short-term (tactical) consequences of supply chain disruptions may cause lost sales and revenue, and long-term (strategic) consequence might be lost market share. (Hopp, Irvani & Liu 2012) Furthermore, supply disruptions may cause lower stock returns relative to benchmarks, increase in share price volatility, drop in operating income and increase in overall costs (Hendricks & Singhal 2012).

2.2 Risk drivers

The following contemporary trends and practices act as potential drivers for supply chain disruptions: single sourcing, global sourcing, limited buffer stocks, focusing on efficiency, poor planning and execution capabilities, a high degree of concentration of suppliers and manufacturing (reliance on suppliers), bottleneck products or association with high-risk geographic areas, industries or products, long lead times, high level of product obsolescence and the potential to lose control over the supply chain operations (Hendricks & Singhal 2012; Christopher 2011). While having reduced the purchasing price and costs of managing the supplier base, single sourcing has also increased the vulnerability of supply chains in a situation where single-source supplier is unable to

deliver on time. When it comes to limited buffers, just-in-time delivery and zero inventory are commonly cited goals for organisations, however these strategies can make the supply chain fragile. The same applies to focusing on efficiency and reducing costs as well as over-concentrating operations at a particular location. (Hendricks & Singhal 2012) The Single Market within the EU and the free flow of products across borders has increased the centralization of production and distribution facilities as organisations are striving for economies of scale. Whilst centralization may lower production costs, the products have to travel longer distances and the flexibility of supply might suffer as centralized production facilities are often designed to produce very large batches. (Christopher 2011) Poor planning and execution instead result in more incidents of mismatched demand and supply (Hendricks & Singhal 2012).

Outsourcing, being one of the drivers of globalisation, affects the organisation and its immediate relationships as well as changes the structure and processes of the supply network (Harland, Brenchley & Walker 2003). Organisations can get access to global markets through outsourcing activities, which enables them to focus on their core capabilities, get access to key technologies and share risks with other network members, thus, strive for improved performance and cost savings (Harland et al. 2003; Christopher 2011; Hallikas et al. 2004). Other drivers for globalisation are strategic intent, economies of scale and scope, value chain management, free-trade, comparative advantage, market access and information technology (Harland, Brenchley & Walker 2003). Increased dependence of outsourcing and partnering has increased interdependency between the different nodes of supply network. This increases the chance of disruption in one link of the supply chain which can then rapidly spread through the chain. (Hendricks & Singhal 2012) Hence, actions taken by any company within the supply network may increase risks for another company involved in the network (Chopra & Sodhi 2004).

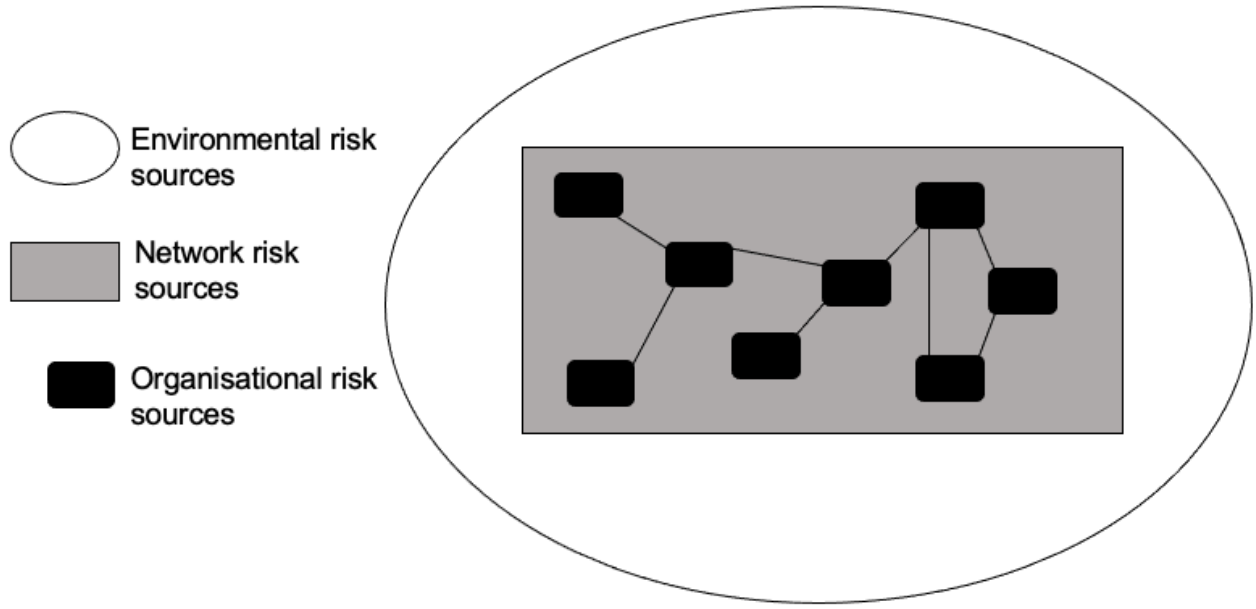

Figure 3 Supply chain risk sources (Adapted from Jüttner, Peck & Christopher 2003, 10)

In most cases the sources of supply chain risk arise from individual supplier failures or market factors and can be environmental, organisational or network related (figure 3) (Zsidisin 2003; Jüttner, Peck & Christopher 2003). Environmental risk sources arise from uncertainties regarding supply chain's interaction with the environment, such as accidents, socio-political actions or natural disasters. Organisational risks lie within the boundaries of each individual supply chain member organisation, ranging from e.g., labor, production, or IT-system uncertainties. Network-related risks arise from interactions between the supply chain members and can be distinguished into three categories: chaos, inertia, lack of ownership and lack of confidence. These concepts are explained in detail in the following paragraphs.

The uncertainty within a supply chain can increase the 'chaos' risk which results from e.g., over-reactions, mistrust and distorted information (Christopher & Lee 2004; Childerhouse et al. 2003). Information distortion increases as a result of inadequate information about demand within the upstream supply chain (Chopra & Sodhi 2004).

The ‘bullwhip’ effect related to increased fluctuations of order patterns throughout the supply chain is an example of distorted information causing chaos (Christopher & Lee 2004; Lee, Padmanabhan & Whang 2004; Chopra & Sodhi 2004). Inertia on the other hand refers to a lack of responsiveness to changing environmental and market conditions and can result in inability to react to unpredicted events arising from environmental or organisational risk sources (Jüttner, Peck & Christopher 2003).

Lack of confidence in supply chain related concepts such as order cycle time, demand forecasts, supplier’s capability to deliver, quality of the products or transportation reliability to name a few, might increase supply chain’s risk exposure. If these factors are not reliable, it means that there is not enough visibility in the upstream and downstream flows of the supply chain. This leads to precautionary measures such as building excessive inventory buffers, which again distorts the supply chain visibility. (Christopher & Lee 2004) Followingly, the forecast risk increases when there is a mismatch between the projected and actual demand. Other factors increasing the forecast risk include long lead times, short product life cycle and high product variety. (Chopra & Sodhi 2004) Another network-related risk triggered by trends such as outsourcing is the ‘lack of ownership’ which refers to confused lines of responsibilities between buyers and suppliers within a network caused by insufficient interaction (Jüttner, Peck & Christopher 2003).

2.3 Supply chain risk management

Any change within the supply network has the potential for systemic or disruptive risk. Regardless of the scale of the change or whether it is anticipated or not, organisations typically have the ability and experience to manage the risk. (Lynch 2012) However, supply chain risks might be challenging to manage because individual risks are often interrelated and therefore actions to mitigate a specific risk can exacerbate another (Chopra & Sodhi 2004). In addition, the consequences of risks are difficult to manage, and critical incidents may affect others heavily and change their perception of a company or brand (Harland, Brenchley & Walker 2003). Therefore, company’s risk

management has to be holistic and comprise of multiple approaches in order to be efficient in avoiding risks (Smallman 1996). To deal with supply chain risks, companies must develop robust capabilities which requires leadership, detailed and careful planning and commitment of resources (Hendricks & Singhal 2012). Firms that passively accept the supply chain risks, leave themselves exposed to financial and market-share losses (Tomlin 2006). Companies must carefully balance between the appropriate level of inventory, capacity and other business elements to succeed in the dynamic contemporary business environment (Chopra & Sodhi 2004).

Researching the supply chain deficiencies can be problematic as supply chains or networks are often complicated and dynamic by nature and consist of wide range of operators from different parts of the world (Harland, Brenchley & Walker 2003). With a well-designed and risk-oriented supply chain management companies can improve their overall performance, competitiveness and thus their ability to bring value to the stakeholders in their value chain (Teuscher, Grüninger & Ferdinand 2006). The structure of a supply network influences the performance of the network in a disruptive event. Factors related to the network structure include the number of levels and nodes at each level, type and location of the nodes as well as coordination of them. A node in a supply chain may be a raw material or component supplier, a manufacturer, a distribution center or a retailer. (Hopp, Irvani & Liu 2012) The more nodes and links there are in the supply chain, the greater the risk of failure (Christopher 2011). According to Ritchie & Brindley (2007) a successful management of risks is an important measure of the overall management performance of an organisation. Chopra & Sodhi (2004) argue that organisation's level of preparedness as well as the type of supply chain disruption define how the organisation fares against supply chain threats.

According to Lynch (2012), the basic risk terminology and elements of supply chain risk measurement and management are: threats, vulnerabilities, likelihood, impact and investment. Threats are elements that might potentially cause harm to the organisation. Vulnerabilities are weaknesses or points in the supply network where the organisation might be exposed or exploited. Likelihood is the possibility of a detrimental

event occurring, and a threat realizing. Impact means the direct and indirect effects of a negative event and can be measured e.g., in loss of revenue, margin, loss of brand, strategic value or inability to comply. (Lynch 2012; Zsidisin et al. 2004) Finally, investment refers to the amount of resources the organisation is willing to allocate to risk mitigation and risk-finance issues (Lynch 2012).

A key way to avoid supply chain disruptions is to conduct risk assessment and mitigation strategies and to strive for designing resilient supply chains (Ward & Hargaden 2019). To deploy a supply chain risk management system, commonly used process includes the following steps: identify, assess, measure, mitigate, validate and monitor risks (Lynch 2012; Hallikas et al. 2004; Jüttner, Peck & Christopher 2003). Figure 4 represents a tool for identifying, assessing and managing risk and can be used to conduct research on risks in complex supply networks. The supply network risk tool helps organisations in understanding the sources and outcomes of supply risks related to the operation of their firm and the supplier network. The process starts by mapping the supply network, then identifying, assessing and managing risk and finally, collaborative supply network risk strategy should be formed and implemented. (Harland, Brenchley & Walker 2003)

Figure 4 Supply network risk tool (Adapted from Harland, Brenchley & Walker 2003, 56)

Zsidisin, Ragatz & Melnyk (2005) state that many popular supply chain design principles focus on increasing efficiency and/or responsiveness of the supply chain rather than decreasing the risk of supply chain disruptions. Chopra & Sodhi (2004) suggest that when constructing a supply chain risk management strategy, managers should do two things: first thing is to create an organisation-wide understanding of supply chain risk, and the second thing is to determine how to adapt general risk mitigation approaches to their company and circumstances. According to Christopher (2011), the first stage of strategic risk management is understanding the company's internal processes in order to find the most relevant and critical threats. Only after that the external environment should be monitored for relevant threats in terms of how severe effects a failure would have on the supply chain performance. Then, developing

mitigation and contingency strategies accordingly can be initiated. In complex supply chains it is advisable to focus only on the critical paths.

Factors that contribute to choosing the optimal disruption-management strategy include cost, supplier characteristics, capacity, flexibility, risk tolerance of the focal firm and the length of disruption (Tomlin 2006). Often used risk management strategies include risk transfer, risk taking, risk elimination, risk reduction and further analysis of individual risks (Hallikas et al. 2004). The most successful companies mitigate supply risks by implementing various risk management strategies such as inventory, capacity and redundant suppliers concurrently (Chopra & Sodhi 2004; Tomlin 2006). According to Tomlin (2006), active disruption management strategies build upon mitigation and contingency actions. However, in some circumstances the best strategy might be passive acceptance of a risk, as risk mitigation and management actions are not free (Tomlin 2006). The challenge in dealing with supply disruptions is to find approaches that do not sacrifice the efficiency achieved by following the practices and trends presented in above chapters. Choosing the appropriate approach depends on the firm's operating environment and systematic process for risk management is needed to find out which strategies each firm should adopt. (Hendricks & Singhal 2012)

2.3.1 Risk identification and assessment

Identifying risks enable organisations to become aware of events causing uncertainty. Risk identification is vital in recognizing future uncertainties and to be able to proactively manage those scenarios. (Hallikas et al. 2004) Collaboration between supply chain partners should be increased to collectively identify the critical nodes and links within the supply chain, and to react to them in an appropriate manner (Christopher & Lee 2004). In addition, to mitigate and manage risks, they also need to be measured (Hallikas et al. 2004). Risk assessment and prioritization are needed both at the company and network levels to be able to choose the most suitable risk management practices according to each situation. Risk assessment consists of evaluating the likelihood of occurrence, exposure, triggers, and possible losses (Harland, Brenchley & Walker 2003). Risks are related to each organisation's

objectives, which is why risk assessment should be carried out from the company's own perspective as the risk transfer in a network may increase risks for some companies and decrease them for others. However, the dependencies on other organisations in a networked environment must be taken into consideration in the risk identification process. (Hallikas et al. 2004) When proactive supply management tools, especially those focusing on supplier quality issues, improving supplier performance and preventing supply disruptions, are implemented, supply risk assessment may occur as a secondary benefit (Zsidisin et al. 2004). Figure 5 illustrates how the risk analysis process has the task of identifying and quantifying risks along the extended supply chain (from suppliers through production and logistics to customers) and helping to determine appropriate risk mitigation and response strategies.

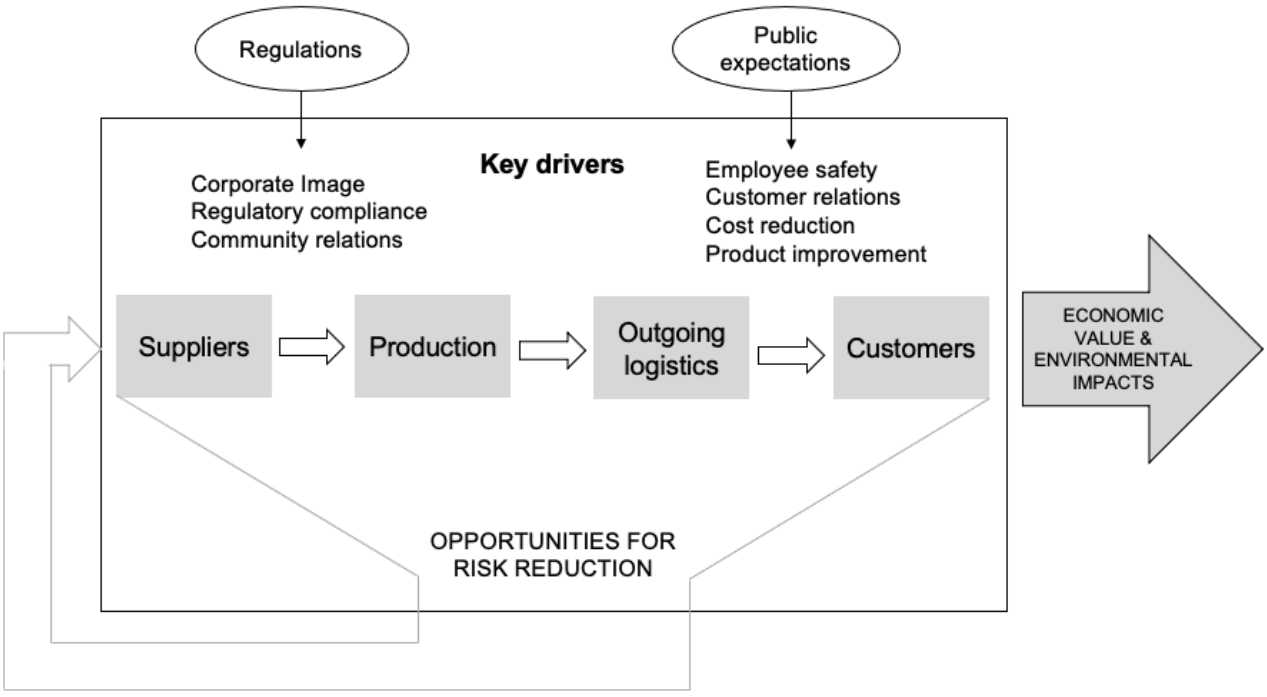

Figure 5 Risk analysis in the extended supply chain (Adapted from Kleindorfer 2000, 16)

To find out where the greatest vulnerabilities lie in the supply chain, and what is the likelihood of a disruption, a supply risk profile should be established for the business. To identify the risk profile, a risk audit can be carried out to examine the main sources of potential risks across the supply network and the likelihood of occurrence and possible impact of them. The risk profile also changes constantly, as economic and market conditions as well as the regulatory environment change. (Christopher 2011) It is important to realize that different events causing supply disruptions may vary greatly in terms of likelihood and severity (Hopp, Irvani & Liu 2012). Some events are not likely to happen but when they do, they may potentially cause severe consequences. Whereas some events occurring more likely or frequently might not have as dramatic consequences. This is why risks should not be solely looked at in terms of total impact (likelihood of occurrence times consequence) but rather inspect the events through the qualitative effects they might cause for the firm. (Hopp, Irvani & Liu 2012) Each strategic decision should be considered also in terms of how they may affect the vulnerability of the firm's supply chain (Christopher 2011).

2.3.2 SCRM strategies

Ritchie & Brindley (2007) argue that classic supply chain risk management systems such as buffer stocks and built-in slack in delivery lead times are becoming less practicable in the contemporary world, as with lean thinking, just-in-time production and material requirements planning, the requirements are included in the contractual arrangements. Harland, Brenchley & Walker (2003) suggest that scenario planning, use of expert panels and prediction through statistically based forecasting methods should be incorporated in modern risk management. According to Chopra & Sodhi (2004) leading companies use holding reserves that include excess inventory, capacity and redundant suppliers to deal with the range of supply chain risks. Succeeding in managing the costs and benefits of holding reserves however requires a good understanding of supply chain risks and remedies. The organisation's operating environment strongly affects the choice of a risk mitigation strategy. Motivating factors such as trust and dependence also influence the choice. (Mishra, Sharma, Kumar &

Dubey 2016) Identifying the events that may cause supply disruptions and evaluating the likelihood of those events are means to prepare for disruptions and reduce their impact (Hopp, Irvani & Liu 2012; Christopher 2011).

Hendricks & Singhal (2012) suggest the following approaches to balance the trade-off between supply chain efficiency and supply disruption risk: improving the accuracy of demand forecasts, integrating and synchronizing planning and execution to avoid supply-demand mismatches, reducing the mean and variance of lead time, collaboration and cooperation with supply chain partners, increasing visibility of the supply chain, building flexibility in the supply chain and investing in technology. Christopher (2011) divides supply chain risk mitigation strategies into two categories: redundancy and flexibility. Redundant solutions include increased inventory, backup systems and long-term supplier relationships. Flexible responses include delayed product differentiation, flexible manufacturing practices, lead-time reduction, dynamic inventory planning, supply chain visibility and cross-training of employees. Whilst redundant solutions are common traditional risk-management approaches, flexible responses not only manage risks but also increase the competitive capabilities of an organisation. Miller (1992) distinguishes five risk mitigation strategies, out of which four can be adapted to supply chain context according to Jüttner, Peck & Christopher (2003). These four strategies are avoidance, control, cooperation and flexibility. Some of the supply chain risk mitigation measures related to these four strategies are presented in table 1 and in detail in the subsequent chapters.

Table 1 Risk mitigation strategies in supply chains (Adapted from Jüttner, Peck & Christopher 2003, 19)

Avoidance	Control	Cooperation	Flexibility
purposely choosing specific suppliers, products or geographical markets	vertical integration buffer inventory excess capacity contractual obligations/incentives for suppliers	improvement of supply chain visibility information sharing collaboration	postponement multiple sourcing localised sourcing

Avoidance

In order to avoid negative impacts of inevitable supply disruptions as much as possible, firms must protect against them (Atan & Snyder 2012). Even though it is impossible to prevent events causing supply disruptions that are beyond human control, it is possible to reduce the likelihood of the event triggering a supply disruption (Hopp, Irvani & Liu 2012). One way to protect against disturbances in supply is to avoid factors that have great potential to cause disruptions. From a supply chain risk management perspective, avoidance strategy can include dropping specific products, suppliers or markets if they are seen unreliable in terms of supply (Jüttner, Peck & Christopher 2003). For example, sourcing from regions that are not prone to earthquakes from the risk avoidance point of view is more rational than sourcing from areas that have a high risk of natural disasters (Hopp, Irvani & Liu 2012).

Control

Organisations should try to control contingencies from risk sources rather than passively accept that they must operate under uncertainties (Miller 1992). Examples of control in SCRM context include i.a. vertical integration, buffer inventory, excess

capacity or imposing contractual requirements on suppliers (Jüttner, Peck & Christopher 2003). Supply chain members should also possess contingency plans and tools for making corrective actions in a disruptive event (Christopher & Lee 2004). Supply disruptions may cause problems for firms competing for limited supplies of backup capacity, so a quick and decisive response to a disruption may help the firm in avoiding disruptions for the customers. Response strategies can be further divided into detection and speed strategies. Detection strategy requires coordinated efforts in several business dimensions, such as distinguishing disruptions from normal day-to-day variations, locating the disruption in the supply chain and efficient transfer of information to where it is most needed. Speed strategy instead refers to quick detection and response to events that may cause supply disruption, e.g., locking up the available backup supply. (Hopp, Irvani & Liu 2012) Furthermore, a rapid access to information about supply disturbances is a prerequisite for building supply chain resilience (Christopher 2011).

According to Hopp, Irvani & Liu (2012) the consequences of an inevitable supply disruption will not reach the end customers if there is enough extra capacity and downstream inventory within the supply chain. Capacity plays a crucial role also in the supplier's recovery in the aftermath of a disruption (Tomlin 2006). Inventory is an effective tool to mitigate the negative effects of supply disruption (Hopp, Irvani & Liu 2012; Atan & Snyder 2012). Considering possible supply disruptions, the optimal inventory management system requires higher inventory levels than what are needed in normal circumstances. This however causes extra costs and since disruptions are considered rare events, holding high inventory levels might not be desirable by managers. (Atan & Snyder 2012; Chopra & Sodhi 2004) Excessive buffer inventory or capacity might also distort the supply chain visibility which makes it less feasible to react to irregularities or unexpected events within the supply chain (Christopher & Lee 2004). Thus, holding inventory might be an appropriate strategy for products with low holding costs whereas responsive delivery strategy might be more suitable option with expensive products with short life cycle (Chopra & Sodhi 2004).

In case of long-lasting supply disruptions, also other protective strategies are required besides inventory. Inventory is expensive and traditional models for the strategic design of supply networks primarily aim to cost-efficiency and lean strategies, which is why just-in-time (JIT) supply chains are often considered an appropriate strategy and are very commonly used in many industries. However, JIT supply chain is based on an assumption that all elements of the supply chain always perform as planned. This makes the supply chain very vulnerable in case the elements do not perform as planned. (Hopp, Irvani & Liu 2012) Thus, the main concern in inventory management is to find the optimal policy as to when, how much and from whom to order (Atan & Snyder 2012). Although single sourcing eliminates the costs and intricacies related to diversification, it may pose the supply chain to vulnerability and disruptions if there is high demand for the single supplier's products from other firms as well. All significant factors, including the disruption profile, inventory costs, fixed and variable supplier costs, capacities and response times need to be taken into consideration when choosing a sourcing strategy for a firm. In addition, the strategies are not mutually exclusive and in many cases a combination of strategies is the most reasonable solution. (Schmitt & Tomlin 2012)

When the flow of supplies is disrupted at a particular node of a supply network, firms can use alternative 'back-up' sources to ensure the material flow continuation. Securing extra capacity is another form of redundancy protection and contingency planning and can be divided into already existing physical capacity and virtual capacity which can be created if it is needed. (Hopp, Irvani & Liu 2012; Kleindorfer & Saad 2005) Fully owned redundant capacity is the quickest type of capacity to bring online but also the most expensive form of redundant capacity. Virtual capacity on the other hand is less expensive but not as quickly accessible. (Hopp, Irvani & Liu 2012) Securing excess capacity also lowers the amount of inventory needed, however excess capacity must be flexible in order to avoid it negatively impacting the financial performance of an organisation (Chopra & Sodhi 2004).

Cooperation

By forming strong linkages with other supply chain members and improving the vertical integration, firms can protect against the disruption risk. Trust between the exchange partners is beneficial for strengthening the long-term relationships. Also, the more there is dependency between a buyer and a supplier, the more there must be trust between them to reduce risks. (Mishra et al. 2016) Collaborative information sharing among supply chain partners is vital in identifying vulnerabilities and executing effective crisis management (Kleindorfer & Saad 2005). Working with suppliers and customers and insisting them to monitor and manage supply chain vulnerabilities would potentially cause a snowball effect if each node of the network were to work with their first-tier supplier to achieve better performance in supply chain risk management (Christopher 2011).

According to Kleindorfer & Saad (2005) disruption risk alignment should provide incentive alignment and collaboration for risk reduction and avoidance among all supply chain partners as one weak partner in the supply chain may cause undesirable consequences for all supply chain members. Thus, early-warning and crisis-management systems must be applied across the whole supply chain to detect vulnerabilities. Also, Hallikas et al. (2004) suggest that sharing risk management process and developing collaborative means to manage risks in the business network is useful as the interconnections between the companies make them interdependent.

Limited visibility is a common problem in many supply chains. It means that a certain entity in the supply chain is not aware of the status of upstream and downstream operations of the network. (Christopher 2011) Increased visibility throughout the supply chain will prevent risk exposure. The relevant data should be accurate and timely and available for all key members of the supply chain. (Christopher & Lee 2004) Increasing visibility means that firms are aware of what happens in their supply chain, including their internal operations, suppliers, customers and the location of inventory, capacity and critical assets. Through increased visibility and control over the supply chain

organisations are able to tackle the lack of confidence in supply chain processes as well as inhibit the bullwhip-effect (Christopher & Lee 2004; Chopra & Sodhi 2004). To increase visibility firms can use indicators of supply chain performance to collect and analyse data and to monitor them against benchmark (Hendricks & Singhal 2012). The key to improved visibility is information sharing among supply chain members, as shared information reduces uncertainty and thus increases the responsiveness of the supply chain (Christopher & Lee 2004).

Flexibility

As even the best managed supply chains might be affected by events that cannot be forecasted, it is vital that resilience is built into them. Resilience indicates a system's ability to return to a desired state after being disturbed, thus, system's resiliency means that the system is flexible and agile. (Christopher 2011) Flexibility and agility of resources reduce risks and increase the speed of response to disturbances (Kleindorfer & Saad 2005). Furthermore, building flexibility in the supply chain enhances its responsiveness and the appropriate dimension of flexibility for each firm depends on the firm's operating environment (Hendricks & Singhal 2012).

Tomlin (2006) suggests that volume flexibility i.e., supplier's capability to ramp up production when needed, is a strategy which provides substantial benefit and can lower the costs of the focal company. It is an alternative for inventory in managing temporary imbalances of demand and supply. Schmitt & Tomlin (2012) focus on two alternative sourcing strategies: diversification and emergency backup sourcing. Diversification refers to diversifying supply sources i.e., using multiple sourcing to acquire same product on a regular basis. Kleindorfer & Saad (2005) argue that full potential of risk minimization can be achieved only with multi-dimensional diversification which includes diversification of facility locations, sourcing options, logistics and operational processes reduces risk. Diversification is time-consuming and requires constant investment in multiple supplier relationships, however it ensures the

material flow in a situation of interruption if at least one supplier remains operating (Schmitt & Tomlin 2012).

On the other hand, making a firm's supply base leaner offers clear savings so firms must weigh the risk-mitigation benefits of diversification against the cost of extending the supply base (Schmitt & Tomlin 2012). However, Kleindorfer & Saad (2005) point out that extreme leanness and efficiency may increase the level of vulnerability across the supply chain. Fang et al. (2013) suggest that as adding additional suppliers to the supplier base increases fixed costs, it is preferable to choose the sourcing strategy between contingent sourcing (single supplier and a backup supplier) or dual sourcing (two regular suppliers). Instead of routinely sourcing from multiple suppliers, firms may choose single sourcing under normal circumstances and when the primary supplier is unable to supply, an emergency backup supplier can be used. Other means of increasing flexibility include the postponement strategy and localized sourcing. Postponement refers to organisations delaying the decision to produce, label or ship a product to increase supply chain flexibility. Postponement strategy increases flexibility as it reduces an organisation's dependency on forecasts and increases the ability to respond to variations in demand. Localized sourcing may also contribute to reducing supply risk through shortened lead-times and potential for quick responses in fluctuating demand and supply. (Kleindorfer & Saad 2005)

3 MEDICINE SHORTAGES

Medicine shortages affect every stakeholder (suppliers, manufacturers, healthcare professionals and patients) of the health care system causing i.a. difficulties and extra workload for healthcare professionals, additional costs, and compromising patient safety (Besancon & Chaar 2013; WHO 2016; Jenzer et al. 2019). Causes for medicine shortages often arise from manufacturing problems but may also involve economic factors (Pauwels et al. 2015). According to EAHP medicine shortage report 2019 a large majority of hospital pharmacist's that took part in the survey, agreed that medicine shortages are frequently encountered in their hospital. Medicines affected by shortages include i.a. those used for treating cancer, infections, emergencies, neurology and cardiovascular conditions as well as anaesthetic products and nutritional support products (Jenzer et al. 2019; Mazer-Amirshahi, Fox, Farmer & Stolbach 2019).

A harmonized definition of medicine shortages should be determined as the first step of alleviating the issue (Ward & Hargaden 2019; Jenzer et al. 2019). The definition of medicine includes in addition to drugs, also medical devices, foodstuff for special medical purposes as well as nutraceuticals (Barbosa-Povoa, Jenzer & de Miranda 2019). WHO (2017) has proposed two co-existing definitions for medicine shortages, which emphasise the needs of patients, the important role of medicines as well as the natural characteristics of the healthcare system's environment and the pharmaceutical market. On the supply side "A "shortage" occurs when the supply of medicines, health products and vaccines identified as essential by the health system is considered to be insufficient to meet public health and patient needs. This definition refers only to products that have already been approved and marketed, in order to avoid conflicts with research and development agendas." (WHO 2017, 10) On the demand side "A "shortage" will occur when demand exceeds supply at any point in the supply chain and may ultimately create a "stockout" at the point of appropriate service delivery to the patient if the cause of the shortage cannot be resolved in a timely manner relative to the clinical needs of the patient." (WHO 2017, 10) Two concise definitions of

medicine shortages are provided by Bogaert et al. 2015 and Pauwels et al. 2015. Bogaert et al. (2015, 2) define medicine shortage as “a situation in which the current or projected demand of a medicine at user level is inadequately met.” According to Pauwels et al. (2015, 1) a medicine shortage can be described as “a shortcoming in the supply of a medical product that affects the patient’s ability to access the required treatment in due time.”

Medicine shortages cause harm for the patients but also negative consequences for the economy (Jenzer et al. 2019). In most cases there are available treatments available for substituting the primary treatment in case of a supply disruption yet finding a substitutive requires considerable amount of time from healthcare professionals (Pauwels et al. 2015; Besancon & Chaar 2013). In some cases, however there is no feasible substitutes available which may require doctors to choose which patients to treat (Besancon & Chaar 2013). Using a substitutive medicine increases risks caused by using other excipients, concentration or untranslated package information leaflets (Jenzer et al. 2019). Medicine shortages also increase medical care costs from both the patient’s and the society’s perspective (Sarnola & Linnolahti 2019). Shortages increase costs for healthcare systems directly, but also indirectly by increasing invisible costs in terms of for example time spent in solving the shortages and changes in management procedures (Barbosa-Povoa, Jenzer & de Miranda 2019). According to Fox, Sweet & Jensen (2014) the estimated financial effect of medicine shortages in the U.S. is hundreds of millions of dollars annually. Patients instead might be negatively affected by clinical impact such as medication error, adverse effects, delays in medical care and disease progress caused by using substitutive medicine (Pauwels et al. 2015; Sarnola & Linnolahti 2019).

According to EMA (2012) reflection paper, the risk management in the pharmaceutical industry often tends to be more reactive than proactive. However, both reactive and proactive measures are needed as the medicine shortage issue cannot be tackled by a single act alone. Reactive measures include i.a. increasing transparency, carrying out risk assessments and redirecting medicines to individual patients when and where

they are needed. Proactive measures include i.a. the adoption of prudent tendering practices to avoid ‘the winner takes it all’ solutions as well as to lower the risk of single supplier dependence. (EAHP 2019) Reduction of risk and the management of emergency situations where shortages of critical medicines occur, are critical aspects that need to be controlled. The risk associated with different elements can be reduced by conducting analysis of the likelihood of occurrence and severity of risk factors. Evaluating the supply chain risk factors should be the key point in starting the risk assessment of medicine supply chain. (Battistini 2019)

3.1 Causes and mitigation strategies

Reasons for medicine shortages are often multifold because the manufacturing and distribution of medicines include the operation of various different actors such as the raw material supplier, manufacturer, wholesaler, pharmacy or hospital and regional authorities (Lääketeollisuus 2020a; Jenzer et al. 2019). The manufacturing of European medicines is largely outsourced and centralized into countries of low labour costs and often medicine manufacturers use subcontractors for production and testing. Furthermore, in many cases pharmaceuticals that belong to the same product category, but are sold by different pharmaceutical companies, are all actually manufactured in the same production facility, in most cases in China or India. This is a factor that makes the supply chain of medicines vulnerable and prone to disruptions. (Besancon & Chaar 2013; Junttonen 2017)

To avoid medicine shortages in the market, ensuring supply continuity is one of the main aspects and to succeed in ensuring supply continuity, mitigation activities and long-term strategies must be distinguished from each other. Mitigation activities are targeted to preventing supply disruptions from turning into medicine shortages whereas long-term prevention strategies should address the root-causes of shortages to be able to prevent supply disruptions from occurring in the first place. (Battistini 2019) Tackling medicine shortages can be done both, in national and multi-national levels (Sarnola & Linnolahti 2019). Designing predictable, redundant and resilient

supply chains that are able to quickly react to changing demand or problems at a manufacturing site helps in preventing medicine shortages (Battistini 2019; Yaroson, Breen, Hou & Sowter 2019). Battistini (2019) also stresses out the importance of supply chain agility in mitigating medicine shortages. In addition, consolidating quality and implementing systems that proactively identify, measure and monitor risks across the whole supply chain are the key aspects to be taken into consideration.

Due to increased outsourcing of medicines and raw materials, the range of potential causes for disturbances in the supply of medicines is wide and these causes can originate from either supply or demand related reasons (Lääketeollisuus 2020a; Pauwels 2015). The causes can be related to economic, business, political, manufacturing or distribution issues (Battistini 2019). On a more practical level natural disasters, epidemics, lack of raw material, problems in the production process, unexpected demand, or shortages in a competing company's product may result in medicine shortages (Lääketeollisuus 2020a; Birgli 2013). In addition, insufficient inventories, strict regulation regarding medicine production and quality, hoarding of medicines by some purchasers, counterfeit medicines, grey markets (stockpiling medicines at risk of being in shortage and selling stock at extremely high prices once a shortage occurs) and imperfect purchasing policies further contribute to hinder supplying medicines where they are needed when they are needed (Besancon & Chaar 2013). It should be taken into consideration that the perceptions about the reasons causing medicine shortages may vary for example between different professional groups or geographical location of the market in question. The differences between professional groups may reflect the differences in the tasks and responsibilities of each group. (EAHP 2019)

Battistini (2019) listed eight overall business strategies for reducing the risk of medicine shortages from the viewpoint of supply chain. These strategies are business continuity planning, supply chain management, safety stock of raw materials, safety stock of intermediates and finished products, backup internal and external manufacturing facilities, dual-source suppliers, ability to add a shift to an existing manufacturing line

and warm starts. Also, periodic risk assessment reviews, periodic assessment of supply chain performance, trending reports, issue management communication system and improvement of processes and analytical standards should be considered in order to reduce the risk of supply disruptions.

3.1.1 Economic and market factors

Fluctuating market demand can affect, and sometimes lead to, medicine shortages. Factors affecting demand include i.a. price, tendering and epidemics. Forecasting the demand is challenging as it often relies on seasonal trends and scarce historical data. Also, special attention should be given to the internal demand of emerging economies, such as China and India, producing API's and manufacturing medicines. If this demand is not appropriately met with increased capacity, the provision of medicines between international and internal markets may cause tensions as already seen for example in China. Economic factors such as limited financial purchasing capability or corruption may also hinder the distribution or acquisition of medicines and thus, cause shortages. (Besancon & Chaar 2013)

Market entry for new pharmaceutical producers is costly and unpredictable process due to challenges related to maintaining quality systems, attaining regulatory approval and frequently changing regulatory requirements (WHO 2016). Furthermore, globalisation, increasing competition and diminution of patent protection add pressure to new product development and market entry. The time-to-market of a new pharmaceutical product takes a long period of time, from 2 to 15 years, and after the clinical trials only a few promising compounds will be filtered out of substantial amount of new chemical compounds and reach the market. (Gatica, Papageorgiou & Shah 2003) The production of certain medicines such as antibiotics, hormones and cytotoxic drugs also requires specific production facilities and knowledge or complex standards of quality assurance in production (Besancon & Chaar 2013; Battistini 2019). Establishing redundant production capacity is challenging if manufacturing requires specialised, segregated or self-contained production lines. The setup of these kind of

facilities requires a great amount of investment and the profitability of them is uncertain if the demand is not stable and the margins for products are low. (Battistini 2019)

Most developed countries usually impose stricter national regulations for medicines to ensure and improve quality which may result in weakened availability (Besancon & Chaar 2013). In the U.S. for example, increased FDA inspection and compliance activities as well as their scrutiny of manufacturing process have resulted in temporary stops of medicines manufacturing and thus may result in supply disruptions (Mazer-Amirshahi et al. 2017). Policy mechanisms and harmonization efforts should highlight the support for good manufacturing practices (GMP), coordination of strategies for the notification of medicine shortages as well as appropriate supply chain management (Besancon & Chaar 2013; Iyengar, Hedman, Forte & Hill 2016). Proactive risk management should be promoted by marketing authorization holders by requiring submission of risk-analysis identifying any weaknesses in their manufacturing processes and possibly also providing contingency plans and proposals to tackle the weaknesses (EMA 2012). Also, to adequately address certain causes of medicine shortages a strong EU commitment is required (EAHP 2019). Legal and organisational strategies should be coordinated by EU institutions to address the issue of medicine shortages between all member countries and measures taken at the European level should be supported by national action (Bogaert et al. 2015; EAHP 2019).

Applicable civil penalties could be established and enforced for manufacturers who fail to notify the respective authority about a medicine shortage on time (Jenzer et al. 2019). On the other hand, Battistini (2019) suggests that more incentives should be provided for manufacturers so that they would enhance production in a situation where another producer leaves the market or there is otherwise a risk of disruption in the medicine supply. Clinicians and responsible organisations should work together to make medicine manufacturers responsible for the availability of medicines and adaptation to shortages (Rinaldi, de Denus, Nguyen, Nattel & Bussières 2017) Harmonization of regulation and standards on manufacturing as well as product approval between countries could help minimize the fragmentation of the medicines

market and thus facilitate the allocation of medicines to places and situations where shortages are experienced (Besancon & Chaar 2013).

Countries that consume only a small percentage of the overall medicine consumption, and do not have a viable manufacturing industry for medicines, are more prone to medicine shortages compared to countries that have bigger consumption for medicines (Besancon & Chaar 2013). Bigger markets might be prioritised by pharmaceutical companies and wholesalers as they may consider that as market and volumes are small, but production and remediation costs are high, the market may seem unattractive and have low-profits (Heiskanen et al. 2017; Mazer-Amirshahi et. al. 2017; Besancon & Chaar 2013). As a result, pharmaceutical companies might opt out of the market as it is not desirable to cope with limited volumes and profits. In the long run, this may lead to limited number of companies operating in the market which decreases the redundancy of the manufacturing system and thus may contribute to increasing medicine shortages. (Sarnola & Linnolahti 2019; Mazer-Amirshahi et. al. 2017)

3.1.2 Supply related factors

Main causes for medicine shortages connected to manufacturing include i.a. unexpected shortages of starting materials, intermediates and auxiliary materials as well as contamination, quality issues and unforeseen results of monitoring in routine manufacturing (Battistini 2019). The scarcity of raw material producers and medicine manufacturers contribute to shortages as these suppliers cover a significant part of the global demand and thus it is hard to replace shortages on a short notice (Heiskanen et al. 2017; WHO 2016). In addition, even if there were multiple potential suppliers available in the global level, only few of them are included in the marketing authorisation to the EU (EMA 2012). Many API suppliers are nowadays wholly located outside the EU, mostly in China or India. Medicine manufacturers' reliance on just a few suppliers on a global level poses medicine supply chain a risk factor potentially causing instability within the global supply chain. (Besancon & Chaar 2013)

Ensuring that API producers meet quality standards should be given closer attention and audit reports of API suppliers could be shared between different stakeholders in the supply chain (Besancon & Chaar 2013). Following the principles of Good Manufacturing Practices (GMP) in medicine manufacturing is considered a critical aspect in the process of mitigating medicine shortages. GMP compliance issues and quality defects are often linked to manufacturing problems. (Battistini 2019) To ensure appropriate and continued supply of medicines, it is the marketing authorisation holder's responsibility to ensure that GMP are being complied across the manufacturing supply chain. An arm's length relationship between the marketing authorization holder and the manufacturer may result in GMP compliance remaining marginal and causing potential quality issues within the production. (EMA 2012)

Ensuring a diverse set of suppliers for medicines as well as raw materials and API's would increase supply chain resilience and thus prevent supply disruptions (EAHP 2019; Besancon & Chaar 2013; Jenzer et al. 2019). When medicine shortages occur, using alternative suppliers increases the flexibility of sourcing (Ward & Hargaden 2019). Greater domestic manufacturing was also considered to reduce the risk of medicine shortages according to Heiskanen et al. (2017). In addition, supplier selection should be carried out diligently by manufacturers in order to avoid quality and GMP non-compliance risks and partnering with the supplier should be considered to help improve their quality systems as well (Battistini 2019). Thus, more attention should be paid to increasing collaboration between the different operators in the medicine supply chain to enhance quality and GMP compliance.

Heiskanen et al. (2017) found out that when It comes to manufacturing issues long and complex production chain is the most common reason behind medicine shortages. Controlling the reliability of the production chain becomes more difficult, the risk of quality issues increases, and manufacturing costs may potentially get higher as the production chain becomes longer or more complex. Thus, long and complex production chain causes more shortages compared to shorter, direct production chain. (Heiskanen et al. 2017) The consolidation of pharmaceutical manufacturing means that

there is little redundancy or spare capacity built in the global supply chain. Organisations' pressure to meet their economic targets means that production is highly optimized and when something unexpected occurs, there is a risk of production capacity being exceeded. (EMA 2012) Also, in case of a shortage, an alternative manufacturer may not be able to increase its production if it is already producing at full capacity (Fox, Sweet & Jensen 2014). Thus, capacity issues are also potential threat to ensuring the supply of medicines.

Whenever a manufacturing site stops production, the consequences for medicine supply chain can be substantial (Besancon & Chaar 2013; Battistini 2019). A manufacturing site may stop or reduce production due to malfunction of a production line, quality issues detected by the manufacturer itself through quality assurance or by an inspection of a medicine's regulatory authority (Besancon & Chaar 2013; Heiskanen et al. 2017). Quality defects and GMP non-compliances might cause a sudden gap in the supply of medicines if a batch is withdrawn from the market or not released at all as precautionary measure (Battistini 2019; Besancon & Chaar 2013). The inspection itself may lead to supply disruptions by delaying production but also the corrective measures taken to fix the problem may result in shortages. Maintenance shutdowns at the production site also cause supply disruptions if the manufacturer has not produced enough stock to cover the demand whilst the production is in standstill. (Besancon & Chaar 2013)

Inventory practices can have a crucial role in preventing or enabling medicine shortages. Incidents and supply disruptions at the manufacturing level can be compensated with inventory buffers of medicines. However, often inventories are just-in-time inventories which contributes to the impact of medicine shortages. Stock piling is in use only in a few countries and often contingency plans are not systematic. (Besancon & Chaar 2013) Low stock levels across the distribution chain are considered to cause medicine shortages (Heiskanen et al. 2017). According to Sarnola & Linnolahti (2019) it is necessary to have enough resilience towards disruptions in the medicines' distribution network. To help prevent negative patient impacts in case of a

supply disruption, manufacturers should ensure that there are enough raw material stocks and production capacity in multiple locations. In addition, sufficient volumes of alternative products should be stocked by wholesalers and retailers. However, Jenzer et al. (2019) argue that stockpiling of drugs should be prohibited to prevent medicines from being shifted away from healthcare facilities where there are patients in need of those medicines. Low stock levels might also be a conscious business decision in order to minimise warehousing costs as e.g., in Finland warehousing costs are higher than in some other European countries (Heiskanen et al. 2017). Regardless, it is important that optimal use of medicines is promoted to ensure accurate and clinically appropriate demand (Iyengar et al. 2016).

3.1.3 Information sharing and collaboration

According to EAHP (2019) improving communication and obliging medicine manufacturers to inform about medicine shortages in a timely manner were brought up among the top three proposals by hospital pharmacists to alleviate the medicine shortage problem. There are also gaps in the risk management practices regarding medicine shortages in hospital pharmacists. The lack of oversight and systemic indicators pointing out possible supply disruptions along the medicine supply chain as well as the lack of information regarding the current cases of drug shortages contribute negatively to the availability of medicines (Besancon & Chaar 2013). To be able to proactively and promptly react to a supply disruption or a medicine shortage, identifying the information sources in order to collect available data is required. However, data collection is not always straight forward as some key drivers of drug manufacturing and distribution are not always transparent. These key drivers may include production schedules, distribution of production volume across contract manufacturing facilities or supply or purchasing practices of the wholesaler or a pharmacy. (Battistini 2019)

According to Jenzer et al. (2019) a critical issue is that the stakeholders in the medicine supply chain do not collaborate sufficiently to ensure the supply of essential medicines. Marketing authorisation holders should promote clear and transparent communication and proactive risk management as integral measures in maintaining trust between all

stakeholders (EMA 2012). Communication and transparency between regulators and medicine manufacturers could enhance the development of corrective measures before shortages happen. Also, when regulators make decisions that affect the medicine supply chain, it is important that these decisions are communicated to other stakeholders as well. An open dialogue between purchasing officials and manufacturers could improve forecasting and planning. (Besancon & Chaar 2013) Modern communication systems should be developed on the national level in cooperation with the pharmaceutical industry, operators of the distribution chain, healthcare professionals and regulatory authorities in order to share information of medicine shortages (Sarnola & Linnolahti 2019). A system for reporting and tracking medicines in or at risk of shortages should be established to support health systems in identifying where the shortages occur or are likely to occur, and also the estimated length of the shortages (Jenzer et al. 2019; Ward & Hargaden 2019). Early warning systems should also be employed when possible to find substitutive medicines, alternative suppliers or other mitigation measures (Jenzer et al. 2019; Iyengar et al. 2016). In order to enable better response efforts, timely reporting of shortages is essential (Ward & Hargaden 2019).

4 RESEARCH METHODOLOGY AND DATA COLLECTION

The empirical part of the study was conducted as a qualitative multiple case study. There are a wide variety of approaches and methods included in the term of qualitative research. Primarily the information or data that is collected is nonquantitative in character and consists of textual materials such as interviews and documents or visual materials such as video recordings and internet sites. There can be multiple goals for qualitative research depending on the purpose of the study or project in question. The outcome of the research often consists of essential findings from the analytical synthesis of the data. It can include for example new insights and understandings on already existing research knowledge, evaluation of the effectiveness or a certain policy or program as well as critique of a certain course of action or method. (Saldana 2011)

There are several different types of qualitative research, case study being one of them (Saldana 2011). In a qualitative case study either single, or multiple cases are examined in order to gain real-world insights within the context of the research (Farquhar 2012; Saldana 2011). A multiple case study can be used to compare different cases and explore the differences between them. The aim is to get repetitious findings across the cases so that the researcher can predict either similar or contrasting results regarding the presented theory. (Yin 2003) A qualitative case study provides a tool to study phenomena within specific contexts and can be a valuable method for developing in-depth analysis, theories and interventions as well as evaluating programs (Miller 2007; Baxter & Jack 2008). According to Yin (2003) a case study approach should be considered when the study aims to answer in “how” and “why” questions.

Qualitative case study was regarded as suitable research method for this master’s thesis as the aim was to gain in-depth, real-life information on a specific phenomenon, to examine the reasons for it as well as to evaluate the methods behind it. The empirical research was conducted through semi-structured interviews which means that the interviews followed a certain guide but also allowed flexibility and adaptation in respect

to the context (Farquhar 2012). Using semi-structured interview method allowed complementary questions to be presented in addition to those that were in the interview frame. This way it was possible to gain more in-depth information from the interviewees.

The aim for the empirical part of this study was to find out what are the supply chain related root causes behind medicine shortages occurring in the Finnish market, and which supply chain risk management actions are currently applied to tackle or mitigate the medicine shortage issue. The empirical study was conducted by interviewing representatives from pharmaceutical wholesale licence holders and wholesalers. It was presumed that interviewing medicine wholesale licence holders and medicine wholesalers operating in Finland would best serve the objective of this research as representatives of these organisations are supposedly acquainted with how the medicine supply chain is built as well as the characteristics typical for medicine's industry. Furthermore, the outbreak of COVID-19 pandemic influenced the global economy drastically in 2020, and Mazer-Amirshahi et al. (2019) foretold that the pandemic has potential to further increase medicine shortages due to production and export interruptions of API's from China and India. Thus, the possible effects of the pandemic were also briefly studied in the empirical part. The interviewees were asked if the pandemic has affected medicine availability in Finland and how pharmaceutical companies have been able to prepare for or mitigate the possible negative impacts for medicine availability caused by the pandemic.

The interviewees represent four pharmaceutical wholesale licence holders and a wholesaler operating in Finland. Some of the wholesale licence holders have their own production of pharmaceutical products in Finland and/or elsewhere in Europe. Some also sell products of partner companies. Each company either has international operations of their own or is a part of an international corporation or group. The wholesale licence holders supply pharmaceuticals both to pharmacies and hospital usage through the wholesaler. The size of supplier base differed between the case companies, however, each interviewee stressed out that the supply chain behind

finished pharmaceutical products is almost without an exception long and consists of multiple actors. The interviewees also stressed out that the pharmaceutical industry differs considerably from other industries due to regulation regarding manufacturing, pricing and distribution. Interviewees, their job title and case company's field of operation are listed in table 2.

Table 2 Interviewees

Interviewee	Job title	Case company
A	Demand Planning Manager	Pharmaceutical wholesaler
B	Manager New Business and Hospital Sales	Pharmaceutical wholesale licence holder
C	Head of E2E Supply and Planning	Pharmaceutical wholesale licence holder
D	Supply Chain Head Finland	Pharmaceutical wholesale licence holder
E	Associate Director Portfolio & Business Development / Supply Chain & Customer Service	Pharmaceutical wholesale licence holder

In total, five interviews (one interview per each case company) were held for the empirical research. Interviews were held through video-calls and each interview lasted about an hour. Interviews were recorded to facilitate data analysis and reviewing the material afterwards. Interviews were held in Finnish so the empirical material and the citations in chapter 5 have been translated from Finnish into English. The interview frame consisted of eight open questions about themes medicine supply chain risks, medicine shortages and risk management measures against medicine and raw material availability issues. The eighth question handled COVID-19 pandemic and its possible effects for medicine availability. During the interviews, additional questions were also asked to complement the actual interview questions which were designed with a view to find answers to the research questions of this thesis. The interview

question frame was sent to the interviewees beforehand to allow them the possibility to become acquainted with the questions prior to the actual interview.

Based on the interviews, data that was substantial relative to the context of this thesis was firstly collected and then categorized into two main categories and multiple sub-categories. Categorisation was used to distinguish the substantial data relative to the scope of this thesis from the data that do not provide value for the objectives of this thesis. Even though the interviewees mostly kept to the point during the interviews, the discussion occasionally got side-tracked. Finally, once the interview findings were organised and categorised, they were then written out and analysed in the empirical section of this thesis. Direct quotes were also picked up from the interviews and written out in the report to emphasize some of the statements and to support the analysis.

5 RESEARCH FINDINGS

In this chapter the results and findings of the empirical study are presented and analysed. In chapter 5.1 an overview on the pharmaceutical market in Finland, based on existing literature, is provided as background information for the empirical findings. In chapter 5.2 the main risks for medicine availability based on the interviews are presented. Lastly, in chapter 5.3 ways to prevent or mitigate medicine shortages through SCRM efforts are proposed based on the interview findings.

5.1 Pharmaceuticals market in Finland

Finnish pharmaceuticals market covers approximately 1,1% of the European pharmaceuticals market and the Finnish market share of the global pharmaceuticals market is approximately 0,3% (EFPIA 2019; Elo 2018). In 2019 the total sales of pharmaceuticals at wholesale prices in Finland was 2,711 million euros and pharmaceutical imports were worth 2,011 million euros which indicates that Finland is heavily reliant on imports and foreign manufacturing of medicines (EFPIA 2019; Lääketeollisuus 2020b). Majority of the pharmaceuticals sold in the Finnish markets originate from other EU countries (Sarnola & Linnolahti 2019).

There are just a few wholesalers specialising in medicine distribution operating in Finland, largest being Oriola and Tamro. According to the single-channel principal, a pharmacy or a hospital can only use one wholesaler to procure a specific pharmaceutical company's products and each pharmaceutical company makes an exclusive distribution contract with the wholesaler, including all its products. (Pharma Industry Finland 2020; Heiskanen et al. 2017) Privately owned community pharmacies and university-owned pharmacies have the exclusive entitlement to sell prescription medicines and over-the-counter medicines in Finland. The trade and purchasing of medicinal products by the hospital districts and expert responsibility areas (ERA's), also known as hospital trade, is organised through obligatory competitive tendering procedure. (Heiskanen et al. 2017) To avoid counterfeit and to secure the availability of medicines, the whole distribution channel in Finland is closely and strictly controlled

by professionals (Pharma Industry Finland 2020). According to the Medicines act (395/1987) chapter 2 section 8 “medicinal products may only be manufactured industrially by medicinal product manufacturers that have acceptable production facilities and equipment and a license from the Finnish Medicines Agency (Fimea).” In addition, medicinal product’s wholesale trade is subject to a license issued by Fimea (Fimea 2020b).

The availability of medicines is critical for securing patient life and safety which is why legislation and regulation have been set by the EU and Finnish government, aiming to ensure medicine availability at all circumstances. The availability of medicines in a situation in which such availability is restricted, is ensured by the legislation concerning mandatory medical supplies reserve including critical and widely used medicines for 3 to 10 months’ average supply, depending on the medicine. (Fimea 2020a; Sarnola & Linnolahti 2019) The legislation applies to pharmaceutical companies, importers, health care units as well as the National Institute for Health and Welfare in Finland (Fimea 2020a). The mandatory reserve supply chain system, like any other national distribution system, is heavily reliant on the quality and continuous supply of medicines (Sarnola & Linnolahti 2019). According to the Medicines act chapter 5 section 37 the pharmaceutical wholesaler is obliged to inform breaks in medicines distribution and the estimated duration of them to Fimea and pharmacy, hospital pharmacy or veterinary who have ordered medicines.

All EU member states must comply with the EU rules and requirements regarding medicine authorisation and monitoring. All medicines must be authorised before they can be released to market in the EU. (EMA 2016) Regardless of where the medicine has actually been manufactured, a medicine factory located inside the European Economic Area (EEA) area must always release the medicine for distribution if it is to be sold in the EU. These factories must ensure that each production and testing phase of the medicine batch is carried out according to related EU regulation and instructions. Mostly also the final testing of pharmaceutical products is carried out in laboratories located inside the EEA. The manufacturer releasing the medicine for distribution, the

marketing authorisation holder and the pharmaceutical authority that has granted the sales permit for the medicine, must be aware of the complete production chain of the medicine. (Junttonen 2017)

Figure 6 illustrates a simplified version of production and supply chain of pharmaceuticals sold in the Finnish market. First 6 phases can be applied to any EU country as all member states must comply with the EU rules and requirements regarding medicine authorisation and monitoring (EMA 2016). The last phases instead illustrate the Finnish distribution system. In the first two phases raw materials needed for the API are procured and the API is produced. Then, the API with other substances is refined into a medicine either outside or inside Europe. Medicines are then packed in their primary package and delivered to destination before they are packed in their retail packages which have the required information leaflets attached. After that, medicines can be distributed to pharmacies or hospitals. (Junttonen 2017; Lääketeollisuus 2020c) Customers in Finland have access to medicines either through a hospital pharmacy, a community pharmacy or a university-owned pharmacy which acquire medicines from the wholesaler according the one-channel principal (Pharma Industry Finland 2020; Heiskanen et al. 2017).

Figure 6 Medicine supply chain (adapted from Lääketeollisuus 2020c)

As can be seen from figure 7, according to the annual number of shortage notifications reported to Fimea by the marketing authorization holders, medicine shortages have increased by approximately 180 percent in the Finnish market between 2010 and 2019. Based on previous research, the most common reasons, according to pharmaceutical companies and wholesalers, behind medicine shortages in Finland are small size of the pharmaceuticals market, sudden or fluctuating demand, small stock sizes, long lead times (from the point of placing an order to the point of the order being delivered to Finland) and dependence on foreign manufacturing (Heiskanen et al 2017). Small size of the market refers to small purchasing volumes, limited number of operating companies in the market and small language area with two native languages (Lääketeollisuus 2020a; Heiskanen et al. 2017). Delivery times can take up to 24 months and sometimes the medicines ordered do not arrive in Finland in time which may cause a shortage. Long delivery times also make forecasting the sales

challenging as pharmaceutical companies and wholesalers have to place orders well in advance of the actual sales. (Heiskanen et al. 2017)

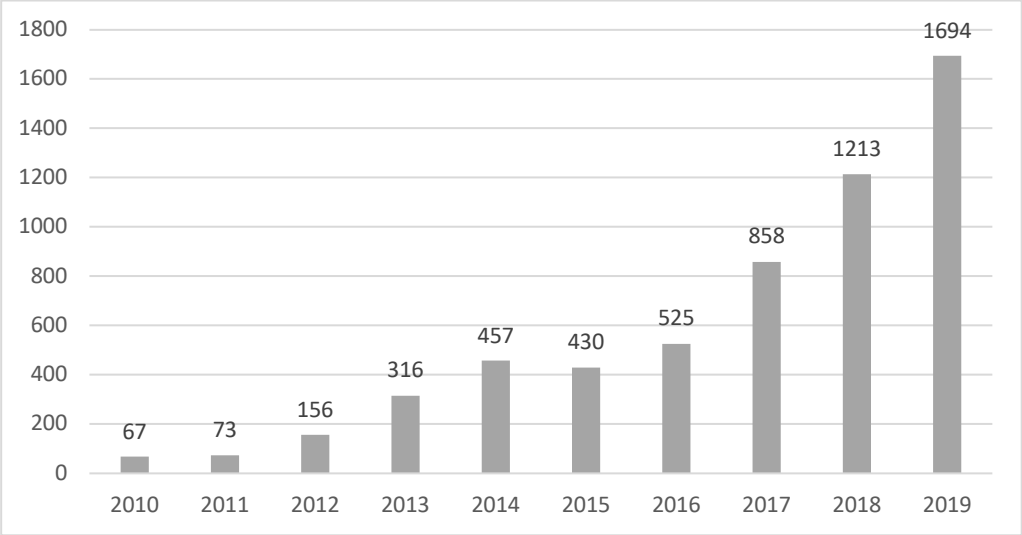

Figure 7 Shortage notifications reported to Fimea (Adapted from Fimea 2020c)

Other supply related reasons contributing to shortages in Finland include mandatory reserve supplies, issues or changes in distribution, production, capacity and quality, changes in marketing authorization holders, tightened regulation, insufficient communication and monitoring (Heiskanen et al. 2017). The single-channel system that is in place in Finland, may potentially also lead to medicine shortages if the wholesaler faces major disruptions. In addition, the limited number of medicine distributors operating in the market poses a risk to medicine availability in case of a supply disruption and other wholesalers not being able to handle the large number of orders. (Sarnola & Linnolahti 2019) However, Heiskanen et al. (2017) point out that often the reasons behind medicine shortages are complex and that there is in most cases more than just one reason affecting behind a shortage. Supply-related reasons commonly interface with the country-specific characteristics of Finland. Demand-related reasons instead are often associated with the attractiveness and predictability of the market and some reasons such as raw material shortages are considered global.

Reasons considered global thus have similar effects on other countries as well. (Heiskanen et al. 2017)

5.2 Risks behind medicine shortages

Each interviewee recognized the issue of medicine shortages and agreed on the issue being topical and complex and thus in need of intervention. Referring to medicine shortages statistics from the last decade (figure 7), the majority of the interviewees admitted that medicine shortages have been increasing during the recent years both globally and in the Finnish market. However, interviewees pointed out that a change in the compilation of statistics on medicine shortages in Finland have contributed to increased numbers and that actually the security of medicine supply in Finnish pharmacies is almost 100%. Interviewee E also pointed out that the number of generic medicine providers in the market has increased noticeably during the last two decades and as the number of operators in the market increase, so does the number of shortage notifications. Thus, the medicine shortage issue is actually not as critical, at least not in Finland, as the statistics and media imply. Interviewees also noted that not all shortages are long-lasting and have drastic impacts which is why shortages should be categorized i.a. according to their criticality. Thus, interviewee E suggests that it would be appropriate to revise Fimea's medicine shortage notification system. This would enable transmitting more realistic image of the situation as in the light of statistics the situation might appear worse than it is in reality. Interviewee C also points out that the effects medicine shortages cause in the supply chain, vary depending on the product in question. Shortages of generic medicines are not as likely to cause drastic consequences as shortages of rare or patented medicines.

However, each interviewee found that shortages in raw materials and API's used for medicine manufacturing, as well as finished medicines, cause extra workload and increase costs for the supply chain members from the manufacturer to the pharmacy. In case of a raw material shortage, a manufacturer must find alternative raw material supplier or turn to buffer inventory. Pharmacies and doctors instead must take time

and effort to find substitutive product for the end-user in case of a finished medicine shortage. Shortages may thus cause harm and confusion to patients in terms of changing clinical practice or having to use substitutive treatment. However, in Finland patient safety is rarely compromised because of medicine shortages. Furthermore, according to interviewee A issues in medicine availability may cause sanctions for pharmaceutical companies.

The interviewees were all quite unanimous about the main risks behind medicine shortages. Each participant listed unexpected peaks in demand as the most considerable reason causing shortages in the Finnish market. Then again supply-related reasons were also recognized as substantial and often more complex set of risks. The perception of risks and the significance of them differed slightly depending on the interviewee's field of operation. In the subsequent chapters, the most significant risks that arose from the interviews are being listed and analysed in more detail.

5.2.1 Demand risk

As already mentioned, each interviewee highlighted the significance of sudden demand peaks in creating medicine shortages. These peaks were considered challenging and causing extra workload, even though demand peaks can be predicted to some extent. Interviewee A noted that the demand for medicines is rather predictable and stable by nature, especially regarding medicines used for treating chronic diseases such as diabetes and seasonal conditions such as hay fever. However, small buffer stocks in pharmacies as well as long lead times hinder rapid and flexible response in situations where demand increases quickly and exceeds supply. Interviewee E pointed out that some medicines are only produced very rarely, maybe once a year. This combined with long lead times and strictly regulated supply chain emphasizes the importance of careful demand planning. Thus, the interviewees agreed on that it is preferable to use proactive measures rather than reactive, to prepare for availability issues and minimize the harmful effects of them. Factors such as the pricing system of medicines (reference price system), tendering of hospital medicines and changes in clinical practice further contribute to demand peaks.

Furthermore, as there is usually a limited number of companies offering generic medicines, a market exit of a particular company can cause unexpectedly high demand for other companies' products. The same applies if some of the companies providing generic products faces shortages. These kinds of situations negatively affect the predictability of demand. For example, if a company that holds 70% market share faces product shortages or leaves the market, the remaining demand will be spread for other companies in the market to cover. These companies are used to having only 30% market share which means that they have probably not prepared for such high demand, thus it is probable that they will also face difficulties in serving the demand. Interviewee B notes that this is especially risky in the hospital medicines' sector where there are often just a few suppliers for each pharmaceutical product category.

5.2.2 Regulation and country-specific risks

The quality requirements for medicines are extremely strict which is why the medicines industry is highly regulated. Despite strict quality requirements contributing to i.a. patient safety, these requirements also affect the flexibility of supply especially in a shortage situation. According to interviewee D the administrative and legal requirements also change constantly and implementing them is costly and time-consuming for pharmaceutical companies. Revision of authorization, documentation or trading license procedures can potentially result in shortages as implementing and processing these changes take time both at the pharmaceutical company's end as well as at the authority's end. Depending on how long it takes for the authority to go through the changes, the process can create supply interruptions.

Interviewee D pointed out that in case there is a shortage of a particular medicine in the Finnish market, the product can be imported from another EU country with an exceptional permit granted by Fimea. The package leaflets however need to be replaced with new ones including all information in Finnish and Swedish which in some cases is not possible due to the legislation regarding the prevention of falsified medicines. Hence, interviewee B pointed out that medicines are one of the few exceptions to the free movement of goods within the single market in Europe.

Furthermore, the marketing authorization also defines on a very detailed level e.g., the contents of a medicine. Interviewee E gave an example that if a medicine manufacturer's primary supplier for a certain raw material is unable to supply and the manufacturer wants to use raw material from another supplier, depending on the product an exceptional permit might be required to be able to replace the original supplier with another one. Thus, the quality requirements for medicines are much stricter than for example for electronic devices. Also, according to the interviewees the permit of exception process is heavy, time-consuming and costly, which reduces the flexibility of the system.

Country-specific factors of Finland were also brought up by almost every interviewee as contributing factor to medicine shortages. Finland is a small market with small order volumes when compared to other, bigger markets such as the United States or Germany. Interviewee A pointed out that as the pharmaceutical manufacturing is largely centralized, a small market such as Finland may not be seen attractive by the manufacturers. Big, international pharmaceutical companies strive for economic advantage so it might be that supplying for smaller markets, especially in a shortage situation, is not considered profitable enough. On the other hand, interviewee E pointed out that small size of the market can sometimes be an advantage as small orders can be covered more easily and on a shorter notice than larger ones. However this applies mainly to generic medicines.

The geographical location of Finland means that lead times are comparably long which puts a high emphasis on demand planning. Interviewee E noted that some companies do not necessarily have a proper organisation for each smaller market. Thus, some pharmaceutical companies have a joint management organisation for all Nordic countries which may result in poor ability to react to each specific market's requirements or circumstances. Furthermore, Interviewees B and D pointed out that even though the mandatory reserve supplies of medicines is a useful system, the legislation regarding it needs revision. The content of the law is partly outdated and at the moment approximately 20% of the reserve end up expiring on a regular basis.

Through revision the mandatory reserve supply law would better serve the contemporary needs as well as contribute to more efficient and appropriate procurement and warehousing of medicines.

5.2.3 Medicine supply chain risks

According to the interviews, demand can be predicted and also affected to some extent whereas supply is more challenging to manage, especially in the pharmaceuticals market where the manufacturing and distribution is very much centralized, and the number of suppliers and alternatives is rather limited. In most cases supply disruptions are not predictable and sometimes a medicine shortage can last up to a year. Thus, supply chain risks, especially supply risk, are considerable threats to medicine availability. In the following paragraphs the most substantial factors causing supply risk based on the interview results are presented.

Supply chain structure

The supply chains behind medicines are usually long and comprise of various actors, however the roots for many pharmaceutical products are in Asia, where the raw material and active ingredient production are largely concentrated. All interviewees were unanimous about the fact that the scarcity of raw material and active ingredient producers cause significant risk for medicine availability. Manufacturing, packaging and distribution of medicines are also highly centralized operations. High level of centralization is largely due to the pricing of medicines, in fact dumping, as medicines cause one of the biggest expenditures for governments annually. Thus, the most inexpensive alternatives and economies of scale are pursued especially in the generic medicines segment even though some medicines have high holding and inventory costs. This results in low margins and profits. Centralization of operations and scarcity of suppliers naturally results in increased vulnerability and risk exposure in the supply chain if something detrimental happens for example in the production facilities. Producers might face raw material shortages, a natural disaster may destroy production facilities or stocks, or staff in a certain facility might fall ill due to an epidemic.

In worst cases these kinds of events result in production stops which again may result in shortages throughout the supply chain and can cause major consequences around the world. Interviewee B stated that when the risks of centralization are combined with the country-specific risk factors and demand alterations, the issue of medicine shortages multiplies and becomes ever more complicated.

Some of the interviewees told that they do not precisely know how long the medicine supply chain behind the end product actually is. Interviewee C pointed out that as the beginning of the medicine supply chain comprises of chemistry and processing industry, it takes a long time before the raw material and active ingredients are even ready to be used for medicine manufacturing or assembling. Each interviewee agreed that long supply chains result in long lead times which in turn may cause delays in raw material and finished product orders. Long lead times also put a high pressure on demand forecasts as they must be made well in advance. For a small market like Finland, the order quantities are usually optimized which means that one order can cover up to a year's usage of a certain medicine. It is not feasible to place small just-in-time orders as the lead times are up to 6 months but also because it is not desirable from the suppliers' point of view. Interviewee A pointed out that the obsolescence of medicines must also be taken into consideration when planning orders and warehousing as medicines must e.g., have enough duration of use left after the customer has purchased it from the pharmacy.

Manufacturing

Based on the interviews, the optimization of medicine manufacturing has caused manufacturing and distribution to be spread for rather a small group of manufacturers and contract manufacturers. Yet the whole process of medicine manufacturing from extracting the raw materials until the distribution to pharmacies and hospitals is scattered to multiple operators. Interviewee B pointed out that very few medicines are produced at one place from start to end which means that medicine supply chain

consists of multiple different phases and operators which in turn increases the number of potential risks within the manufacturing and distribution processes.

Problems related to manufacturing include quality issues and capacity issues. According to interviewee D, quality issues in production or in batches may result in batch recall or sometimes even a production stop. The length of production stop might also vary as the source of the quality defect must be localized and fixed. Interviewee C stated that as the quality requirements for medicines are extremely strict, pharmaceutical companies and authorities do not take any risks that would compromise product quality. Capacity issues include e.g., staff falling ill and machinery breakdown which negatively affect the production capacity availability. Because of the scarcity or producers, quality issues and capacity issues create vulnerability and a high risk for medicine supply disruptions. In case one production facility stops operating, there might not be alternative suppliers available even for generic medicines but especially for patented medicines. In addition, interviewee D pointed out that changes in the manufacturing firm's operations might cause product shortages if the changes have not been communicated to the parties concerned. For example, if the production of a specific product is shifted to another location, enough bottle-neck stock must be produced beforehand to ensure product availability during the transfer-period.

Transparency and information sharing

According to the interviewees, often the information about shortages on raw materials, API's or finished pharmaceuticals reaches the wholesale licence holders, wholesaler or distributors at the last minute. All medicine shortages should be notified to Fimea two months in advance, however in reality only a small fraction of them is notified on time. Naturally, shortages are often difficult or impossible to predict however the information sharing could be improved between the operators of the supply chain, so that other supply chain members could prepare for the shortage in advance. Of course, companies reach for economic advantage which means that sharing certain information would possibly cause disadvantage for their business. Interviewee A noted

that some essential information relative to shortages might be classified as trade secrets and thus does not become public and interviewee E noted that it is against the principles of competition legislation to share certain information outside the organisation. However, late notices on medicine shortages cause extra workload and complications for other supply chain members. Also, if quality issues are detected in e.g., raw material production, the information does not always reach other related supply chain members directly. As interviewee C pointed out:

"Sometimes we receive the information (about quality problems) in a roundabout way so that we do not actually find out about the problems from the supplier but for example from the authorities. If the authorities detect a quality defect through an audit at the supplier's end, we get the information from the authorities although primarily we should be able to receive the information directly from the supplier."

Interviewee B mentioned that despite quality control systems and supplier audits, medicine manufacturers do not have continuous control over their suppliers. Medicine shortages can originate from a situation where the supplier of a raw material for example, suspects that they may face shortages in the near future but does not share the information further in the supply chain. Instead, the raw material producer starts to prepare for the shortage situation quietly by limiting or redirecting their delivery capacity and allocating products to prioritized clients rather than smaller, less significant customers. The wholesale license holder that uses the raw material for manufacturing finished medicines usually receives the information about a shortage too late to conduct any corrective or preventive actions and thus the issues caused by the shortage cumulate further in the supply chain.

5.3 Medicine SCRM

Based on the interviews, certain supply chain risk management strategies emerged that are being used at the interviewees' respective companies or were suggested by the interviewees to be utilized against medicine shortages. These strategies are being presented in detail in this chapter. According to the interviewees, a key aspect in a

company's risk management strategy is continuous improvement of processes which is especially important in the medicines industry.

5.3.1 Manufacturing and inventories

"There are hardly any tricks against the actual supply risk, we (as a wholesaler) just need to trust that the supplier has enough goods. – We cannot affect the logistics chain behind the first-tier supplier as each company is an independent actor." (Interviewee A)

Based on the above citation, the wholesaler does not have much control over the supply chain behind medicine manufacturers of marketing authorization holders, and the responsibility over the supply chain remains with them. Although other interviewees did not agree on the complete lack of measures against supply risk, the means to influence the operation of suppliers, especially behind the first tier are limited which is why each interviewee stressed out the importance of holding enough buffer stocks as a protective measure against shortages. However, warehousing is expensive, and some medicines also require special conditions, for example regarding the temperature of warehousing and logistics. Holding stocks is pricy which is why especially pharmacies with limited warehousing capacity, favor JIT deliveries and lean warehousing, however pharmacies are obliged to have inventory equivalent to 2 weeks' use to secure availability. The wholesale license holder is also obliged to constantly have in stock the quantity equivalent to wholesaler's and pharmacies' demand. Other strategies such as dual sourcing or using back-up suppliers are in use in the case companies if only there are alternative suppliers available in the market. Interviewees also stressed out the importance of up-to-date demand forecasts to facilitate order planning and to mitigate negative consequences of possible availability issues. The mandatory reserve supply was also considered a great means to protect against shortages, however as already pointed out in chapter 5.1.2 the associated law needs revision to better serve the demand.

Regarding inventories, Interviewee C pointed out that storing raw materials is more preferable than storing finished medicines. Raw materials have longer preservability and they do not have strict shelf-life. Instead, raw materials will be re-tested for usability before refining them into medicines to make sure they are still fit for use. Storing finished products is more risky and costly from the manufacturer's point of view not only because plenty of resources have been invested in the product but also because finished products usually have a fixed shelf-life. Thus, warehousing gets more costly as the product gets more refined which is why it is only reasonable to store raw materials and postpone refining them until there is demand for finished products. Interviewees also pointed out that printing the package labels and leaflets to end products in different languages enables marketing the same product in multiple markets. This strategy is often used for the Nordic countries, for instance.

Nearshoring was also brought up in the interviews as a means to decrease the supply risk. According to interviewee E, European medicine manufacturing is vital for the security of supply and as a matter of fact there are already a lot of medicine and API production facilities in Europe. Especially the production of critical medicines should be secured in Europe to ensure more responsive and flexible supply in a shortage situation. However, nearshoring medicine manufacturing to Europe on a larger scale requires investments and political cooperation. It would be very difficult for Europe to compete with the economies of scale that other big manufacturer countries have. Furthermore, if medicine manufacturing were to be restored to Europe on a larger scale, low prices should not be the biggest incentive as it would be very challenging for Europe to compete with Asia in prices. Instead, nearshoring should be considered through factors such as sustainability, responsibility, shorter lead times and improved availability. As interviewee B pointed out:

"EU has the objective of moving more of the production to Europe, however it is not very easy. Europe does not have the infrastructure needed for such large-scale medicine manufacturing. – To be able to shift the production to Europe, the bigger infra is lacking which exists in, for example, China and USA."

As already mentioned above, importing medicines from other EU countries in shortage situations is one way of mitigating the effect of shortages. It is usually a strategy for acquiring rare medicines that do not belong to mandatory reserve supply or do not have substitutes in the market. However, as the exceptional permit process is sometimes lengthy and inflexible, interviewees emphasized that the flexibility and speed of the process should be increased. This could be done i.a. through enhanced cooperation between the authorities and pharmaceutical companies. Also, interviewee E suggested that modern information technology should be harnessed more effectively for flexible and rapid transaction between pharmaceutical companies and controlling authorities.

In a shortage situation, or in circumstances where shortages are likely to form, medicine manufacturing capacity can be focused to manufacturing specific products. Interviewees C and E emphasized that in their respective organisations patient critical medicines are always prioritized and their availability is ensured at all circumstances. This sometimes means that these products are being produced detriment of other products. This usually applies to products that are non-generic or that are generic but non-exchangeable to other generic products. For these products risk assessment is conducted very thoroughly and on a regular basis to avoid shortages as well as possible.

5.3.2 Supplier monitoring and collaboration

According to the interviewees, each pharmaceutical company must have a quality system and each supply chain member has to comply with e.g., GDP and GMP to ensure sufficient quality throughout the entire chain. Both authorities and organisations set quality requirements for suppliers and perform monitoring i.a. through audits and quality agreements. The authorities conduct audits on a regular basis for all actors in the pharmaceutical supply chain. Interviewee B told that the quality assurance system obliges the wholesale license holder to audit its suppliers as well as the first-tier supplier to audit second-tier suppliers and so forth. The auditing is mainly conducted through following the auditing reports from partners or suppliers and ensuring that each

supply chain member has conducted audits as supposed. Thus, a continuous chain of quality assurance throughout the chain will be ensured. The auditing system also works the other way around and suppliers audit the wholesale license holders. Interviewee B noted however, that they do not always know exactly where in the supply chain the risks exist as the object of auditing is that sufficient quality in the entire supply chain is ensured. Interviewee C told that in their respective organisation, they also audit their first-tier suppliers, first tier suppliers audit second-tier suppliers etc. In addition, interviewee C's organisation monitors the operation of subsequent tiers together with the first-tier supplier especially with key suppliers. The object is to cooperate with suppliers from different tiers to find out supply chain problems and risks as early as possible to be able to prepare for them efficiently.

Because of authority supervision, quality control systems and quality agreements with suppliers, the information on medicine shortages reach pharmaceutical companies and wholesalers. However as already mentioned earlier, in some cases the information comes last minute and thus causes problems in the supply chain. According to interviewees, there are not many means for facilitating the problem as the issues causing shortages are often unforeseeable. Interviewee D pointed out that in order to facilitate the information transfer in the supply chain competing organisations should be able to discuss and share information on possible upcoming shortage situations. This however is contradictory as organisations seek for economic advantage and the stakeholders in the medicine's industry aim for profit making. It is also against the principles of competition legislation. Thus, interviewee E suggested that authority interference is needed to facilitate the process of improving information exchange regarding shortages.

Interviewees also emphasized the role of good supplier relationships in preventing shortages on a company level. Interviewee C pointed out that especially for smaller organisations it is important to hold good relationships with suppliers and ensure that the supplier regards them as a major and important customer. This way the customer may gain advantage in relation to other companies in terms of access to supplies in a

shortage situation. Also, the information transfer between the supplier and the customer is usually enhanced if they have a close relationship.

6 CONCLUSIONS AND DISCUSSION

In this chapter, answers to research questions are given by summarizing the main findings of the empirical study and reflecting them to the theoretical part of this thesis. In addition, in chapter 6.2 the effects the COVID-19 pandemic has had on medicine availability are briefly discussed and in chapter 6.3 the limitations regarding this study are presented and suggestions for future research are proposed.

6.1 Answering the research questions

The aim of this thesis study was to research which supply chain risks contribute to medicine shortages occurring in the Finnish market. In addition, the objective was to find out how medicine shortages could be mitigated or prevented through supply chain risk management practices. The conclusions were drawn, and research questions answered based on a theory chapter about supply chain risks and SCRM, a review on medicine shortages based on existing literature and an empirical multiple case study on shortages in Finnish medicine supply chains. The findings of the empirical research are summarized in table 3.

Why do medicine shortages exist?

The main research question aimed at investigating why medicine shortages occur globally and why the issue has escalated during the last decades. According to previous research, increased outsourcing and centralization of medicine manufacturing and distribution have drastically contributed to increasing medicine shortages. This has increased the potential causes for supply disruptions in the medicine supply chain as well. (Lääketeollisuus 2020a; Pauwels 2015) The findings of the empirical study also indicate that increased centralization of raw material, API and medicine manufacturing contribute heavily to medicine shortages. The root cause for outsourcing and centralization lies in the pricing systems of medicines. Systematic dumping of medicine prices globally has left pharmaceutical companies basically no other option than to outsource operations to countries of low labour costs. This applies

especially to the generic medicines' segment. While medicine manufacturing, research and development require a lot of resources and investment, but prices are being pushed down, the margins remain low for pharmaceutical manufacturers and wholesale licence holders. Thus, generic medicine manufacturing is mainly volume business and companies having economies of scale are the most profitable ones. This further decreases the attractiveness of the market in the eyes of new companies aiming at entering the market.

Concentration of the medicines industry means that the number of manufacturers is limited which emerged as one of the main reasons behind shortages according to the empirical study of this thesis. Heiskanen et al. (2017), Junttonen (2017) and Besancon & Chaar (2013) also found out that in the global medicine supply chain, there is not enough redundancy or spare capacity which increases the chain's vulnerability and risk of disruptions. Furthermore, Christopher (2011) argued that flexibility of supply may suffer when centralization of production increases. Similar findings emerged from the empirical study and majority of the interviewees agreed on the scarcity of producers resulting in weakened flexibility and responsiveness among the production chain. On the other hand, the scatteredness of medicine production chains due to multiple refining and production phases results in long and complex supply chains and also increases the vulnerability within them. Supply risk increases as supply networks get wider and thus, risks may occur in different parts and processes of the network (Harland, Brenchley & Walker 2003; Kleindorfer & Saad 2005). Based on the empirical study, the same applies also to medicine supply chains.

The attractiveness of the medicines industry emerged, both in the theoretical research and the empirical study as another reason indirectly affecting the availability of medicines. Regulation and quality requirements in the pharmaceutical industry are stricter than in many other industries which, according to the empirical study, undoubtedly contributes to the number of operators in the market. In addition, According to WHO (2016) market entry for new pharmaceutical producers is costly and unpredictable process due to challenges related to maintaining quality systems,

attaining regulatory approval and frequently changing regulatory requirements. The argument was also supported in the findings of the empirical study and it was emphasized that medicine manufacturing, distribution and warehousing especially in the generic medicines' industry are costly operations and as the gross margins remain relatively low, the industry is not actually seen as a money-spinner.

Both previous research and the findings of the empirical study indicate that demand fluctuations have a substantial role in generating medicine shortages. Besancon & Chaar (2013) argued that fluctuating market demand can affect, and sometimes lead to, medicine shortages. Demand alterations cause medicine shortages globally, but based on the case study findings, there are some factors especially related to the Finnish medicines market such as the reference pricing system and tendering of hospital medicines that may cause sudden demand peaks. Also, if a medicine manufacturer leaves the market unexpectedly, if a pandemic breaks out or if the consumers are provided with information which pushes them to hoard medicines, unexpected demand arises. The scarcity of producers and lack of alternative products add to the negative effects which unexpectedly high demand can create for medicine availability.

Finally, the lack of systemic indicators and monitoring pointing out possible supply disruptions along the medicine supply chain as well as the lack of information regarding the current cases of drug shortages contribute negatively to the availability of medicines according to Besancon & Chaar (2013). In Finland, Fimea collects data on medicine shortages, however the case study results suggest that the reporting practices should be revised to provide better and more realistic overview on the situation. This could be done for example by distinguishing critical or long-lasting shortages from non-critical and short shortages in the reporting which is currently not done in the reporting system. When it comes to information sharing between supply chain members it is, to some extent, restricted by trade secrets or competition legislation which is why increasing the supply chain visibility through enhancing information transfer is not as straight forward.

Heiskanen et al. (2017) pointed out that often the reasons behind medicine shortages are complex and, in most cases, there are more than just one reason behind a shortage. The interviewees of the case study also stressed out the complexity of the issue and noted that if there were simple solutions for overcoming medicine shortages, such issue would not exist in such a large scale. Sarnola & Linnolahti (2019) argued that tackling the medicine shortage issue must be done in both national and multi-national levels. In addition, according to EAHP (2019) and Bogaert et al. (2015), strong EU commitment is required to address certain causes of medicine shortages and legal and organisational strategies should be coordinated by the EU to address the issue at the European level. The empirical study findings also support the above arguments, and it was emphasized that both national and multi-national efforts and political commitment are needed to manage the issue, and to support and facilitate the efforts against shortages.

Which supply chain risks cause medicine shortages in Finland?

The aim of the first sub-research question was to find out which supply chain risks cause medicine shortages, or negatively contribute to medicine availability in the Finnish market. The findings of the empirical study as well as previous research indicate that the risks causing medicine shortages on a global level influence the situation in Finland as well, and that Finland is heavily reliant on imports and foreign manufacturing of medicines. The factors causing risk for supply globally include single sourcing, global sourcing, limited buffer stocks and a high degree of concentration of suppliers and manufacturing (Hendricks & Singhal 2012; Christopher 2011). In addition to the global risks, there are also risks that arise from, or have to do with the country-specific factors of Finland. According to the study of Heiskanen et al. (2017), reasons behind medicine shortages in Finland include the small size of the pharmaceuticals market, small stock sizes, long lead times, dependency on foreign manufacturing, reserve supplies, issues or changes in distribution, production, capacity and quality, changes in marketing authorization holders and tightened regulation. All these factors

are related to the supply chain and also, in one way or another, appeared in the empirical study as potential risk factors for medicine availability.

According to Lääketeollisuus (2020a) and Heiskanen et al. (2017), small size of the market means small purchasing volumes, limited number of operating companies in the market and small language area. All these factors were recognized as contributing to medicine shortages in the Finnish market according to the empirical findings as well. The small size of the market was considered as a disadvantage relative to the supply of medicines especially in a global shortage situation where the global production capacity is likely to be exceeded. On the other hand, also contrasting views on the small size of the market were presented as in some cases it might be easier to cover the demand of a smaller market as the volumes are usually marginal compared to bigger markets. In addition, the limited number of operators in the market was considered an issue in shortage situations due to the lack of alternatives. The scarcity of suppliers is especially emphasized in a situation where one operator leaves the market, and the demand is left for the remaining operators in the market to cover. Small language area was also regarded as a risk factor due to the language requirements regarding medicine package leaflets as these requirements may hinder the flexibility of supply in some cases.

As the starting point of many medicine supply chains is located in Asia and the chains usually consist of multiple phases the lead times can get very long. Due to the geographical location of Finland, the lead times are relatively even longer if compared to e.g., central Europe. Due to long delivery times, sometimes the medicines ordered do not arrive in Finland in time which may cause a shortage in the market. As already mentioned, long lead times also put pressure on demand planning and stock management and sometimes decrease the flexibility of supply. Long delivery times make forecasting the sales challenging as pharmaceutical companies and wholesalers have to place orders well in advance (Heiskanen et al 2017). This finding was emphasized in the empirical findings also. In addition, it was pointed out that small markets typically place medicine orders relatively seldom as otherwise the ordered

quantities would be comparably small which is unattractive for large, international manufacturers. Some medicines are produced seldom, such as once a year only, which makes demand planning ever more challenging.

Chopra & Sodhi (2004) pointed out that since disruptions are considered rare events, holding high inventory levels might not be desirable by managers. Heiskanen et al. (2017) also noted that low stock levels might be a conscious business decision to minimise warehousing costs, as in Finland warehousing costs are comparably higher than e.g., in other European countries. Based on the empirical study high warehousing costs result sometimes in insufficient inventory levels especially in pharmacies which might result in availability issues. The mandatory reserve supplies of medicines were also considered a risk factor in a way, as the legislation regarding the system is not optimal regarding the present-day demand and needs. Sarnola & Linnolahti (2019) emphasized that the system is heavily reliant on the quality and continuous supply of medicines. Thus, if the contents of the law concerning the reserve supply system are out-dated, the system will not serve its purpose optimally.

According to Besancon & Chaar (2013), most developed countries usually impose stricter national regulations for medicines to ensure and improve quality, which may result in weakened availability. The EU and Finnish government have set strict regulation regarding the quality standards of medicine manufacturing, prevention of grey market and counterfeit medicines. Based on the empirical study findings, grey markets and counterfeit medicines are not considered great threat for medicine availability in Finland. Strict regulation and quality standards however were considered as sometimes causing a risk for medicine availability. Especially the authorisation process of medicines was considered inflexible and slow which sometimes causes medicine shortages if for example exceptional permits for medicine imports are not received in time. Also, fewer pharmaceutical products get the marketing authorisation to EU or Finland because of the regulation and quality standards.

Finally, according to the single-channel principal that is in place in Finland, a pharmacy or hospital can only use one wholesaler to procure a specific pharmaceutical company's products (Pharma Industry Finland 2020; Heiskanen et al. 2017). Thus, Sarnola & Linnolahti (2019) pointed out that the single-channel system may potentially lead to medicine shortages if the wholesaler faces major disruptions and if other wholesalers are not able to handle the demand. The empirical study results also indicated that the system has occasionally led to shortages in pharmacies in a situation where the wholesaler has not had enough stock to cover sudden demand peaks. Shortages have arisen as the wholesaler has not been able to cover the demand even though the marketing authorisation holder would have had products in stock.

How to mitigate medicine supply chain risks?

The aim of the second sub-research question was to find out how medicine shortages or critical medicine supply disruptions could be prevented or mitigated at any point of the supply chain. Ward & Hargaden (2019) suggested that to avoid supply chain disruptions risk assessment and mitigation strategies should be conducted and that organisations should strive for resilient supply chains. The empirical study indicated that risk assessment and mitigation strategies are conducted extensively in the case companies as well. Risk assessment is conducted especially carefully with patient critical medicines to ensure their availability at all circumstances. Resiliency is also built in the supply chain as well as possible, however due to industry specific factors resiliency may sometimes be compromised. Mishra et al. (2016) proposed that organisation's operating environment strongly affects the choice of a risk mitigation strategy. Thus, the specific requirements and characteristics of the pharmaceutical industry must be taken into account when designing supply chain risk mitigation strategy. According to Chopra & Sodhi (2004) and Tomlin (2006), the most successful companies mitigate supply risks by combining various risk management strategies such as inventory, capacity and redundant suppliers. Most of the interviewees also told that different risk mitigation strategies are implemented concurrently in the case companies.

Supply risk mitigation strategies that are in place in the case companies, are discussed below by categorizing them according to Miller's (1992) risk mitigation strategies control, cooperation and flexibility. The fourth strategy, avoidance, was excluded from the discussion as none of the interviewees referred to the avoidance strategy as being in use in their respective organisations. This might be due to the characteristics of the medicine's industry as avoiding specific suppliers or manufacturers located in certain geographical areas is presumably not reasonable due to the scarcity of suppliers operating in the market and because the regulation of the medicines industry automatically eliminates from the market operators that do not meet the demands.

The first risk mitigation strategy, control, entails demand forecasts, inventory, quality control and product categorisation. As already mentioned, mased on the empirical study accurate demand forecasts play a significant role in preventing medicine shortages locally. Most of the interviewees stressed out the importance of careful demand planning. In addition, buffer inventories were the most cited means to mitigate shortages among the interviewees. Inventories play a big role in protecting against demand peaks and supply disruptions especially for small organisations. However as holding excessive buffer inventory is costly, it was pointed out that it is preferable to store raw materials rather than finished products. Raw materials do not have precise shelf-life thus their preservability is better than finished products'. Also, more resources and money have been spent in finished products than in raw materials. The so-called postponement strategy increases flexibility as it reduces organisation's dependency on forecasts and increases the ability to respond to demand alterations. (Kleindorfer & Saad 2005) The mandatory reserve supplies of medicines was considered a useful system in protecting against major shortages among the case companies, however two of the interviewees addressed the issue of the mandatory reserve supply system being outdated and in need of an update.

Following the principles of GMP in medicine manufacturing is considered a critical aspect in the process of mitigating medicine shortages (Battistini 2019). Quality control was also considered very important in the case companies. Each pharmaceutical

company should carry out a quality assurance system and it is important that adequate levels of quality are ensured throughout the supply chain. GMP and GDP compliance is monitored through audits carried out by authorities, pharmaceutical companies and their suppliers. Differing from other case companies, Interviewee A who represents a medicine wholesaler, told that the wholesaler can hardly affect the supply chain behind medicine manufacturers or marketing authorisation holders. Other interviewees emphasized the role of conducting quality monitoring for the first-tier supplier but also beyond the first tier to ensure quality throughout the supply chain and to act as an early warning system. Finally, the case companies categorise their products according to i.a. their patient-criticality to prioritise and ensure the availability of the most critical products and e.g., risk assessment is conducted diligently for these products.

Second risk management strategy, cooperation, entails collaboration between pharmaceutical companies and the authorities, supplier collaboration as well as improving the communication between supply chain members and reporting systems of medicine shortages. As Hallikas et al. (2004) proposed, it is inevitable that organisations form networks and collaborate to be able to respond to changing market environment. When it comes to collaboration between pharmaceutical companies and authorities, the flexibility of authorisation processes could be improved. Based on the empirical research, the exceptional permit process regarding the import of medicines or accepting new raw materials for medicine production can be troublesome, time-consuming and costly. According to the interviewees, these processes could be facilitated by utilising modern information technology solutions. The empirical study results also indicated that fostering good supplier relationships is vital in securing supply, especially for smaller companies.

According to EAHP (2019) improving communication and obliging medicine manufacturers to inform about medicine shortages in a timely manner were brought up as a way to alleviate the medicine shortage problem. Kleindorfer & Saad (2005) emphasized that collaborative information sharing among supply chain partners is vital in identifying vulnerabilities and executing effective crisis management. The

interviewees of the empirical research also recognized the issue of inadequate information sharing along the medicine supply chains. However, as already mentioned, sharing information openly is not always in organisations' interest. Battistini (2019) also argued, that collecting supply chain data is not always straight forward as some key drivers of drug manufacturing and distribution, such as production schedules or distribution, supply and purchasing practices are not always transparent. Thus, in the empirical study it was suggested that stronger political commitment and participation is needed to facilitate the information transfer between the supply chain operators to improve the notification about factors contributing to possible shortages.

Third and final risk mitigation strategy, flexibility, includes different sourcing options and near-shoring of medicine manufacturing. According to Ward & Hargaden (2019), using alternative suppliers increases the flexibility of sourcing when medicine shortages occur. The empirical research findings also support this perception. However sometimes there are no alternative suppliers of raw materials or API's available due to the scarcity of manufacturers and suppliers in the medicines industry. The marketing authorisation of medicines also sometimes defines very strictly for example, that only a specific raw material supplier's product can be used in the production of the medicine. Thus, utilising multiple sourcing is not as straight forward in the medicines industry, as it would be for example in the electronics industry. According to Hopp, Irvani & Liu (2012) and Kleindorfer & Saad (2005), securing extra capacity is a form of redundancy protection and contingency planning. Based on the empirical study, case companies that have their own medicine manufacturing, aim for diversifying API and medicine manufacturing locations to increase the supply resiliency. Thereby the supply of these products is secured if something detrimental happens in the production facilities at one location. The manufacturing capacity can also be redirected to producing certain products detriment to other products in a shortage situation or if a sudden demand peak arises.

Finally, near-shoring of medicine, raw material and API manufacturing to Europe appeared as a preferred risk mitigation strategy based on the empirical study findings.

Heiskanen et al. (2017) also found out that greater domestic manufacturing was considered to reduce the risk of medicine shortages. According to interviewee E, establishing medicine manufacturing in Finland would not be sustainable or profitable, however in Europe there already exists a good number of API and medicine manufacturing capacity and thus it was considered that moving more production to Europe would be feasible. Interviewee B however pointed out that Europe is lacking the required infrastructure which enables establishing medicine manufacturing on a larger scale. Europe could not compete in low prices with the Asian manufacturers so if medicine manufacturing were to be established in Europe on a larger scale, low prices cannot be the sole motive when choosing a supplier. Other factors such as increased flexibility of supply, environmental aspects and sustainability should weigh more in organisations' decision making.

Table 3 Summary of results

CAUSES	RISKS	MITIGATION STRATEGIES
Outsourcing	• Long supply chains • Long lead times • Quality issues • Scattered supply chain • Capacity issues • Scarcity of manufacturers • Inflexibility of supply	• Nearshoring production • Product categorisation • Supplier quality controls • Buffer stocks • Postponement of production • Joint packaging for multiple markets • Multiple sourcing • Diversification of manufacturing locations
Centralisation of manufacturing and distribution		
Regulation in the medicines industry	• Inflexibility of the authorisation process	• Authority involvement and political commitment • Accurate demand forecasts • Improved medicine shortage reporting system
Changes in demand	• Reference price system • Tendering • Companies leaving the market	
Poor supply chain transparency	• Distorted information • Belated information on shortages	

Due to the outbreak of COVID-19 pandemic in 2020, it was considered important to include the possible effects of the pandemic for medicine availability in this thesis. Thus, the interviewees were asked if the pandemic has affected medicine availability in the Finnish market. Each interviewee told that the pandemic caused some short-term shortages of especially painkillers in Finnish pharmacies due to increased hoarding in the spring 2020. Consumers were preparing for possible availability issues by hoarding medicines and the Finnish government had to set some restrictions for purchasing quantities per customer to ensure availability. However, according to the case study shortages were not critical at any point. According to interviewees A and E, the hoarding was more or less unnecessary and caused by distorted information given to the consumers.

Pharmaceutical companies had prepared for increased demand by increasing production capacity and inventory buffers as soon as the virus started spreading in the beginning of the year 2020. In addition, protecting the staff working in the production facilities was a top priority to prevent any production stops caused by staff falling ill. Interviewees B and E pointed out that the mandatory reserve supply of medicines also contributed to the ensured availability of medicines in Finland. Interviewee B instead noted that some manufacturers focused in producing critical medicines related to treating COVID-19 diseases which in some cases caused shortages of other medicines as their production capacity was reduced. The interviewees told that by the end of 2020 they had not confronted any major raw material or API shortages as the production as well as logistics had been functioning well and without major interruptions.

6.2 Limitations and suggestions for future research

Due to the research methodology, there are some limitations regarding the empirical study of this thesis. First, as the interviewees chosen for the empirical study represent a medicine wholesaler and medicine wholesale license holders, the result of the study are not generalizable to the scope of the entire medicines industry. Also, one of the

interviewees work in a different branch than the others, thus has slightly different perspective to the topic. However, it is considered that the empirical study provided reliable results as the findings go mainly hand in hand with the already existing research and literature about the topic. Thus, it is also considered that the interviewees chosen for the study shared reliable and well-informed insights, as they were well acquainted with the subject and the context of this thesis. Regarding future research, the issue of medicine shortages still has multiple research gaps. The topic has not yet been extensively studied, especially in the Finnish context as the issue has drawn attention only recently. It would be especially important to define the players who would start leading the conversation about the topic and systematically investigating sustainable solutions for the medicine shortages issue. On a concrete level, conducting research on other fields by interviewing e.g., representatives from the national competent authority (Fimea) or multinational authorities would provide valuable information from other perspectives than those presented in this thesis.

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