Aalto University
School of Business

# Supply Chain Management in a Highly Regulated Environment – a Case Study of Supplier GMP-Compliance Management in the Pharmaceutical Industry

Master's Thesis
Samuli Vaittinen
Fall 2016
MSc programme in Management and International Business

Aalto University
School of Business

Aalto University, P.O. BOX 11000, 00076 AALTO
www.aalto.fi

**Abstract of master's thesis**

**Author** Samuli Vaittinen

**Title of thesis** Supply Chain Management in a Highly Regulated Environment – a Case Study of Supplier GMP-Compliance Management in the Pharmaceutical Industry

**Degree** Master of Science

**Degree programme** Management and International Business

**Thesis advisor(s)** Nina Granqvist

**Year of approval** 2016 **Number of pages** 90 **Language** English

**Abstract**

The purpose if thus study is to explore the impacts of high authority regulation and enforcement to supply chain management practices. As one of the most regulated industries, the pharmaceutical industry was chosen as the research context. More specifically, this study concentrates on the process of managing supplier's compliance to guidelines imposed by the European Commission, commonly called as the Good Manufacturing Practice (GMP). The research context provides a prominent ground for researching the main effects of rigorous authority supervision that may have significant impacts to both business and society.

Theoretical part of this study concentrates on the relevant literature on supply chain management, supplier management, supply chain risk management and supply chain sustainability management. This literature review serves as a theoretical framework to understand what are prevalent, or normal, processes and assumptions in these different practices. This understanding is important for identifying the anomalies brought by high authority regulation and enforcement.

The research was conducted by interviewing informants from six different pharmaceutical companies on their personal perceptions and company's processes. All the informants had a major role in their company's supplier GMP-compliance process, thus having significant internal knowledge. A general framework on the supplier GMP-compliance management process is proposed based on the findings.

I conclude that rigorous authority regulation and enforcement has several major impacts on how companies manage their suppliers, including disintegration of sub-processes, creation of departmental silos and shifting focus towards compliance itself rather than efficiency or rationality of the process. Furthermore, regulations limit risk management options that companies can exercise, which can lead to severe supply chain disruptions. Finally, through authority enforcement and certification programs, there is an unintentional shift of responsibility from industry towards the authorities.

Contributions of this study reach beyond expanding theory – the balance between industrial internal self-control and need of regulatory interference and supervision is in headlines now perhaps more than ever before, not least because of the rise of sustainability initiatives. While adding regulation may at first seem as straight-forward approach, it has implications that are critical to recognize before imposing new requirements.

**Keywords** supply chain management, supplier management, compliance, authority enforcement, risk management, sustainable supply chain management, Good Manufacturing Practice, pharmaceutical industry

**TABLE OF CONTENTS**

## LIST OF TABLES AND FIGURES

**ABBREVIATIONS**

AS – active substance

EMA – European Medicines Agency

FDA – U S Food and Drug Administration

GMP – good manufacturing practice

GSCM – green supply chain management

ISO – International Organization for Standardization

MA – marketing authorization

NGO – non-governmental organization

SCM – supply chain management

SCRM – supply chain risk management

SSCM – sustainable supply chain management

# 1. INTRODUCTION

## 1.1 The pharmaceutical industry, GMP-compliance and impacts of regulation

Surprisingly little research has been done in relation to the pharmaceutical industry practices in general, given its formidable size and undisputed importance. The industry has many specific features, which may hinder the generalization of research results to other industry fields and vice versa, but also make the research essential: pharmaceuticals are saving lives, but as can be seen from the history, they have also taken lives when something has gone wrong. It is not unfair to say that pharmaceutical industry has an impact on every one of us, which is also a reason for its intense and strict regulations.

Pharmaceutical industry is perhaps the most regulated industry and, besides regulations, it is also known for intense authority enforcement of those regulations. All critical activities related to delivering the pharmaceuticals to patients are subject to a specific license. In the context of this industry, authorities have a strong mandate in controlling compliance to the regulations, and enforcement acts such as import restrictions or withdrawing licenses are seen regularly. This is in addition to the tight industry self-control.

In the research context of pharmaceutical industry, this study focuses on the significance and nature of GMP-compliance risk, a term that is specific to the pharmaceutical industry. GMP refers to the good manufacturing practices, or the prevalent regulations starting from raw material manufacturing and reaching to analyzing and releasing a finished pharmaceutical batch for sale. Compliance in this context refers to adhering and conforming to pre-defined guidelines and regulations that have been set by an external party (or parties) to ensure safety and benefits of the society rather than individual corporations or industries. This definition includes a notion that industry's self-control has not seen sufficient and reliable, which is quite self-evident from history of the pharmaceutical industry discussed in later chapters. The scope of this study has been further limited to external supply chain GMP-compliance risk, or in other words, the risk arising from outsourcing manufacturing and related activities and not being able to sufficiently control GMP-compliance level of suppliers. In the context of

the pharmaceutical industry, the purpose of this thesis is to study how significant the GMP-compliance risk is seen by the industry today, what are the current supply chain GMP-compliance risk management practices, and how have the regulations and strong authority enforcement shaped them compared to conventional supply chain and risk management.

Motivation for the study and the scope merged from a perceived growth in importance of the topic: different authorities seemed to increase their monitoring and more actively impose sanctions for non-compliances. At the same time, GMP-regulations are being updated to widen their scope and impose stricter requirements: for example, besides adding new requirements, EU GMP chapter 7 was updated in 2012 to concern all outsourced activities, instead of the earlier scope of contract manufacture and analysis. Finally, as with other industries, pharmaceutical supply chains have become much more complex, shifting a lot of activities to developing countries. As the manufacturing is taking place much further, managing one's supply chain becomes more complex and calls for new means.

All this has led to increasing number of pharma supply chain disruptions related to GMP violations, which can have drastic consequences. From the business side, consequences can vary from withdrawing certain batches from the markets to cancelling entire product lines, as well as company image and reputational issues. From societal perspective, these disruptions can cause world-wide supply shortages of critical medicines.

Regulations naturally also exist outside the pharmaceutical industry, even if they would not be overseen and enforced as rigorously as with the pharmaceuticals. Many other industries, such as banking and insurance, are currently experiencing a move to a significantly stricter regulatory environment. Furthermore, ever-stricter regulations related to sustainability are affecting virtually all businesses, regardless of their line of business. It is quite obvious that increasing regulations will have an impact on companies operate, some of them as intended by regulators, but also some unintended impacts as byproducts of the requirements will certainly appear.

These byproducts might have significant negative effects for business as well as for the society and it is thus important to identify and understand them, for businesses to avoid unintentional processes that might cause inefficiencies and harm the company and for authorities to understand these byproducts when developing existing and new regulations. In a more general context within theoretical fields of supply chain management, supply chain risk management and supply chain sustainability management, this study will explore the byproducts that strong regulation produces in supplier management practices. To identify these regulation-caused byproducts, supplier management practices in the pharmaceutical industry are compared to traditional approaches identified from the literature.

The research problems discussed above are reflected in the following questions that together constitute the research question for this thesis:

*What is the significance and nature of Good Manufacturing Practice compliance risk?*

*How is supplier and risk management constructed in a highly regulated and enforced environment?*

*What are the impacts that strong regulation and authority enforcement impose to supplier and risk management practices?*

## 1.2 Outline for the thesis

This thesis situates itself among three main theoretical fields: supply chain management, risk management and sustainability management. From the perspective of this thesis, sub-themes of these main theoretical fields concentrating on supply chain management and supplier management concepts are the most relevant ones. These theoretical fields, even though being their own research areas, are intertwined and borrowing from each other.

The reason for focusing on supply chain management and risk management is quite clear: these are the main theoretical fields explaining the background and the very basic assumptions related to this thesis. Without reviewing these two fields, it would be very hard

to define the upper-level context relevant to this thesis or reflect the study results to areas outside the pharmaceutical industry. Compared to these two research areas, importance of sustainability management to this thesis is not as obvious and requires further elaboration.

As mentioned above, the pharmaceutical industry, and GMP-compliance being one of its specific characteristics, have remained understudied till to date. Furthermore, management of compliance in general has attracted little interest. Sustainability management is one of the rare theoretical fields that studies compliance management in a supply chain context and is thus of special interest for this thesis: it deals with managing compliance to certain standards, and even though there are some differences to the GMP-environment, management of sustainability on supply chains is a fairly good match with supply chain GMP-compliance management.

Sustainability management is still a new area, but it has withdrawn a lot of attention in recent years. Its theoretical context is built around contemporary and complex supply chains, extending around the whole world, that is also characteristic of pharmaceutical supply chains. For this thesis, sustainability management is a mean to extend the theoretical surface to include compliance-specific features from a general, not an industry-specific, perspective. It should be beard in mind, however, that sustainability is not a perfect analogue to GMP: one major difference between the two topics is that where authorities are the main party monitoring and imposing GMP-compliance, NGOs and other non-authority stakeholders are more important in sustainability enforcement.

The higher-level purpose for this thesis can be described as follows: instead of being an empirical testing field for the prevalent theories, the pharmaceutical industry and GMP-compliance provides an interesting setting for researching the effects of high authority regulation and enforcement in relation to these prevalent theories. This thesis will thus research how the assumptions and generally accepted practices are shaped by the specific setting examined.

The outline for the thesis is as follows: first chapters will introduce the relevant literature field, starting from the outlying area of supply chain management in general and specifically supplier management and supply chain risk management practices. The final part of the literature review will concentrate on relevant literature on sustainability from supply chain management perspective. After the literature review, methodology chapter will introduce research questions, research context and how the research was conducted. Before going to the actual results, chapter 5 will act as an introduction to the empirical context of the research, the pharmaceutical industry, and its specific characteristics. This will be followed by presentation of the research results and main conclusions and discussion. I will conclude this thesis with managerial implications and further research suggestions.

## 2. THEORETICAL APPROACHES TO SUPPLY CHAIN MANAGEMENT

One of the earliest academics emphasizing the importance of purchasing and suppliers was Porter (1975), who identified them as two of the five critical forces that affect industry competitive nature. The strategic importance of purchasing and supplier decisions has subsequently been emphasized by many authors and today is a generally accepted notation (for example Hahn *et al.*, 1986 and Ellram & Carr, 1994). Competition between companies has thus extended to competition among supply chains (Li *et al.*, 2006).

Supply chain management (SCM) is a broad research field that holds many themes under it, such as collaboration, demand, logistics, strategic, supplier and marketing management (Soni & Kodali, 2013). Research on SCM has been fragmented and as there is no generally accepted definition for the term, the term has been used in many different contexts (Storey *et al.*, 2006; Grimm *et al.*, 2015). It has originated within the manufacturing industry and contributed to some well-known concepts, such as total quality management, lean management and just-in time management (Burgess *et al.*, 2006). Nowadays SCM research addresses also areas outside the traditional manufacturing industry, including the service industry and virtual enterprises (Grimm *et al.*, 2015).

SCM research borrows from many other research fields: Croom *et al.* (2000) identified 11 different subject literatures that have contributed to SCM, such as purchasing and supply, organizational behavior, contingency theory, institutional theory, strategic management and network literature. Some other tightly linked research fields also borrow from SCM literature, including supply chain risk management (SCRM) and sustainable supply chain management (SSCM), that will be addressed separately in later chapters. This literature review will mainly concentrate on the supplier management aspect of SCM theory, but it should be noted that this grouping is only directional as boundaries between the different SCM areas remain loose and many of them are interrelated.

## 2.1 Supplier management

Supplier management includes many sub-themes such as supplier selection, supplier evaluation, supplier relationship management and supplier development. Besides SCM, it also owes to purchasing management and performance management disciplines. This chapter will concentrate on the problem of supplier selection, qualification and evaluation (SSQE).

The process of selecting, qualifying and evaluating suppliers has attracted a lot of attention from modelling discipline, and there are many articles presenting complex algorithms and mathematical models for managing this process (for example Hammami *et al.*, 2014 and Yadav & Sharma, 2016). A bit surprisingly, there are not many qualitative studies on this process and literature is lacking clear qualitative models for SSQE (Luzzini *et al.*, 2014), even though its importance to organizations' performance is well acknowledged (Carr & Pearson, 1999 and Kannan & Tan, 2000).

In their book *Purchasing and Supply Management*, Johnson & Flynn (2015) divide the supplier selection criteria into three different levels: strategic, traditional and current additional. These levels and the criteria under them are summarized in Table 2.1.

Table 2.1: supplier selection criteria (based on Johnson & Flynn, 2015)

| | |
|---|---|
| **Level 1: strategic** | |
| **Linking sourcing with strategy** | Assessing which suppliers are able to meet organization's (strategic) requirements |
| **Risk assessment** | Assessing supplier risk versus expected returns |
| **Strategy development** | Developing purchasing strategy based on the risk assessment |
| **Level 2: traditional** | |
| **Technical, engineering, manufacturing and logistic strengths** | Evaluating supplier's current and future operational strengths, including quality aspects |
| **Service design, operations and delivery** | Evaluating supplier's current and future service capabilities |
| **Management and financial evaluation** | Evaluating supplier's managerial systems and financial aspects in terms of price negotiations and financial health |
| **Level 3: current additional** | |
| **Financial considerations** | Evaluating means to strengthening purchasing organization's financial aspects, such as tax savings |
| **Environmental impact** | Assessing sustainability aspects |
| **Innovation** | Assessing supplier's potential for innovation |
| **Regulatory compliance** | Assessing supplier's regulatory compliance |
| **Social and political factors** | Assessing social and political concerns related to the supplier |

From the three levels introduced by Johnson & Flynn (2015), strategic level criteria concentrate on how a supplier candidate would support company's strategy, identify risks on this area and how company's purchasing strategy with this candidate should be aligned.

Traditional level criteria concentrate on supplier candidate's operational level strengths and weaknesses as well as management and financial aspects. Finally, current additional level criteria address different areas that have arisen more recently into focus in supplier evaluation and include for instance supplier's potential for innovation, environmental and societal factors and regulatory compliance. The writers emphasize, that the resources, time and attention invested to the process should reflect strategical importance and value of the purchase.

According to study conducted by Luzzini *et al.* (2014), supplier evaluation process can be allocated into six main stages and furthermore assembled into three main processes that are presented in Table 2.2. Even though the purchasing unit is usually in the focal point and managing the SSQE process, other units, such as quality, engineering and finance, usually take part in the design and implementation of SSQE system and its different stages (Luzzini *et al.*, 2014).

In pre-qualification stage, an organization gathers preliminary information about the supplier firm. Potential suppliers may be dropped from the process during each of the stages. First stage is RfO, or request for offer, which in addition to collecting the first economic offer, serves also as a tool to receiving general information from the supplier. RfO is usually followed by a separate questionnaire to assess the supplier in more detail. If not already included in the first questionnaire, it is followed by a second one focusing on the specific product or service offered, concentrating on supplier's technical and operational capabilities in relation to producing the service or product.

Table 2.2 supplier evaluation process steps (based on Luzzini et al., 2014)

| | |
|---|---|
| **Pre-qualification** | *"Collection of preliminary and general information about the supplier firm"* |
| RfO | Economic offer from the product or service and gathering general information from the supplier |
| Questionnaire(s) | Gathering supplier-related information |
| Product & process quality | Gathering information on supplier's capabilities to produce the product or service |
| **Qualification / Selection** | *"Collection of in-depth information about the supplier product or service"* |
| Technical & economic | Assessing supplier's product and process quality |
| Negotiation & budget split | Further negotiations and assigning the supplier a share of the company's total purchase volume |
| **Vendor rating** | *"Comprehensive and continuous evaluation of supplier performance in terms of products and services delivered"* |

If all the pre-qualification steps are passed, supplier enters the actual qualification/selection process, starting with assessing supplier's product and process quality that may include (but not limited to) product sampling, on-site visits or initial discussions on contractual arrangements. If the supplier passes this phase, it formally enters the organization's supplier base, which may be followed by further negotiations and assigning a certain share of organization's total purchases.

The final stage, vendor rating, concentrates on active suppliers that are assessed through different key performance indicators. According to Luzzini *et al.* (2014), typical focus areas are quality, service level and documentation. The purpose of this assessment is to identify the top-performing suppliers and, on the other hand, suppliers with many problems, and take

actions accordingly (such as preferring the top suppliers or implementing improvement plants for poor suppliers).

Luzzini *et al.* (2014) emphasize that the SSQE process is always case-specific, and the indicators and metrics used should be adjusted to firm's strategy and on the nature of product or service being procured. This is addressed by a process presented by Kraljic (1983), who defines a four-step process for strategically managing company's supply: (1) classifying purchased materials according to their impact to profit and supply risk, (2) conducting market analysis regarding the relative power of the customer in regards of its individual suppliers, (3) positioning strategic materials identified in the first step in a matrix of supplier versus company relative power and (4), depending on where the material lies in the matrix, implementing a specific supply strategy (exploit, balance or diversify). Besides concentrating on the individual products or services procured, companies should also review the entire supply profile of their individual suppliers, differentiating long-term strategic suppliers from short-term non-critical suppliers (Luzzini *et al.*, 2014).

### 2.2 Supply chain risk management

Supply chain risk management (SCRM) is not itself a new practice, as risks have existed also in traditional, local and integrated, supply chains (Tang, 2006a). However, as the traditional supply chains have shifted into more modern, global and outsourced supply networks, and the magnitude key suppliers grown significantly, the nature and severity of supply chain risks has risen significantly. Many articles refer to the time of turn of millennium as the big turning point in SCRM research, as many severe and global supply chain disruptions occurred (for example Ho *et al.*, 2015; Sodhi *et al.*, 2012; Tang, 2006a). One of the most known of these incidences is the fire at one of Ericsson's main supplier in 2000 (a semiconductor plant owned by Phillips), that eventually was evaluated to have caused a $400 million loss for Ericsson (Chopra & Sodhi, 2004). Other examples include Dole's banana plantation destruction by a hurricane in 1998 (Biddles, 1998), Dell's recall of 4 million laptops due to defective battery

caused fire hazard in 2006 (Lawton & Dade, 2006) and Mattel's recall of 19 million toys due to lead paint and loose magnets in 2007 (Story & Barboza, 2007).

From a theoretical perspective, SCRM overlaps with SCM in many respects, but these two research fields should not be confused with each other. As was true with SCM, also SCRM lacks a clearly defined and broadly accepted definition (Diehl & Spinler, 2013), which makes locating it on a theoretical map also challenging. Drawing on the previous definitions of other writers, Ho *et al.* propose SCRM to be defined as "*an inter-organisational collaborative endeavor utilizing quantitative and qualitative risk management methodologies to identify, evaluate, mitigate and monitor unexpected macro and micro level events or conditions, which might adversely impact any part of a supply chain".* Even though over-simplifying these two fields, the main difference could in a very general level between SCM and SCRM be considered as follows: SCM concentrates on making the supply chain more innovative, productive and effective, whereas SCRM focuses on identifying, preventing and managing risks laying in the supply chain. As with SSQE, the focus in SCRM research has been more on quantitative models than qualitative research.

Risk management process in the supply chain context can be considered to consist of three different phases, containing six distinct steps, as suggested by Tummala & Schoenherr (2011) and presented in Figure 2.1. In phase I, all the relevant risks are identified, measurement of the severity of effects of the individual identified risks should they occur and assessment of the probability of the individual risk occurrence. On phase II, the individual risks are first evaluated based in their severity and probability and, at least for risk that are not on an acceptable level based on the evaluation, a risk mitigation plan is developed and implemented to manage the non-acceptable risk. The final in phase III focuses on monitoring the individual risks as well as the risk portfolio and the implementation and effectiveness of mitigation plans.

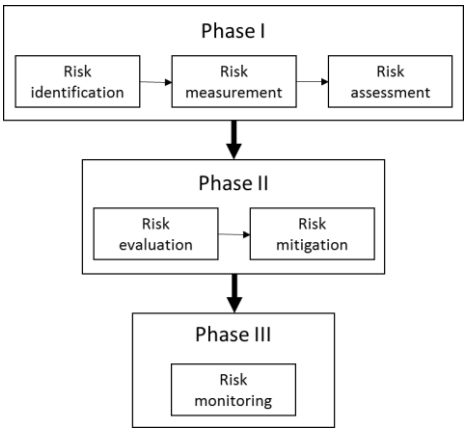


Figure 2.1: risk management process (adapted from Tummala & Schoenherr, 2011)

Perhaps one of the best overview of different risk categories in the supply chain is captured by Ho *et al.* (2015), whose illustration is presented in Figure 2.2. Based on their view, on a broader level the risks can be divided into macro- and micro-level (also catastrophic and operational (Sodhi *et al.*, 2012) or disruption and operational (Tang, 2006a)) risks. As described by Ho *et al.* (2015), macro-level risks are rather uncommon, external occurrences that can have a devastating impact on companies and can be divided further into natural and man-made risks, such as earthquakes or hurricanes and war or political tremor. Micro risks, on the other hand, "*refer to relatively recurrent events originated directly from internal activities of companies and/or relationships with partners in the entire supply chain*", and can be further divided into demand risks, manufacturing risks, supply risks and infrastructural (information technology, transportation and financial systems) risks. For the purpose of this thesis, the remainder of this chapter will focus on qualitative SCRM strategies of macro-level and supply risks.

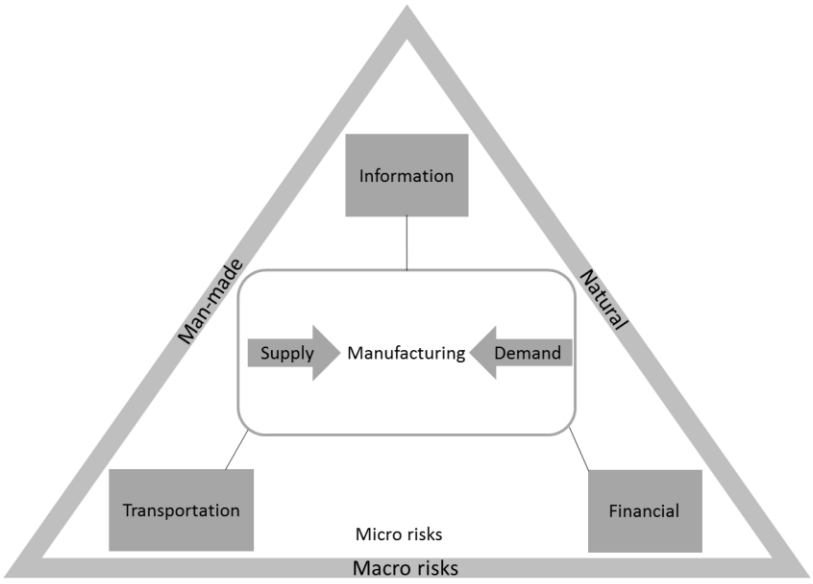


Figure 2.2: conceptual framework of supply chain risks and risk management steps

As companies have been racing to make their supply chains more efficient (or high-speed and low-cost) with initiatives such as just-in-time, the vulnerability of these supply chains to disruptions has grown significantly (Lee, 2004). Besides reducing costs and improve customer satisfaction in normal conditions, supply chain strategies should thus be able to secure company's operations, should a major disruption occur. Tang (2006b) introduces nine different strategies for this purpose that are listed in Table 2.3. Tang (2006b) emphasizes, that these strategies have three main challenges: balancing between the costs and benefits of a specific strategy, fitting the supply chain strategy to company overall strategy and being able to proactively implement a given strategy or being able to identify the need of a given strategy in the first place. Even though same strategies may be applicable to mitigate also supply risks, the different nature between these two risk categories calls for specific means for supply risk management.

Table 2.3 strategies for overcoming macro risks (adapted from Tang, 2006b)

| Strategy | Description | Benefit |
|---|---|---|
| Postponement | Apply product standardization and delay the point of product differentiation | Enables a firm to change the configurations of different products quickly |
| Strategic stock | Maintain a stock of critical components or products in strategic locations | Enables a firm to respond to market demand quickly during a major disruption |
| Flexible supply base | Maintain multiple suppliers | Enables a firm to shift production among suppliers promptly |
| Make-and-buy | Maintain the capability to manufacture critical components or products in-house while outsourcing | Enables a firm to shift production between in-house production facility and suppliers rapidly |
| Economic supply incentives | Provide economic incentives to suppliers for preventing perishment of supplier base | Enables a firm to adjust order quantities quickly |
| Flexible transportation | Enhance multi-modal (air, road and water), multi-carrier and multiple route transportation | Enables a firm to change the mode of transportation rapidly |
| Revenue management | Apply dynamic pricing and promotion when selling perishable products or services | Enables a firm to influence the customer product selection dynamically |
| Dynamic assortment planning | Enhance assortment planning by promoting (displaying) widely available products or services over the ones facing supply disruptions | Enables a firm to influence the demands of different products quickly |
| Silent product rollover | Introduce new products to markets without a formal announcement | Enables a firm to manage the demands of different products swiftly |

Supply risks mean any adverse events or situations with the upstream partner of a company, that may have a negative impact on the company (Zsidis, 2003). Examples of supply risks include poor quality, uncertain capacity, late delivery, lack of supplier involvement and supplier failure in terms that the product is not delivered (Ha *et al.*, 2015). They are in general considered more day-to-day level and not as significant as macro-level risks, but may nevertheless have a notable impact on company's performance. Table 2.4 summarizes different supply risk approaches presented in the literature.

Table 2.4 strategies for overcoming supply risks

| Strategy | Description |
|---|---|
| **Behavior-based management techniques (Zsidis & Ellaram, 2003)** | Focuses on supplier processes rather than outcomes; evaluate suppliers based on their behavior, which will have an effect on the outcome. Requires improved information sharing, monitoring supplier progress and actions and close relationship with suppliers |
| Supplier certification | Certificate suppliers that consistently meet predetermined quality, cost, delivery, financial and volume targets. Helps to reduce time-consuming controls of certified suppliers, generates information on supplier performance and aligns supplier's behavior with the company's processes |
| Quality management program | Establish a quality management program in supplier's premises to achieve company's quality requirements and expectations. |
| Target costing | Establish two-way information sharing and negotiation by sharing company's sales estimates and production schedule and supplier's cost structure and cost drivers and pursue together ways of reducing costs |
| Supplier development | Improve supplier's performance and capabilities by for example developing supplier's technical quality or delivery capabilities and driving continuous improvement. May include giving feedback to and training the supplier, sending company's own employees to supplier's premises and investing to the supplier's facilities and equipment. |
| **Early supplier involvement (Zsidis & Smith, 2005)** | Involve supplier already in an early phase of product development to reduce the risk of supplier failure, quality problems, supplier insolvency, product delays etc. |
| **Reducing supply chain complexity (Choi & Krause, 2006)** | Carefully manage the (1) number of suppliers, (2) differentiation of suppliers including cross-border barriers, technical capabilities and operational practices and (3) inter-relationship among suppliers to reduce supply risks arising from supply chain complexity. Reducing supply base to an extreme, on the other hand, will also increase supply risk significantly. |
| **Contingency planning (Colicciha *et al.*, 2010)** | Develop plans and actions for alternative modes of supply to be activated in case a negative event occurs for secure supply. |

Even though a lot of literature exists around SCRM, many gaps and unexplored topics remain, starting with the fact that a clear definition of SCRM is still to be acknowledged. As SCRM itself contains such a broad variety of topics and different types of risks, it is

challenging to get a holistic view of overall risk management practices instead of concentrating on individual risk types. From practical point of view, even though many conceptual frameworks have been presented, empirical research is still abundant in many respects and many theories are still to be tested in practice. Finally, the lack of qualitative research and "easy-to-approach" SCRM, instead of complicated modelling applications, makes it harder for real-life organizations to apply research to real-life conditions.

## 3. SUSTAINABILITY AND SUPPLY CHAIN MANAGEMENT

Importance of and attention on sustainability has grown as supply chains have become more and more global. Globalization has strongly affected production and consumption patterns on every industrial aspect and will continue to do so in the future. Typical feature of today's supply chain is to organize higher-skill activities, such as product design, marketing and business development, in developed countries, while locating lower-skill manufacturing activities to developing countries. It is also common for brand-owning companies to outsource the manufacturing activities. This division between higher-skill activities and manufacturing operations creates concerns that the social, environmental and economical norms that are expected in company's home country are not appropriately enforced in the countries where manufacturing is taking place.

Globalization, rising importance of supply chains, increased competition, harsher regulations and intensifying scarcity of resources have alone made companies to pay more attention on sustainability (Walker *et al.*, 2008). Besides these drivers, many different NGOs have shifted their focus, or even born, to govern sustainability of modern global supply chains. Furthermore, companies experience pressure towards managing supply chain sustainability from their customers, other firms, governments and even local communities. Governance for sustainability is thus multifold, not something stipulated solely by government agencies, but by several different types of actors with many different instruments. Besides the rising strategic importance of SCM and the purchasing in a traditional sense focusing at lower costs,

quality and flexibility, the growing importance of sustainability demands buyers to do this in a social and environmental manner. This setting has evoked rich literature around sustainability and supply chain management. The purpose of this literature review is not to capture a holistic view on theories of sustainability management in supply chains, but to introduce the main points of relevance to the theme under study.

### 3.1 Basic terms: GSCM, triple bottom line & SSCM

The basis of sustainability management in supply chains started to evolve from environmental aspects in the early 1990s, first focusing on specific activities of SCM such as logistics and purchasing, and then integrating these activities to achieve environmental effectiveness, eventually establishing the term of green supply chain management, GSCM (Sarkis *et al.*, 2011). As described by Beamon (1999), GSCM focuses on minimizing environmental impacts of a product through its entire life cycle as an extension to traditional SCM. Sustainable supply chain management, SSCM, is another established term that is in many respects viewed as an extension of GSCM incorporating the other, social and economic, aspects of sustainability (Ahi & Searcy, 2013).

One widely used framework used in conceptualizing SSCM is the triple bottom line – or the three dimensions of sustainability – that was introduced by Elkington in 1998. According to Elkington (1998), sustainability of organizations at a broad level consists of three components: the natural environment, society and economic performance. Perhaps the most important notion of the triple bottom line is that sustainability is not something that organizations can be profitable in spite of sustainability, but that companies increase their profitability by engaging environmental and social activities that improve their economic performance (Carter & Rogers, 2008). The triple bottom line framework is presented in Figure 3.1.

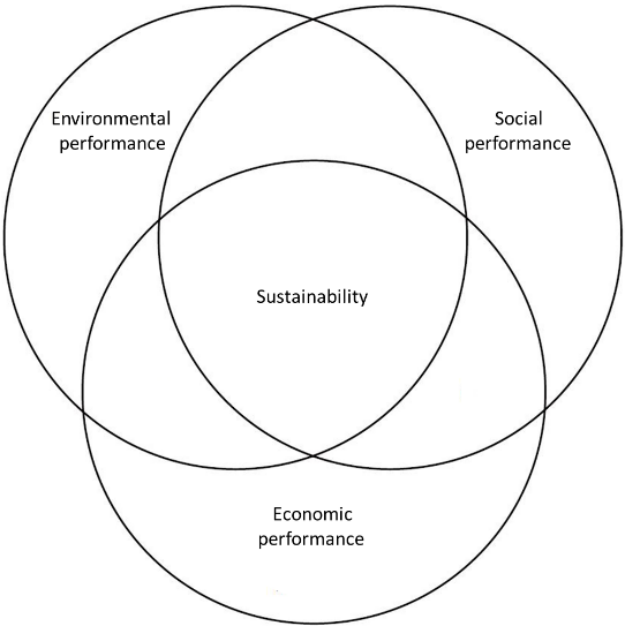


Figure 3.1: the triple bottom line (adapted from Carter & Rogers, 2008)

In their effort to include different characteristics found in the literature, Ahi & Searcy (2013) defined SSCM as *"the creation of coordinated supply chains through the voluntary integration of economic, environmental, and social considerations with key inter-organizational business systems designed to efficiently and effectively manage the material, information, and capital flows associated with the procurement, production, and distribution of products or services in order to meet stakeholder requirements and improve the profitability, competitiveness, and resilience of the organization over the short- and long-term".* As GSCM and SSCM are based on the same principles, only with the difference of GSCM omitting the social and economic dimensions of sustainability, this chapter will use the term SSCM with the notion that it also withholds GSCM and that the literature of GSCM in a broad sense also applies to SSCM. When placing SSCM on a theoretical map, it is obvious that it has the same linkages to and builds on the same theories as SCM. However, SSCM literature has also specifically been linked to several organizational theories by Sarkis *et al.* (2011), including for example the complexity theory, resource based view, institutional theory and stakeholder theory.

## 3.2 Sustainable supply chain management

Even though SSCM refers to the whole supply chain, the literature has usually had its main focus in supplier management practices (Beske & Seuring, 2014). SSCM frameworks tend to rely on a typical SCM orientation that begins from a focal company as an initiator of sustainable practices, which typically has the most power and influence along the supply chain and extends its requirements for sustainable practices to its suppliers (Gimenez & Tachizawa, 2012; Miemczyk *et al.*, 2012). This is also the orientation for SSCM framework introduced by Beske & Seuring (2014), which aims to describe SSCM "*in or through SCM*".

Beske & Seuring (2014) identify five different key categories and prevalent practices under them from SSCM literature. The practices in this framework should be understood as a way of doing things with the aim of improved performance and the categories as a way of dividing and grouping practices under different umbrellas. The five categories are orientation, continuity, collaboration, risk management and pro-activity. These categories are further divided into three underlying drivers: strategic values, structure and processes. The framework is illustrated in Figure 3.2. Each of the five categories and related practices are introduced below.

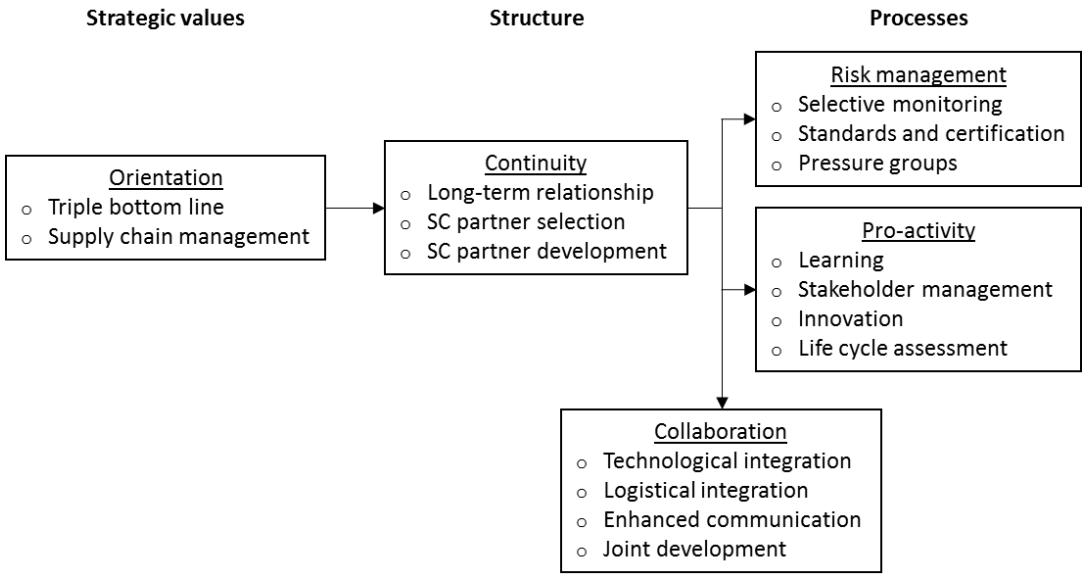


Figure 3.2: Key categories and related practices in SSCM (adapted from Beske & Seuring, 2014)

The first category Beske's & Seuring's (2014) framework, orientation, addresses company's strategic orientation and values: to reach effective SSCM, strategy and top management are obliged to encourage sustainability and supply chain management in the first place. Sustainability has to be integrated to company's strategy and receive top-management support for reaching the full potential of SSCM. Sustainability-oriented companies are usually giving equal weight to all three (economic, environmental and societal) dimensions of sustainability in their decision-making, thus following the triple bottom line practice. Different sustainability goals may conflict with each other and it is important to recognize possible trade-offs between the triple bottom line dimensions. Second practice in this category is SCM, which implicates that traditional SCM practices have to be integrated to the strategy and decision making and also calls for top-management support. This category thus includes conventional supply chain thinking through SCM practices, but is separated from it by including the triple bottom line dimensions in the strategic prerequisite. Orientation category can be seen as the starting point and precondition for encaging SSCM and is built upon strategic values.

Continuity category can be viewed through structural decisions: it defines how the supply chain is set up and how different partners work together. As Beske & Seuring (2014) describe it, continuity underscores mutual and beneficial relationship between the supply chain partners and reflects performance of the entire supply chain, instead of performance of its individual members. In addition, the writers furthermore mention that continuity is about sharing risks and profits along the supply chain. Practices under this category concern building long-term relationship, development of supply chain partners and selection of (qualified) partners. Long-term relationship helps to build trust, common goals and structures, whereas partner development aims at improving performance and capabilities of the supply chain (Beske & Seuring, 2014). Supplier selection is described to include, besides selecting the right partners, reducing the supplier base to a limited number of suppliers.

Beske's & Seuring's (2014) third category, collaboration, is staged between structure and processes: it is defined to be about generating collaboration in the first place (structure), but also about how collaboration is achieved in the operational level in practice. Beske & Seuring (2014) describe collaboration to go one step further than cooperation, for example in forms of inter-organizational learning and long-term orientation. Practices in the category include logistic and technological integration, enhanced communication along the entire supply chain and joint development of capabilities and products.

In general, SSCM is perceived to have different and perhaps even higher risks than the traditional SCM, including significant disruption risk due to a smaller supplier base and reputational risks; on the other hand, supplier base reduction and increased collaboration with the remaining suppliers are thought to reduce risks through lower supply chain complexity and uncertainty (Miemczyk *et al.*, 2012). In Beske's & Seuring's (2014) framework, risk management category is placed in the processes stage and is about reducing the many risks of SSCM. Practices introduced by Beske & Seuring (2014) are selective monitoring through for example audits of an individual partner, standards and certifications that are usually more general and concern several companies, and finally, managing the many sustainability pressure groups, such as NGOs and local authorities.

The final category of Beske & Seuring (2014), pro-activity, integrates sustainability to product development phase, through product life cycle assessment and initial supplier selection. This also concerns involving a wider group of stakeholders to company operations and is about acquiring knowledge and learning from these stakeholders, leading to sustainable innovations. These practices are mainly driven by company processes.

What is, then, the difference between SSCM and conventional SCM? SSCM is commonly seen to be developed from the theories and practices of SCM for the demands of sustainability (Svensson, 2007). From the practices introduced by Beske & Seuring (2014), the writers list the triple bottom line, stakeholder management and life cycle assessment to be exclusive to

SSCM and to bring out significant differences in standards and certification, communication, technological integration and partner selection practices.

### 3.3 Dynamic capabilities in SSCM

The SSCM framework presented above can be seen as rigid and may not be sufficient in describing SSCM in a dynamic environment. Organizations pursuing a sustainability strategy or acting in sustainability-sensitive industries can also in general be seen to be more prone to unpredictable changes than other companies. This chapter has already linked SSCM to resource based view that, according to Teece *et al.* (1997), in a rapidly changing and unpredictable environment is unable to adequately explain competitive advantage of some firms in relation to others. In dynamic markets with rapidly changing competitive environment, long-term competitive advantage can only be achieved with dynamic capabilities, where companies "*integrate, build and reconfigure internal and external competencies to address rapidly changing environments*" (Teece *et al.*, 1997). Dynamic capabilities are thus about adapting to fast and unpredictable changes, risk and opportunities and shaping company's environment to achieve competitive advantage. This is also reflected in the definition of dynamic capabilities by Eisenhardt & Martin (2000): "*The firm's processes that use resources—specifically the processes to integrate, reconfigure, gain and release resources—to match and even create market change. Dynamic capabilities thus are the organizational and strategic routines by which firms achieve new resource configurations as markets emerge, collide, split, evolve, and die."*

Drawing from the literature, Beske (2012) introduces linkages between SSCM and dynamic capability theories in a conceptual level. He identifies some of the major overlapping business environment characteristics to lie in globalized markets, market transparency, market demand, product success and performance; these linkages are highlighted in Table 3.1.

Beske (2012) identifies five distinctive categories of dynamic capabilities to be of particular importance in SSCM. Figure 3.3 presents these categories as part of a SSCM framework first introduced by Beske (2012) and further modified by Beske *et al.* (2014). In this framework, dynamic capabilities are thought to enable efficient use of static capabilities and create new ways of using existing as well as totally new capabilities. Long-term competitive advantage does thus not arise from holding resources, but from the ability to configure and re-configure these resources (Teece *et al.*, 1997; Eisenhardt & Martin, 2000). Next, the five categories of dynamic capabilities are introduced.

Table 3.1 major overlaps between dynamic capabilities and SSCM theories
(adapted from Beske, 2012)

| **Business environment characteristics** | **Dynamic capabilities** | **SSCM** |
|---|---|---|
| **Globalized markets** | Dispersion of the geographical and organizational sources of innovation and manufacturing | Dispersion of the geographical and organizational sources of innovation and manufacturing |
| **Market transparency** | Market boundaries are blurred | Sometimes intransparent buyer-supplier relationships; tacit knowledge and contacts |
| **Market demand** | Market demand changes are nonlinear and unpredictable | Mature, informed customers, instant information sharing; rapidly, dynamically and unpredictably changing demands from stakeholders |
| **Product success** | Product success often based on multiple technologies and companies | Product success dependent on different technologies and companies |
| **Performance** | Competitive advantage is more than just financial performance | Firm performance measured on three dimensions of sustainability |

*Knowledge assessment* category is described by Beske (2012) to comprise of capabilities to access, acquire, understand and share knowledge of the supply chain partners. This category is important as gathering and creating new knowledge and is presented to be essential in maintaining competitive advantage in dynamic markets by Beske (2012)

*Supply chain partner development* is about developing all the actors in a supply chain, which can include customers, to realize their purpose in the supply chain (Beske, 2012). The different actors of a supply chain thus develop each other, and development becomes a continuous routine.

As developing partners to be better partners is considered important, so is the ability to co-evolve, or to develop and implement new competences for the supply chain. *Co-evolving* category includes dynamic capabilities that enable different actors to combine their resources to create new synergistic capabilities (Beske, 2012).

*Reflexive supply chain control* is defined by Beske (2012) as sharing, evaluating and influencing the actions taken by individual supply chain actors to reflect the benefit of the whole chain and, on the other hand, to evaluate the prevailing practices against changes in the prevailing business environment and adapt to these changes. This category is thus about influencing other actors in the supply chain to implement a common strategy and to adapt it as needed.

Finally, s*upply chain re-conceptualization* is described by Beske (2012) as considering a wider set of stakeholders, such as NGOs, as part of, and integrating them to, the SSCM. This category builds upon stakeholder theory that has been introduced in the earlier sections.

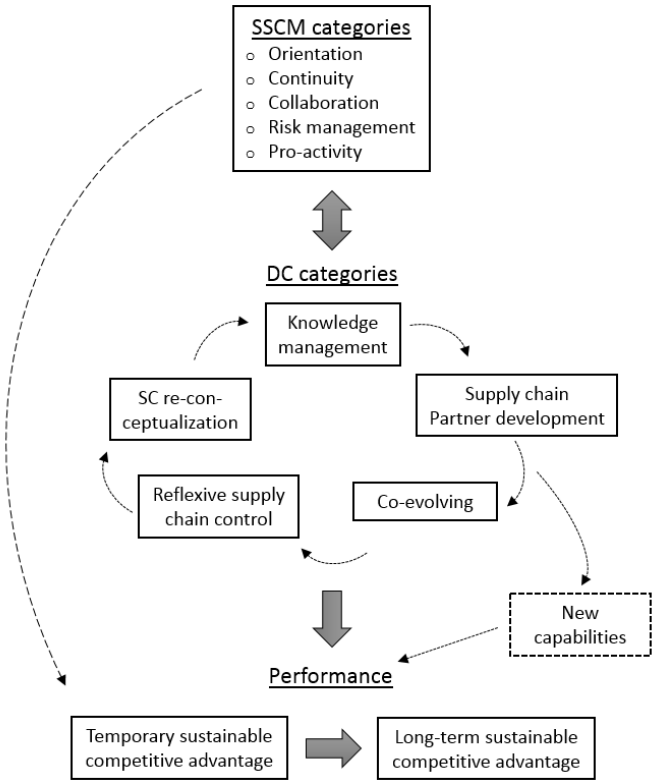


Figure 3.3: framework of dynamic capabilities in SSCM
(adapted from Beske, 2012 and Beske *et al.*, 2014)

The frameworks presented by Beske (2012) and Beske *et al.* (2014) are both relying solely on existing literature, thus the relationship between SSCM and dynamic capabilities is lacking empirical research and the explanatory and predictive value of these frameworks remain to be tested in real-life settings. Empirical studies may also prove some of the dynamic capabilities presented in the frameworks irrelevant for SSCM as well as add new ones yet to be discovered. It is quite obvious that to achieve competitive advantage through dynamic capabilities, supply chain has to be highly integrated among its individual parties and the basic principles of SSCM have to be in place.

### 3.4 Sustainable supplier management

Literature of SSCM exists in a broader level addressing the three dimensions of sustainability, but supplier management in general, and SSQE in particular, in regards of sustainability is not that well established (Zimmer *et al.*, 2016). Figure 3.4 presents one of

the rare frameworks found in the literature of sustainable supplier management processes presented by Zimmer *et al.*, 2016, that consists of three core processes: sustainable supplier selection, sustainable supplier development and sustainable monitoring.

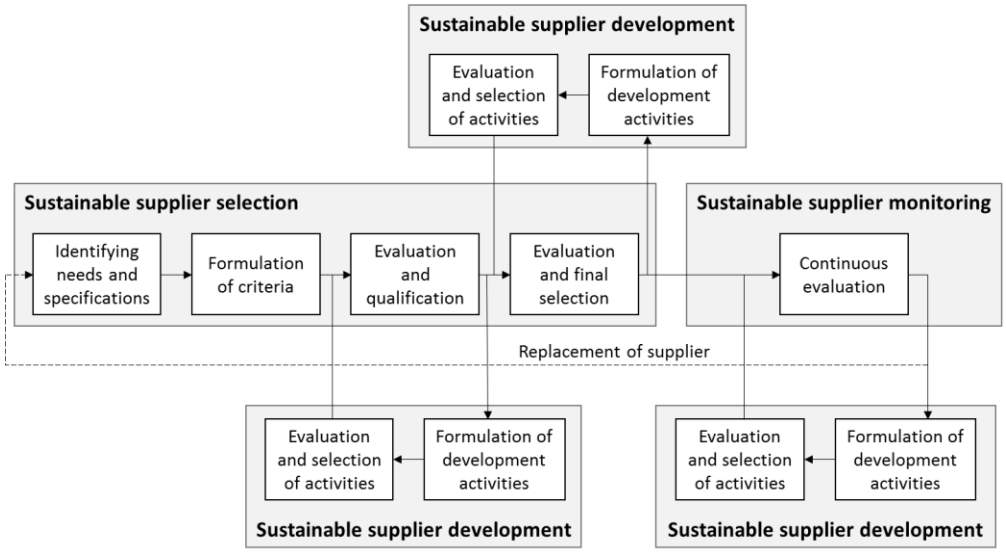


Figure 3.4: sustainable supplier management processes (adapted from Zimmer et al., 2016)

According to Zimmer *et al.* (2016), sustainable supplier selection process consists of identifying and evaluating supplier candidates in regards of the triple bottom line dimensions, the defined criteria serving also the base of evaluation in the monitoring and development processes. Sustainable supplier monitoring process is seen as a continuous evaluation of an existing supplier against defined minimum requirements and improvement in terms of the triple bottom line dimensions, and also serves as a trigger for supplier development or replacing a supplier in case it is not complying to the requirements. Finally, a supplier can be transferred to the sustainable supplier development process from supplier evaluation or monitoring processes. The scope of the three sustainable supplier development processes presented in Figure 3.4 are somewhat different: development during evaluation and qualification usually focuses on achieving established minimum requirements, whereas the other two development phases usually focus on improving the supplier beyond the minimum requirements. As explained by Zimmer *et al.* (2016), sustainable supplier selection,

monitoring and development processes are seen as independent, but interrelated, of each other.

The framework presented by Zimmer *et al.* is a very generic one, and is differentiated from the traditional supplier management only by the focus on sustainability: the core processes and principles are the same. Furthermore, it doesn't describe the meta-processes and actual means of how companies in practice manage the sustainability aspect of their suppliers. The lack of prescriptive sustainable supplier management frameworks shows that the SSQE process in terms of sustainability is not well established in the literature. As with traditional supplier management, there are quantitative algorithm-based models for evaluating supplier sustainability through different parameters, but qualitative methods are virtually nonexistent in the literature. Next, this chapter will examine supply chain sustainability from risk management point of view.

### 3.5 Supply chain sustainability risk management

One of the rare hands-on frameworks for supply chain sustainability risk management is given by Foerstl *et al.* (2010), based on their own study in chemical industry (see Figure 3.5). It includes six different stages: external responsiveness, supplier sustainability risk identification, assessment of supplier sustainability risk, supplier sustainability risk consequences, sustainability risk management response and sustainability risk performance outcomes. As managing external stakeholders such as NGOs has been already discussed above, this chapter will concentrate on the five latter stages.

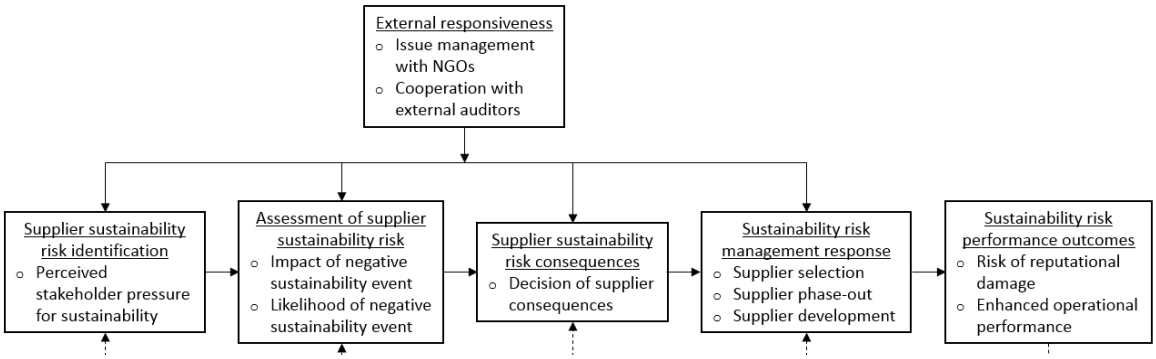


Figure 3.5: supply chain sustainability risk management (adapted from Foerstl et al. 2010)

According to the study of Foerstl *et al.* (2010), purchasing and supply managers experience significant external pressure in terms of supply chain sustainability, primarily from regulatory bodies. This pressure can be in the social or ecological dimension of sustainability, and companies focus on the dimension(s) for which they experience pressure. The identified risk areas thus depend on what kind of external pressure companies experience. Foerstl *et al.* (2010) also conclude, that even though the sustainability dimensions under focus may alter between companies, the processes and techniques of risk assessment are similar. The reason of limiting risk assessment to mainly one of sustainability dimensions was found to be shortage of internal resources. Similarly, suppliers that are seen to impose the biggest risk are given high priority in the sustainability risk management processes.

As presented in the earlier chapters, risk assessment is typically conducted through two components: assessing the consequences (impact) of an event, and the probability (likelihood) for the event to occur (Manuj & Mentzer, 2008). In their study, Foerstl *et al.* (2010) found that the impact-likelihood method is prevalent risk assessment method among the interviewed chemical companies. The companies initially relied on the information available in their supplier database and the probability of occurrence was evaluated through four indicators: physical properties of the supplied product, production process, supplier's geographical location and supplier's past performance records. Assessment of these indicators is done qualitatively and different indicators can be given different weights, depending on the product category. The consequences of a non-compliance were found to be estimated through indicators such as purchasing volume and strategic status of the supplier.

Based on these two components, suppliers were positioned to a two-dimensional matrix and the subsequent action depends on the supplier's position in the matrix. Non-critical suppliers were managed through a self-declaration on sustainability compliance, whereas critical suppliers are managed through self-assessment questionnaire and audited in case there is doubt about sustainability practices. Very critical suppliers are audited automatically. New suppliers taken to the selection process are evaluated through a self-assessment questionnaire

and chosen suppliers have to pass an on-site audit to be considered as potential suppliers for the company.

The probability-impact risk assessment method has been criticized to be static in it nature and thus to be limited on continuous supplier sustainability risk monitoring (Gelderman & Weele, 2003). Even though this was acknowledged by the companies following the method, the probability-impact risk assessment was seen as an easy tool for determining subsequent sustainability risk mitigation strategies and identifying supplier development needs (Foerstl *et al.*, 2010).

The risk assessment is followed by decision of supplier consequences and risk mitigation processes. Foerstl *et al.* (2010) conclude, that for established suppliers, the preferred action in case of violations is to retain the supplier through supplier development. Here, the supplier sustainability criteria are seen as dependent assessment criteria and violations usually result in increased resource allocation from the buying firm. On the contrary, in case of new suppliers, deficiencies in sustainability compliance may easily result in elimination of the supplier from the supplier selection process. Here, sustainability criteria are seen as independent selection criteria that are important in screening new suppliers and preventing high-sustainability risk suppliers from entering the supply base.

As described in the framework introduced by Foerstl *et al.* (2010), sustainability risk assessment divides suppliers into a continuum with insignificant risk in the other end and critical risk supplier on the other. Firms have basically three options to reduce the observed risks among their supplier: ignoring high-risk suppliers when selecting new ones, developing established suppliers above acceptable standards and termination of supplier relationship (phase-out) of an existing supplier. First option is quite straight-forward and is dependent on the efficiency of supplier selection process. It prevents reputational damage brought by new non-compliant suppliers. Second option reduces risks among suppliers as well, but additionally broadens the available supplier base and builds the relationship with suppliers.

It also enhances cross-functional and inter-firm collaboration and thus may have operational performance implications. Third option, terminating supplier relationship, is perhaps the most radical one and usually leads to a moral obligation of the buying firm to implement corrective actions that may be time- and resource taking. It may also mean publicly acknowledging a supply chain misconduct that brings negative publicity for the company.

Supply chain sustainability risk management is thus as much about choosing the right suppliers as it is about neglecting the ones posing high risks. Not every supplier can be considered as a strategic partner, and those that are must be screened carefully. Integration towards sustainability and achieving competitive advantage through SSCM practices (or dynamic capabilities) is not possible if company has chosen wrong partners. It is for example impossible to reach sustainable supply chain if other parties in the chain don't even see the importance of sustainability, nor does it make sense to assign a lot of resources into supplier development if the supplier is not willing to develop.

### 3.6 Challenges in supply chain sustainability management

Enhancing and managing sustainability in supply chains is by far not an easy task and poses some specific challenges. According to Boström *et al.* (2015), global supply chains and networks experience six different kind of challenges (or gaps) in governing their sustainability: geographical, informational & knowledge, communication, compliance, power and legitimacy challenges. These challenges are listed in Table 3.2 and will be further discussed below.

Geographical gaps arise from the distance between the different parties in a global supply chain. This remoteness brings "*a distance from the many serious environmental and social impacts of production, which help to contribute to public ignorance towards these circumstances and make public debate and opinion-formation difficult*" (Boström *et al.* 2015). In other words, it is easier to ignore sustainability violations that occur on the other side of the world than the ones that occur in your proximity. Chkanikova & Lehner (2015)

Table 3.2 challenges in governing sustainability in global supply chains
(based on Boström *et al.*, 2015)

| Challenge | Description/cause | Recommendation |
|---|---|---|
| **Geographical** | Distance between different parties causes ignorance of sustainability violations | Mediated communication<br>• Using local suppliers<br>• Generic standards |
| **Informational & knowledge** | Difficulty of getting reliable, comprehensive and credible information from the supplier, especially in case of long geographical distances | Increasing transparency<br>• Independent information providers<br>• Verification agents |
| **Communication** | Challenge of finding communication tools, strategies and systems to overcome geographical and social distances | Strengthening communication<br>• Standards<br>• Information systems<br>• Direct interaction |
| **Compliance** | Difficulty of ensuring and governing supplier's compliance to legislation and to the established sustainability standards | Establishing effective governance practices<br>• Effective audit program<br>• Networking with external stakeholders (NGOs) |
| **Power** | Due to lack of relative power, buyers are unable to enforce standards and requirements on supplier, and/or suppliers are unable to contribute in shaping these standards | Balancing power distribution along the supply chain |
| **Legitimacy** | Existing governance arrangements give legitimacy to inefficient standards, block innovation and favor and give power to certain stakeholders | Critical evaluation of the efficiency of current governing practices |

propose favoring local suppliers and approaching them directly for simplifying supply chains and overcoming geographical challenges. As majority of supply chains will stay global, Boström *et al.* (2015) encourage using generic standards and other ways of mediating

communication. However, they also point out that several articles underline risks involved in using global generic standards without considering different cultural contexts.

Geographical distances increase need for reliable, comprehensive, verified and credible information, which creates information and knowledge gaps. As shown by the study of Börjeson *et al.* (2014), getting such information can be extremely challenging and a big gap may exist in knowledge of buyer and supplier organizations. The dilemma here that supply chains are facing is how to retrieve delicate information if this information will put the informant in bad light? Not all actors in the chain (producers, buyers, end-consumers, authorities) have the same information, which creates an information asymmetry that Boström *et al.* (2015) propose to be compensated using independent information providers, verification agents and other means for increasing transparency. Transparency, however, is not always straight-forward and there are pitfalls especially in constructing transparency in different societies as presented by Mol (2015): someone always decides what is kept secret and to whom information is revealed. Finally, Boström *et al.* (2015) stress that interpreting information received is seldom explicit and usually needs interaction between suppliers and buyers.

As presented by Seuring & Muller (2008), the need for communication along the supply chain is argued heavily for in the SSCM literature, thus the third challenge introduced here is communication gaps. According to them, several articles bring out challenges in finding communication tools, strategies and systems to overcome geographical and social distances. As presented by Boström *et al.* (2015), communication may be strengthened with standards, information systems and direct interaction between parties, but is weakened by problems brought by language, trust, costs, unequal expertise and cultural codes. Increasing supply chain complexity emphasizes communication problems.

Deviances between recognized global sustainability standards and on-the-ground compliance generates compliance gaps: even global standards can remain neglected in practice as the tools for ensuring compliance are limited (Boström *et al.* 2015). As illustrated in the study of Helin & Babri (2015), compliance gaps may remain even if auditing systems are in place as violations can remain undetected and improvement may remain only marginal, even though there are also successful examples of implementing sustainability standards.

Fifth identified challenge is power gaps, which on the other hand create problems for the buyers if they lack the power to enforce standards and requirements on supplier (Helin & Babri, 2015) and, on the other, create problems for suppliers to whom the lack of power means lack of flexibility and ability to contribute in shaping these standards (Vellema & Wijk, 2015). Boström *et al.* 2015 suggest that equal distribution of power among supply chain is crucial for creating sustainability.

Finally, the article of Miller & Bush (2015) highlights that many global governance arrangements are continued, even though there is little evidence of improvement and much evidence on the flaws that actually prevent improvement. These arrangements have been unable to solve geographical, informational, communicative, compliance and power problems, and on the contrary create new gaps called legitimacy gaps by Boström *e. al.* (2015). These gaps occur when governance arrangements enable operation and authority of inefficient standards, block innovation, favor and give power to certain stakeholders and shape the markets. The efficiency and intends of governance arrangements should thus be critically evaluated.

Boström *et al.* (2015) conclude that generic, global standards alone are not sufficient and that implementation of these standards should be done keeping local context in mind. To overcome the many supply chain management challenges, monitoring and enforcement methods need to be supplemented with education and other means and governance arrangements should be developed through reflexive learning. There is a significant need for

responsiveness in governing supply chains, and it should never be seen as a one-shot effort, but rather a long-term, collaborative reflective and committed process.

# 4. RESEARCH METHODOLOGY

This chapter discusses the research methods applied in this Master's Thesis. First, I will introduce the research question and rationalize its relevance. After going through the research question and motivation behind it, the research approach used in this study is described. Next, the context of this research and the sample studied is introduced. This is followed by research design, or data collection and analysis. The chapter is concluded by discussion about the validity, reliability, generalizability and limitations of the study.

## 4.1 Research question and its relevance

The research question of this thesis is divided into three separate questions:

*What is the significance and nature of Good Manufacturing Practice compliance risk?*

*How is supplier and risk management constructed in a highly regulated and enforced environment?*

*What are the impacts that strong regulation and authority enforcement impose to supplier and risk management practices?*

Using pharmaceutical industry as the research context allows to study supplier and risk management in a very specific setting of high authority regulation and enforcement and the effects of these particularities. Furthermore, managing supply chain compliance in general remains an understudied field, the recent advancements being related to supply chain sustainability management. The purpose of the first question is to ensure relevance of the studied phenomenon to pharmaceutical companies in order to confirm that GMP-compliance risk is something that shapes their behavior. Another motive is to understand the prevalent conjectures around this phenomenon.

The second question addresses the process of establishing and maintaining supplier and risk management practices within the research context as it is necessary to establish the fundamental drivers of supply chain compliance management in the given setting. The final question leans to the results of the two previous ones and draws attention to the more generalizable impacts that regulations may have.

Relevance of the research question can be seen from three different level. First, the pharmaceutical industry and its supply chain practices have not been well addressed in the literature even though their effect to the health of modern societies are significant (emphasized by many recent global drug shortages). This research adds to the current understanding of how pharmaceutical supply chains operate in the prevalent environment. Another societal consideration relates to the balance between industry self-regulation and authority regulation and the effects of emphasizing the latter one. From theoretical perspective, this research contributes to the existing qualitative literature of supply chain management in general and specifically to supplier and risk management and also has clear implications to sustainability management.

### 4.2 Research approach

Research methods can be understood as the methods used to answer the research question, and may also have an impact on producing it (Ghauri & Gronhaug, 2005). In upper level, research methods are divided into qualitative and quantitative methods, from which qualitative research is seen to highlight the fundamental understanding of and insights in to a certain phenomenon and thus being especially important for studies where only little is known about the subject (Marschan-Piekkari & Welch, 2004). This study explores a previously understudied topic of supply chain GMP-compliance and its core objective is to understand the current management practices. For these purposes, qualitative methods seem to be the most appropriate ones.

According to Ghauri & Gronhaug (2005), case study is an especially relevant method, if the research topic is hard to examine outside its natural setting. According to Yin (2003), case study method has been conventionally used when research tries to answer *how*- or *why*-questions. The research question presented above seems to build also from *what*-questions (*what are the…; what is the…)*, but it is mainly due to the chosen wording of the question. The research question could easily be edited to include *how*-questions without changing its content: *how do strong regulation and enforcement impact* instead of *what are the impacts*, and *how significant* instead of *what is the significance.* In addition, the questions are studied in a very specific (but also complex) context of pharmaceutical supply chain. Based on these features, case study approach looks justifiable and is utilized in this research.

Case studies are furthermore divided into single and multiple case studies, where multiple case studies are seen to give more compelling and robust results (Yin, 2003). In this study, the focus is on industry practices in general, rather than practices of a certain company, so multiple case study method is applied.

Another division can be made between deductive and inductive approaches: deductive approach examines a theory arising from existing theory, whereas inductive approach aims to generate theory from empirical research (Saunders *et al.*, 2000). Even though one could see the two approaches ruling each other out, they can also be complementary to each other (Bryman & Bell, 2003). This study has some deductive features: one objective is to find similarities to existing theoretical framework of sustainability management in supply chain context. Furthermore, interviews were planned on a thematic framework arising from sustainability management theory. However, the main focus is in framing a previously understudied phenomenon, supplier and risk management practices in a highly regulated and enforced environment, with only limited existing theory, making the study mainly inductive in its nature. Besides deductive and inductive approaches, also abductive approach can be used especially in cases where researcher aims to discover new things (new variables and new relationships; Dubois & Gadde, 2013). From the parts where this study addresses a new

actor, quality department, and a new sub-process of supply chain GMP-compliance management, and the relationship of these two variable to the traditional and theoretically established supply chain management, it can also be considered as abductive.

## 4.3 Research design and conduction

Research design is defined by Yin (2003) as "the logical sequence that connects empirical data to a study's initial research questions and, ultimately, to its conclusions". Research design is thus an integral part of any research and should thus be done carefully. The purpose of this section is to describe the decisions and steps made within the methodological framework built in the previous section, justify these decisions and explain occasions in which it was necessary to deviate from the initial outline. The section starts with specifying the micro-level research context and then moves to describing the research design process of this study, including choosing research sample, data collection methods and data analysis methods.

### 4.3.1 Research context

As described above (chapter 1.1), the macro context of this thesis is pharmaceutical industry and external supply chain management. From the research topic, the context can be refined to GMP-compliance management within external supply chain management in the pharmaceutical industry. This study did not limit the scope to a certain geographic region, so in principle it concerns the whole global pharmaceutical industry, even though most of the cases included in the study are from Europe and not all major pharmaceutical regions are represented.

Besides geographical division, two other ways to segment the pharmaceutical industry are seen important background information for the study: pharmaceutical companies can be divided into chemical and biochemical companies according to the nature of their products, or to proprietary companies developing, manufacturing and marketing their own products and contract manufacturing pharmaceutical companies selling manufacturing services to

other companies. Naturally, many of the companies have both chemical and biochemical products and manufacture both for their own purposes and for external parties, but usually one of the two features is where main business comes from. The cases studied in this research were all companies concentrating mainly to chemical pharmaceuticals. However, the cases included both proprietary and contract manufacturing companies.

In the meso-context (here corresponding firm-level), supply chain management has traditionally been responsibility of procurement and quality assurance. Further, assuring compliance to GMP-standards, within internal and external supply chain, has conventionally been assigned solely to quality assurance. Supply chain GMP-compliance management in its simplest form has been managing frequent GMP-audits, their reporting and overseeing that audit observations have been met with acceptable corrective actions. Micro-level context, based on this responsibility division, is thus be defined as supply chain GMP-compliance management within the quality assurance department.

Inside the company quality assurance, responsibility can further be placed to corporate level quality assurance, manufacturing site level quality assurance, or to both of them. This research targeted the corporate level quality assurance where it was relevant and accessible. In two of the six cases, the main responsibility of company supply chain GMP-compliance laid in the manufacturing site level quality assurance, and information was gathered from this level.

### 4.3.2 Research design and conducting the study

This research followed the process presented in Table 5.1. This process was presented by Eisenhardt (1989) for "*inducing theory using case studies*" and is thus seen a good fit with the objectives of this study. In her article, Eisenhardt (1989) stresses that the process is highly iterative, meaning that the steps are not necessarily taken in the order presented, and that the researcher goes back-and-forth between the steps and realigns his/her assumptions and

previous work as new data comes in. Nothing is written in stone before the whole process is completed.

*Getting started:* Researcher's experience in the field made it possible to construct a preliminary research question based on what was known from the area and what was initially considered to be the main topics of interest and objectives to be addressed in the study. This preliminary research question helped to concentrate the efforts made in the next step into a certain area. It was kept in mind that the actual research question would arise from literature review, after revealing what had been already done and how could this study best contribute in creating new knowledge.

*Preliminary literature review:* This review was performed to learn what had already been done in the field and find a specific focus area for the study. Supply chain management and supply chain risk management literature review revealed that this general theoretical background could not be directly applied due to the specific features of pharmaceutical industry and compliance management. Similarly, it was realized that supply chain management in pharmaceutical industry in general, and GMP-compliance management in specific, had been addressed only in few studies and there was a very limited theoretical background for the research topic. Sustainability management in supply chains was identified to be the closest link to a solid theoretical framework. Research question was refined accordingly to include some fundamental issues within the research topic (e.g. confirming the significance of the topic in the first place).

*Planning data collection:* External information on companies' supply chain management practices is very limited, therefore it was apparent from the beginning that the data needed for the study would be internal. As mentioned previously, the research topic was rather unexplored, and the existing theoretical ground limited. For this reason, it was not practical to use any structured data gathering methods, as there was no solid framework to build on. This ruled structured interviews and surveys out from the data collection methods. Practicalities also prevented performing narrative research, as in the scope of this study

gathering narrative data would be extensively time consuming in the context of Master's thesis and getting access would could prove to be impossible. Pharmaceutical companies are required to maintain a standard operation procedure system to describe how the company operates in different GMP-related activities, including supplier management. The main purpose of standard operation procedures is to guide internal personnel, which makes them an excellent source of information on how the company operates. However, internal standard operation procedures are usually considered confidential, and getting access is again seen challenging. In addition, the standard operation procedures may not always fully reflect the practice, and the data collected through standard operation procedures is limited.

Table 4.1 Research design and conduction process (adapted from Eisenhardt, 1989)

| Step | Purpose |
|---|---|
| Getting started | Designate a preliminary research question to specify the research area and concentrate efforts to this specific area |
| Preliminary literature review | Review work done within the designated research area and refining the research question based on review findings |
| Planning data collection | Identify and design the methods for gathering data |
| Selecting sample cases | Identify companies relevant to the research |
| Entering the field | Request and interview persons relevant to the study within the identified companies |
| Within-case and cross-case data analysis | Identify unique and common patterns from and across cases |
| Shaping hypotheses | Build solid and justifiable hypotheses from data and search underlying causes |
| Enfolding literature | Search similarities and differences to sustainability management theory |
| Concluding research | Present findings and implications |

For the above reasons, guided and semi-structured interviews were selected as the main data collection method. As Eriksson & Kovalainen (2008) define qualitative interviews, they "*are research vehicles, the purpose of which is to produce empirical materials for the study in question*". According to Eriksson & Kovalainen (2008), guided and semi-structured

interviews are useful when studying *what* and *how* questions, advantages being a rather systematic approach combined with flexibility. Interview outline was adapted from themes identified from supply chain sustainability management literature.

*Selecting sample cases:* Sample of this research consists of six international pharmaceutical companies. Criteria for sample companies was quite straight-forward: the companies were expected to have an international external supply chain, perform supply chain GMP-compliance management in-house and be at least medium-sized. No geographical limitations were used. Sampling aimed to find typical cases fulfilling the above criteria, in order to get a cross-section from the pharmaceutical industry (Patton, 1990).

Interviewees in the sample companies were expected to work in quality department and be responsible from supply chain GMP-compliance management in corporate or manufacturing site level. In one case, the interviewee was in a region level, being responsible from Europe supply. In two interviews, there were more than one participant who were interviewed at the same time in a group interview. Table 5.2 summarizes the case companies and interviewees, their location, title and level in the company.

*Entering the field:* Companies were approached by email and in some cases through a follow-up phone call. Emails were sent to general company emails, but also directly to potential persons identified through social media (e.g. LinkedIn). Interviewees were requested to reserve one hour for the interview.

Interviews were semi-structured and each lasted about an hour. One interview was conducted face-to-face and the others through VoIP software (e.g. Skype). All the interviews were recorded and transcribed into text. For interview outline, main themes and two to four main questions to each theme were prepared before the interview, however, this outline was not strictly followed to maintain flexibility within the research topic.

Table 4.2: Case companies and interviewees

| Company | Interviewee location | Company HQ | Interviewee level | Interviewee title(s) | Main business |
|---|---|---|---|---|---|
| A | Finland | Finland | Corporate | Partner Management Manager, QP | Proprietary products |
| B | India | India | Corporate | President - Corporate Quality | Contract manufacturing |
| C | Spain | Sweden | Manufacturing site | Quality Manager & Qualified Person<br><br>Quality Auditor, QP | Contract manufacturing |
| D | Finland | Japan | Region | Responsible person Finland | Proprietary products |
| E | Switzerland | Switzerland | Corporate | Head of QA/GMP, Director Global Quality Management | Proprietary products |
| F | Finland | Germany | Manufacturing site | Responsible person Finland<br><br>Quality compliance specialist<br><br>Quality compliance specialist | Proprietary products |

*Within-case and cross-case data analysis:* Case-specific data was analyzed through within-case and cross-case analysis as suggested by Eisenhardt (1989). The researcher first familiarized himself with the individual cases, which started already when transcribing the interviews. This phase included open coding of the information collected through interviews

and identifying unique features of each case within themes used in the interviews. These features were further refined, forming an iterative and incremental analyzing process. The case-specific features were tabulated to help the cross-case analysis. In the next phase, common patterns and major differences were searched across cases.

As presented by Dubois & Gadde (2002), a case is not the only parameter affecting to theory creation, but also defined empirical boundaries, analytical framework and existing theory have an effect on this process. In this study, the empirical world was clearly limited to pharmaceutical supply chain management from quality department perspective, and the data analysis focused on identifying patterns concerning the different actors and activities within this empirical boundary.

Data analysis is usually done against an analytical framework that can be of two different types: tight and prestructured or loose and emergent (Dubois & Gadde, 2002). This study did not start with a predefined framework, but rather it was created and re-created during the data analysis and interpretation steps. Loose and emergent analytical framework was necessary for this study as the existing theory is built on traditional supply chain management and could not be used to build a prestructured framework for the study purposes, as this study concentrated on creating new theory under a very specific context to contemplate the existing theory.

On a broader level, the data analysis process used in this study and especially in depicting the framework presented in the results section is well described by what Dubois & Gadde (2002) call matching: going back and forth between transcribed interviews, tabulated case-specific features, empirical context, existing literature and the framework (results). One important method used was to first sketch on paper processes for the individual companies and then, through iterative review of interview data and the sketched processes, refine them and find similarities and common features between the companies. One important feature of the matching process is that data should not be forced to fit a defined model, rather the model

should be developed from the data. Finally, Dubois & Gadde (2002) conclude that the matching process has no obvious pattern as matching theory and reality can take various directions.

*Shaping hypotheses:* A generic framework on supply chain GMP-compliance management practices and insights of the phenomenon was constructed based on the common patterns found in data analysis. The main differences across cases were reflected as well. It was kept in mind that the number of cases limited the generalization of results and jumping into too specific conclusions was avoided. The purpose of the framework is more to outline and describe the phenomena rather than to explain it.

*Enfolding literature:* The framework built above was compared to the frameworks found in relevant literature. Similarities were underlined and main differences reflected against the empirical data gathered from interviews.

*Concluding research:* Conclusion included summarizing the main findings from the previous steps and discussing about theoretical contribution and implications for supply chain GMP-compliance and sustainability management as well as supplier and risk management in general.

### 4.4 Research validity, reliability and ethical concerns

This section will be concluded by a critical evaluation of validity and reliability of this research. Also ethical concerns are discussed. Yin (2003) mentions three different types of validity that are useful in evaluating research quality: construct validity, internal validity and external validity. By construct validity, he means pursuing objective interpretation and avoiding subjective conclusions. Internal validity can be understood as deducing solid causal relationships between conditions, and external validity as the generalizability of the research results (Yin, 2003). Finally, reliability of a study means that the same results would be

received if a study would be repeated by another researcher following the same procedures (Ibid.).

According to Yin (2003), *construct validity* can be enhanced by gathering data from different sources, or submitting case reports for reviewing. In this study, obvious additional sources could have been company standard operating procedures or interviewing additional parties such as case companies' suppliers or additional persons within the company. Unfortunately, in the scope of a Master's Thesis, this would not have been possible even if these sources would have been accessible. Even though full case reports were not reviewed by the interviewees, they remained available after the interviews for clarifying issues and this possibility was used in several occasions. Also, researcher focused on objectivity and fact-based interpretations for the full duration of the study.

*Internal validity* was constructed through thorough data analysis. Special attention was given to justifiability of conclusions made. The data itself was rather unambiguous and the research topic tightly defined, which helped drawing conclusions. If the data was not fully supporting conclusions, this is clearly brought up in the results section.

*External validity* in the context of this study is the hardest to evaluate of the three types of validity, as there are no other studies to compare to. Case companies were quite different from each other in terms of main business and location, but their management procedures and views on the topic were similar, which implies that the results should be generalizable to the industry. There were, however, only six companies and this conclusion would need support from other studies to be confirmed. Furthermore, the differences between the case companies may limit generalizability of the study as well. As the research topic itself exists only within pharmaceutical industry, it is obvious that the specific results are not applicable to other industries. Nevertheless, there were many similarities to supply chain sustainability management theory, which would imply that the results may be partly applicable to sustainability field as well. There is more discussion on this topic in the results section.

To ensure *reliability* of the study, the methodological procedures as well as research design and conduction steps have been described accurately and in detail. Data gathering performing was performed coherently, recording and transcribing the interviews, and the data was analyzed systematically. Possible biases between the interviewer and interviewee were decreased by creating an open and trustworthy interview environment. All in all, transparency is reinforced whenever possible.

A lot of effort was also put to minimizing *ethical concerns*. Name of the companies are not published and their description kept minimal, keeping in mind the demands of the study. In few cases where the case companies could be identified from their description, the interviewee was contacted and agreed that the possible compromise of company name is alright. At the end of every interview, interviewees were asked whether anything confidential aroused from the discussion, and they had the possibility to contact interviewer also after the interview.

### 4.5 Limitations of the study

There are several limitations that are good to keep in mind. First, the number of case companies is quite limited to catch all the features of the studied phenomenon. The study results are to be considered more directional than precise. Second, as there was no theoretical framework about the studied phenomenon and interviews were semi-structured, it is possible that something essential was left outside the interview themes. Interviews were kept as open-ended as possible, but this possibility remains. Third, the researches has been working in the pharmaceutical industry for several years, and might have brought some biased views to the study. This possibility was identified from the beginning and objectivity was enforced throughout the study. Finally, one has to consider the possibility that interviewees were biased, describing more how they would want the situation to be than how it actually is. A good example of this is the following question: *when evaluating new suppliers, what kind of weight are compliance issues given compared to price, HSE and other factors?* The interviewees as quality assurance representatives were quite consistent in answering that

compliance issues are the most important ones, but does this really reflect the reality? Unfortunately, in the scope of this study, it was not possible to confirm interview data from secondary sources or additional interviews, so the question of interviewee bias remains open.

# 5. THE PHARMACEUTICAL INDUSTRY

## 5.1 Introduction

Pharmaceutical industry is by far the most regulated industry there is, which can be explained by the prevalent risks. Regulations have evolved step-wise, usually as a reaction to severe occurrences causing deaths or other health effects among patients. One of these occurrences is the thalidomide crisis, where pregnancy related morning sickness was treated with thalidomide-based products without appropriately studying the health effects of the drugs as regulations were basically nonexistent. Thalidomide products caused severe birth defects for approximately 10 000 newborns before the products were withdrawn from the markets. Thalidomide case is the basis for today's stricter regulation and post-marketing pharmacovigilance activities.

Besides using understudied drugs, health risks may arise for example from mixing up drugs in the user level, mixing up raw materials at the manufacturing phase, contaminating drug products with toxic materials or using infected injectables. Furthermore, many active substances (the core raw material of medicines) have a very narrow therapeutic window and are very potent, meaning that the intended health effect may easily turn into health-threatening effects if wrong amount of the active substance (AS) is administrated. As different active substances are many times handled in the same manufacturing facilities, cross-contamination of different active substances is also seen as a serious threat.

There is a big array of different regulations posed to oversee and prevent these threats, starting from the very early steps of development (good laboratory practice, GLP; good clinical practice, GCP) and reaching to the actual manufacturing stage (good manufacturing

practice, GMP), distribution (good distribution practice, GDP) and also to post-market actions (good pharmacovigilance practice, GVP). As the topic of this thesis is related to the manufacturing activities of products intended to the EU region, the most relevant set of regulations for this thesis is good manufacturing practice in the European Union, or the EU GMP. Before going further to GMP specifics, the next paragraph explains the regulatory requirements for individual pharmaceutical products.

### 5.2 Marketing authorization

To sell a pharmaceutical product in the EU region, the product has to be granted a marketing authorization (MA) by the relevant authority. There are several application pathways, but for the purposes of this thesis, the most relevant topics are contents and maintenance activities. MA is assigned to a certain legal entity, usually a pharmaceutical company, called the marketing authorization holder. Marketing authorization holder is responsible for maintaining the MA and keeping it up-to-date. From the authority side, the MA is maintained by the relevant authority, which can be on national or EU-level, depending on the route that the MA has been applied.

MA consists of different modules describing different aspects of the product, such as quality, safety and efficacy. The exact content may vary between products, but MAs usually specify for example detailed composition of the final product, manufacturing plant(s) for active substances and the final product and description of manufacturing process and control steps, location of chemical and microbiological testing, chemical and physical specifications of the final product and description of the analysis methods, description of the packaging material quality, dimensions and artwork and so forth. The intention of this listing is to show that, as every pharmaceutical batch produced have to comply with the registered MA, changing something such as the AS manufacturer, is never quite as simple as in many other industries. In case of changes, the marketing authorization holder must update the MA by a variation, from which basically all considering other than minor changes must be pre-approved by the relevant authority before the applied change can be implemented. To get an approval to the

variation, the marketing authorization holder has to show that the product quality is not affected, which may mean costly and time-consuming studies.

### 5.3 Good manufacturing practice

The foundation and legitimacy of EU GMP is laid out in two European Commission directives, 2003/94/EC for medicinal products for human use and 91/412/EEC for veterinary use. The principles and guidelines set by these directives are interpreted into more practical level by Commission's Guide to Good Manufacturing Practice that is divided into three different parts and 19 related annexes. Even though there are different GMP guidelines written by different organizations or consortiums for many different purposes (for example manufacture of excipients), official GMP begins from the manufacture of active substances and reach to the manufacture of medicinal products and related activities. These related activities include maintaining premises and equipment, documentation, personnel training and qualification, quality control and quality assurance of products, managing outsourced activities, handling product complaints and product recalls and so forth. Other authorities outside the EU, such as FDA in United States or Anvisa in Brazil, have their own GMP guidelines that are mainly harmonized with the EU GMP, some differences remaining. EU regulations place the marketing authorization holder as in the center of requirements: the responsibility of compliance and product quality and safety remains with the marketing authorization holder, never mind where and by which party different manufacturing practices are performed.

GMP guidelines are strongly enforced by the different authorities. Manufacturing pharmaceuticals (or active substances) is subject to a manufacturing authorization granted by the local authority, usually after a rigorous on-site inspection. To bring pharmaceuticals to the EU markets, for example, a manufacturing site also has to have a GMP certificate granted by an authority of an EU member country. These inspections are perhaps the most important way of enforcing the GMP guidelines and usually last several days with several inspectors. The EU GMP certificate, if granted, is valid from one to three years, depending on the amount

and criticality of deficiencies found, after which a re-inspection is needed to receive an updated GMP certificate. In case the company fails to pass the inspection, a non-compliance report is issued to the manufacturing site and importation of products to the EU region is usually banned. Both EU GMP certificates and non-compliance reports are published in EudraGMDP database public for everyone. In addition to the authority inspections, every pharmaceutical batch has to be fully analyzed within the EU region before it can be released to the markets, meaning that imported batches have to be re-analyzed within the EU. Also other regulations exist, but the purpose of this chapter is not to give a holistic view of the prevailing requirements, but rather to give an overview of the regulatory environment pharmaceutical companies and their supply chains are working in.

Compared to the sustainability governance where NGOs are one of the most important pressure groups, in GMP-compliance governance they hold only a very minor role, limited mostly to publishing guidelines. This might be due to the strong role that authorities have taken, making it unnecessary for NGOs to play a bigger role.

### 5.4 Nature of pharmaceutical supply chains

Considering the nature and risks related to pharmaceutical products, GMP requirements and MA procedure, it is obvious that pharmaceutical supply chains tend to be quite rigid. To transfer production of a certain product from one supplier to another one, an organization has to include evaluation of risks related to the new supplier, conduct process validation, transfer analytical methods into a new laboratory, assure product stability remains unchanged and update the MA through variations. These tasks are time-consuming (year may not be enough), require a great amount of effort and resources and are costly. One would therefore think that initial supplier qualification would be considered essential in pharmaceutical supply chains.

According to the EU GMP requirements, an organization has to audit its AS suppliers as well as any supplier taking part in the pharmaceutical product manufacture and ensure that they comply with GMP. These audits should usually be conducted with 3 year's frequency for active suppliers. Only for excipients suppliers there's a possibility to follow a risk-based approach. This audit requirement creates an interesting setting for the supply chain management: whereas in other industries audit is rather something that's performed if supplier is considered high-risk, in the pharmaceutical industry one has to audit even smallest of its suppliers (if they belong to the categories defined above). This is in addition to the fact that authorities are usually auditing the same suppliers in parallel. Moreover, one of the supplier audit goals may well be to ensure that the supplier can pass an authority audit and thus be able to receive and maintain the needed certificates for supplying its products to the EU market.

There has been a lot of discussion around the shift of pharmaceutical production to Asia and its effects on product safety (for example Drakulich & Van Arnum, 2009; Rosania, 2010; Harris, 2009; Harris, 2014), but detailed information about the proportion of pharmaceutical products actually manufactured outside EU is scarce. One reliable information source is the EudraGMDP database maintained by European Medicines Agency (EMA) and listing for example issued EU GMP certificates & non-compliance reports. Based on a report run from this database, Figure 4.1 presents the number of AS GMP certificates issued since 01.01.2013 in the top 20 countries and Figure 4.2 presents the number of issued GMP certificates for pharmaceutical production for human use since 01.01.2013 in top 20 countries.

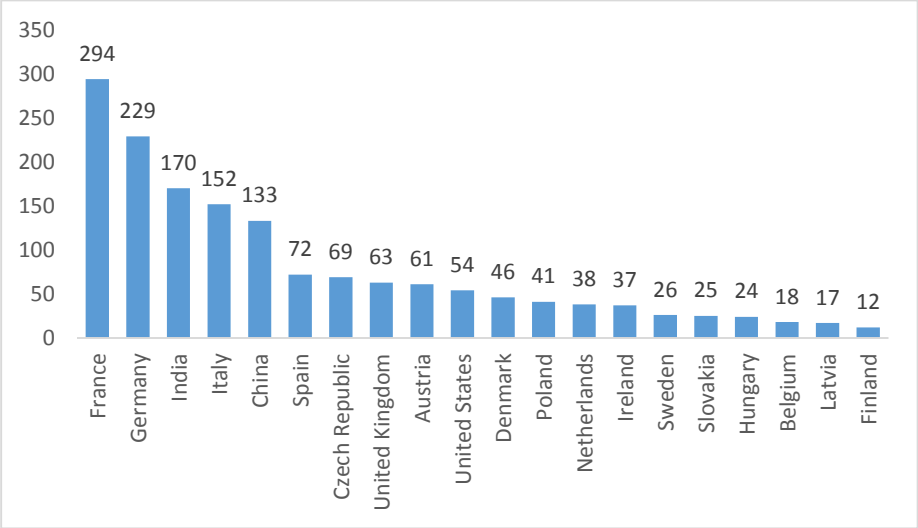


Figure 5.1: EU GMP AS certificates issued since 01.01.2013 per country, top 20 countries (numbers obtained from a report run from EudraGMDP database on 28.03.2016)

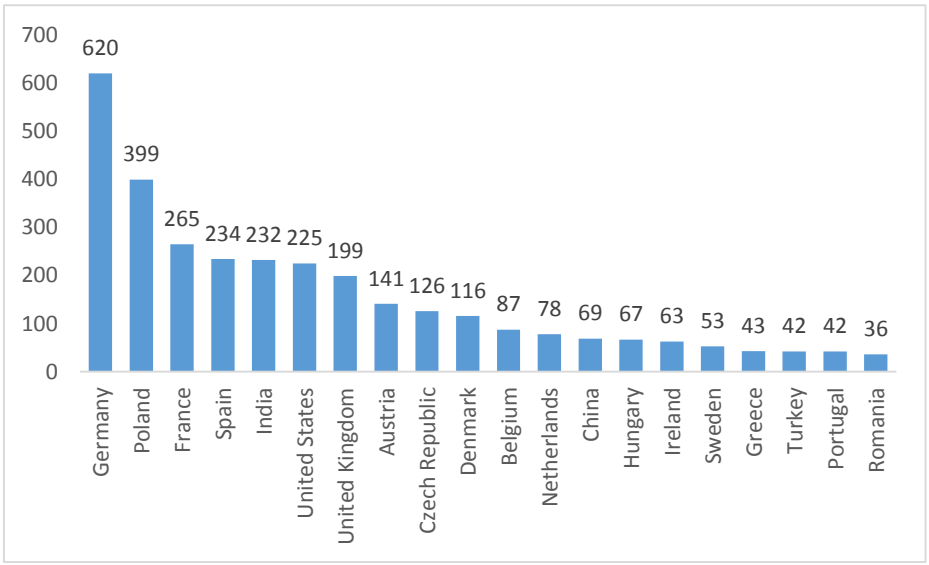


Figure 5.2: EU GMP certificates for pharmaceutical production for human use (not including packaging, analysis, importation, exportation and batch certification activities) issued since 01.01.2013 per country, top 20 countries (numbers obtained from a report run from a report run from EudraGMDP database on 28.03.2016)

From these figures alone, it is quite obvious that India and China are major players in the AS side and especially India in the pharmaceutical production side. However, a big majority of GMP certificates have still been issued to EU member countries, especially to sites in Germany and France. It should be noted that these figures do not take into account the number of products or production volumes, as one production site and all its products are usually under one GMP certificate, be the site's production volume in grams or tons. If it is assumed that the production in EU is more specialized into novel and smaller-volume products and that the production in India and China is directed more to production of bigger 'bulk' products, the relevance of these two countries grows even bigger. This assumption is backed up by statement the European Medicines Agency already in 2005 stating that "*approximately 80% of active substances used in the manufacture of medicinal products within the EEA are manufactured outside of the EEA*". It is also commonly acknowledged that United States is highly dependent on active substances manufactured in Asia (Harris, 2009).

### 5.5 Globalization of pharma supply chains and authority enforcement

The rising importance of Asia and specifically India and China in pharmaceutical production has raised product safety and quality concerns, especially after the Heparin crisis of 2008 (Rosania, 2010). Heparin produced in China from pig intestines and used as AS caused nearly 150 deaths in the United States, when several heparin batches were (possibly deliberately) contaminated with another substance so similar to heparin that the used analytical methods were not able to separate the two substances (Rosania, 2010). Later on, it was acknowledged that the related heparin manufacturing site had not been inspected by US FDA or the Chinese regulators.

After the heparin crisis, the US FDA has increased number of its oversees inspections significantly (Rosania, 2010), which has revealed many misconducts of Asian AS and pharmaceutical manufacturers, such as data fraud and data integrity issues (for example Siddiqui & Chatterjee 2014; Siddiqui, 2015; Edney, 2016). Figure 4.3 presents the number of companies per country listed in FDA's list of manufacturing sites under import alert (sites

that are restricted to export some or any AS pharmaceutical products to the United States). It is however not only the FDA that has increased its oversee focus – also European authorities have issued many non-compliance reports to foreign manufacturers. Figure 4.4 presents the number of issued non-compliance reports issued by EU authorities since July 2009 per country.

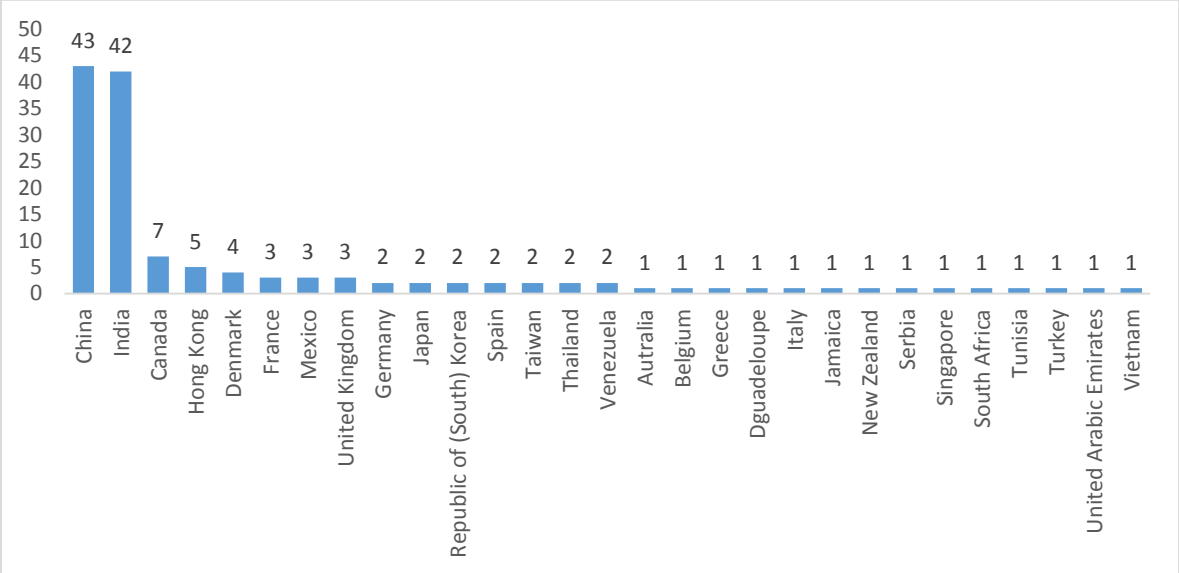


Figure 5.3: number of manufacturing sites currently under U.S. import restrictions (http://www.accessdata.fda.gov/cms_ia/importalert_189.html?source=govdelivery&utm_medium=email&utm_source=govdelivery, accessed on 29.03.2016)

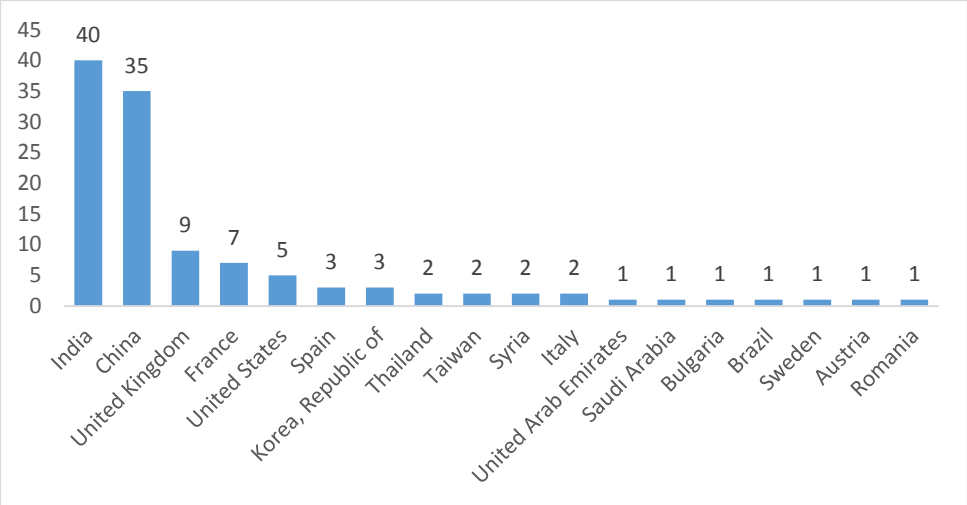


Figure 5.4: GMP non-compliance reports issued by EU authorities since 07/2010 per country (numbers obtained from EudraGMDP database on 28.03.2016)

Both China and India clearly stand out from the above figures. Even though there is a number of other countries in the list and both India and China are bigger in number of pharmaceutical companies than their peers, the differences are drastic. The motives behind the enforcement acts of especially US FDA have been questioned and they have been accused of politicizing to protect domestic industry from international competition (Harris, 2014). Nevertheless, a company choosing a supplier from China or India seems to be taking a bigger risk of supplier compliance issues than a company favoring Western suppliers.

It should be noted that placing an import alert to a manufacturing site by US FDA and issuing a non-compliance reports by the European authorities are the ultimate steps, and the authorities in both continents have other, softer, means to handle observed deficiencies that may already limit the supply of products. On the other hand, the number of companies listed above represent a small fraction of the listed countries' pharmaceutical manufacturing sites and when comparing to the number of EU GMP certificates presented in Figures 4.1 and 4.2, it becomes obvious that a much bigger fraction has passed an authority inspection.

# 6. GMP-COMPLIANCE MANAGEMENT IN PHARMACEUTICAL SUPPLY CHAINS

The results of this study are presented in the following order: this chapter will begin by presenting nature and perceived significance of the studied phenomenon, and then move to describing the actual management processes and organizational aspects.

## 6.1 Pharma supply chains and significance of compliance risks

When acquiring of the biggest risks in company's supply chain, the views of different companies varied somewhat. Four of the six informants directly mentioned supply shortage risks, either with active substances or pharmaceutical products. The possible shortages were thought to arise from several different reasons, varying from GMP-compliance issues to natural accidents such as fire. Two interviewees brought up risks to products or materials

during transportation, such as temperature excursions. Also the risk of "not being aware of what's happening at supplier's end", or losing control, was mentioned by two informants. Compliance risks were directly brought up in two of the interviews, even though indirectly it can be interpreted to concern all the companies (for instance insufficient change control or insufficient transportation controls can be perceived as compliance issues). The emphasis on different risks is interpreted to rise from companies' different supply chain profiles: with some companies the weight is more on raw materials, whereas with others in actual pharmaceutical products. Also the size of external supplier pool and geographical factors may have an effect.

When asking of the biggest challenges, one of the informants mentions that "with today's regulations, when one has to be aware of everything even though you are not the manufacturer, that is quite a challenge". Another informant describes the challenges as follows:

> *The biggest challenges are continuous communication, and transparency between the suppliers. What I am trying to say, as we are sitting in a remote place, we cannot control every day their operations in terms of compliance. So we need to have a process, which ensures the transparency, what is happening at their plant, so we can assure our quality of the product*

This theme was clearly a common concern for almost all of the interviewees: establishing and maintaining trust, transparency and open communication between the separate suppliers and the company. One informant raised the challenge of acquiring appropriate control of transportation and another one the challenge of getting company products prioritized with suppliers that are supplying for several other customers.

All of the interviewees considered compliance risk to be of relevance in the pharmaceutical industry. As the individual companies had quite different supply chains, the risk perceived in the company's own supply chain varied. It was obvious that the interviewees from companies with more complex supply chain considered the risk to be bigger compared to their peers

from companies with simpler supply chains. None of the informants considered the risk to be big in their internal supply chain, but the risk was considered to lie within the external supply network. A general view was that the risk is bigger with Asian companies, compared to their peers in Europe or North America, where the risk was perceived to be much smaller. Nevertheless, one of the informants described that "the world has changed in a way that compliance issues raise more often and losing [manufacturing] license occurs ever more. And not only in India, but also in Europe and these cases have become closer"

The consequences of supply chain GMP-violations were considered to vary from rejecting individual batches to large-scale product recalls and ultimately effects on patients through supply shortages. From the company perspective, most severe consequences were thought to be export limitations on some certain markets or withdrawal of a manufacturing license. In only two out of the six interviews were reputational damages brought up, but clearly they must be existent and are basically two-fold: the reputational costs from patients' side in case of supply shortages, especially with life-saving drugs, and the reputational costs of being publicly notified in the authority websites or databases.

All the informants expressed that there has been an increase in the authority compliance enforcement, basically through two different routes: through establishing new requirements and guidelines that establish new or stricter requirements, especially from the European authorities, and increased authority inspection activity, especially form the US FDA. One of the interviewees stated that from her view, the product quality has remained the same and real risks related to product quality have not increased, but 'authority risk' has increased through stricter standards and requirements. The interviewees seemed to experience this change in two ways: on one side, they have to oversee that their suppliers are adapting to the new requirements, and on the other side they have to be more alert regarding authorities inspecting their suppliers. Five out of the six interviewees experienced that compliance risk has increased during recent years: one had actually experienced a rise in the number of compliance-related incidences, one perceived the increased risk through increased authority

activity, two through increased requirements and one saw the overall risk to be the biggest with new suppliers. One of the six informants experienced that the compliance risk has been reduced as the authorities have taken more control, reducing the number of non-compliant suppliers. Four of the six interviewees saw efficient supplier management to bring competitive advantage, whereas the two remaining saw it more as something that has to be managed carefully in order to enable business continuity, but not as a real source of competitive advantage.

One observation that ought to be noted is that none of the companies had established their own standards for their suppliers, but all based their requirements on GMP-guidelines. Companies may imply some company-specific requirements above the GMP-regulations, especially in case of non-standard products, but GMP was always the basis of these requirements. One of the companies was also producing medical devices and thus following the relevant ISO-guideline, but otherwise no other international quality standards than GMP was mentioned. Relying solely on GMP is probably due to the fact that this gives the companies the most legitimacy over their suppliers: GMP is not a standard that the company alone would require, but is based on legislation and compliance by the suppliers is required to run their business in the first place. GMP is thus more enforcing than for instance ISO standards, as they don't limit the license to manufacture products if a company fails to comply.

One shortly covered topic during the company interviews was the importance of networks. None of the interviewees considered their informal networks to be of importance in supply chain compliance management and only half of the companies belonged to a formal industry consortium where supply chain management is addressed. In these consortiums, the main benefit was seen to be saving audit resources through sharing audit reports instead of organizing separate audits for each company. Other benefits included benchmarking, sharing knowledge and to some extent training. The consortiums, however, were nowhere near replacing companies' own supplier management or even some parts of it, instead they were

more of an extension of it. There might be an element of gaining power through networking over big global suppliers, but this was not brought up during the interviews.

### 6.2 Organization of GMP-compliance management

Among the six companies, there were essentially two different approaches into organizing the supplier GMP-compliance management: in four of the six companies, the responsibility was in the corporate level, whereas in two of the companies, individual manufacturing plants were responsible for managing their own suppliers. If the GMP-compliance management lied in the corporate level, the role of individual manufacturing plants was mainly to report the possible incidences with suppliers to corporate:

> *Manufacturing plants have lesser responsibilities, because what we do is, this central team will qualify and approve the supplier… The only sites would do, is, they should only agree on suppliers. And any non-conformance comes, from those suppliers, they will come back and inform the central supplier group, so that they will see the performance of the supplier*

If, on the other hand, the responsibility lied within the individual manufacturing plants, the role of corporate level was coordinating, information sharing between different sites and setting up and maintaining the supplier GMP-compliance management system to be locally adjusted and followed by the individual manufacturing plants. In this case, the corporation could also assume responsibilities of GMP-compliance management for suppliers supplying materials to several of the individual manufacturing sites. The level of corporate coordination varied between the two companies, one being more stand-alone and the other more dependent on corporate oversight. The reason for choosing one of the two approaches was not apparent from the interviews, but the researcher was left with an understanding that it is strongly related to the uniqueness of the individual manufacturing sites, with companies having standard manufacturing sites following the corporate model and companies having unique manufacturing sites following the stand-alone model.

The main responsibility from supplier GMP-compliance management lied within quality department in all of the six companies, which is not surprising as this is required by the GMP-guideline. Some of the companies had established a separate compliance department for managing supplier GMP-compliance management system, its activities including sending and evaluating questionnaires, performing audits and maintaining the system. In other companies, these tasks were not assigned to dedicated persons or departments, but were performed by the quality department personnel along with their other responsibilities. Even though the responsibility lied within the quality department, all interviewees emphasized the importance of cooperation with other department, such as procurement, research and development and own production.

### 6.3 Supplier GMP-compliance management process

Before going to details of the GMP-compliance management process, it should be emphasized that all the companies had a traditional supplier management (and supply chain management) process that was managed by the company's purchasing (or equivalent) department. GMP-compliance management was thus not something that would replace or make the traditional supplier management obsolete. The GMP-compliance management process was discovered to be independent from, but also interrelated to, the traditional supplier management process. The traditional supplier management process in the companies, even though not in the scope of this thesis, is outlined in this chapter from the parts being relevant and connected to the GMP-compliance management process.

Figure 6.1 presents a descriptive framework of the supplier GMP-compliance management process and its linkages to traditional supplier management process, depicted based on the conducted interviews. The process was similar in all of the six companies and followed on a broad level the same phases and principles. To outline the differences and avoid over-generalization, the differences between companies are outlined in the following chapters and steps that were omitted by half or more of the companies are marked to Figure 6.1 with grey colour. As presented in the figure, GMP-compliance management is divided into two

different phases, new supplier qualification and existing supplier management, each having three separate steps.

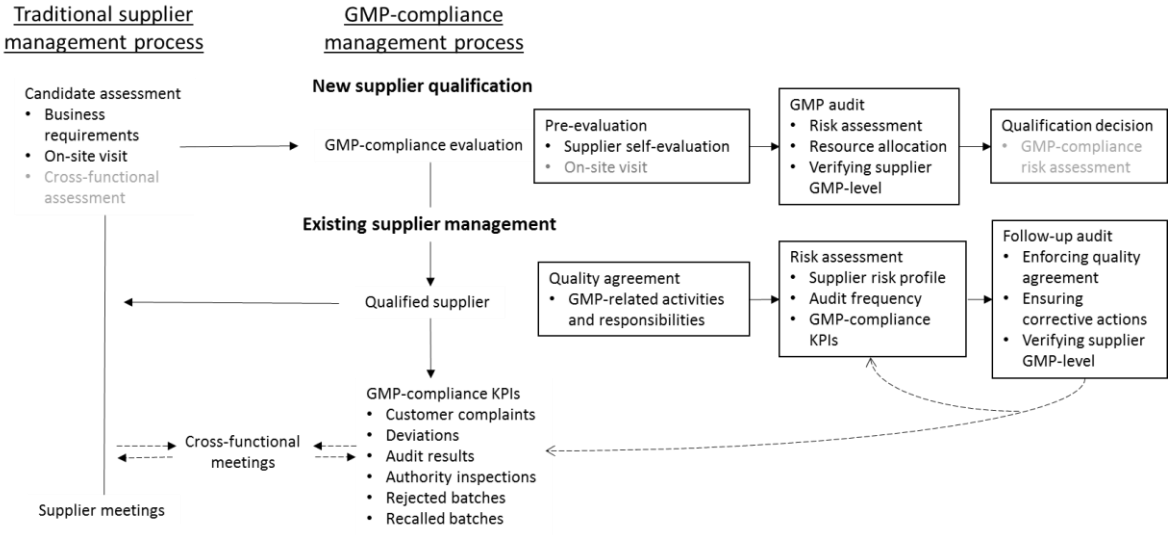


Figure 6.1: supplier GMP-compliance management process and its linkages to traditional supplier management process

## 6.4 New supplier qualification

Evaluation of new suppliers begins from the traditional supplier management process, where procurement department searched the possible candidates and was in charge in selecting the ones to be assessed further based on business requirements. Even though managed by department, also other departments including quality, own production and research and development, were usually participating in this assessment phase. In four of the companies the candidate assessment included an on-site visit to the supplier and a general-level review of the supplier's quality management system to already eliminate suppliers clearly not fulfilling the basic GMP-requirements. In two of the six companies, the candidate assessment was based purely on business requirements and didn't include an assessment of supplier's quality management system. In its simplest form, the process is as described by one of the informants:

*Purchasing unit chooses the supplier and proposes it to quality. According to our procedures, we have to collect some information from the supplier in order to decide if the supplier [can] be certified… This is indicated in procedure and purchasing department [will] ask for this information*

After the supplier assessment in the traditional supplier management process, the remaining candidate(s) were passed on to the GMP-compliance management process. As described in earlier chapters, the main responsibility of this process lied always within the quality department, but the interviewees also emphasized the importance of cooperation with other departments. The companies had some differences in their new supplier process, but all of them had three clear steps: pre-evaluation, GMP-audit and qualification.

### 6.4.1 Pre-qualification

The purpose of pre-qualification in all companies was to make sure that the remaining supplier candidate(s) pass a minimum GMP-compliance threshold, gather more information on them and evaluate whether the candidate can be passed forward to the audit phase. As audits require a lot of resources, not all the supplier candidates could be audited and it was deemed highly important to be able to eliminate suppliers clearly not complying to GMP-requirements already at the pre-evaluation phase. Pre-evaluation step included in all of the companies gathering pre-defined information on company's quality management system, mostly in form of a supplier self-evaluation questionnaire. It also utilized information gathered on the candidate assessment phase. Two of the six companies used questionnaire as the only pre-evaluation tool, whereas others could also organize a visit to the supplier's premises to gather more information and review the physical manufacturing facilities. This visit could take place already in the supplier assessment phase. There were some differences between active substance and final product supplier evaluation: with active substances, pre-evaluation also included analyzing the material according to defined specifications and, depending on the nature of the final product, performing trial manufacturing with the supplier's active substance. Only one of the six informants mentioned analyzing final

products to be included in the pre-evaluation step. Pre-evaluation was followed by supplier candidate GMP-audit.

### 6.4.2 GMP-audit

The purpose of this research was not to describe the audit process itself, but to concentrate on the nature, purpose and limitations of this supplier qualification step. As mentioned earlier, supplier GMP-audits are required by the EU-GMP and thus performed by default, before the supplier can be taken into use. The purpose of this step is quite obvious: to verify that supplier is complying to the current GMP-requirements, including that there are no issues risking the end user's health. That said, some of the limitations of auditing in general are also commonly acknowledged: audits capture only a specific moment in time, and what takes place after the audit can't fully be reflected by the audit. Secondly, there is always a time limitation, and not all relevant topics can be covered during an audit. This fact produces a sampling-kind of a nature of audits: auditor(s) will always have to choose what to include to, and what to exclude from the audit, taking samples of the company's performance.

All the interviewees placed a very high importance to the GMP-audit, and it was clearly the main tool in evaluating supplier candidate's compliance level. One challenge in audits that all informants raised was time constraint: as audits demand a lot of resources also from supplier candidate's end, the number of audit dates accepted by the supplier can be quite limited. When enquiring about the audit days assigned to a given supplier, one of the informants described this challenge as follows:

> *[We assign] one day. It is hard to get more time because companies receive a lot of audits… if you buy a lot of product then it is possible. In some cases, you have to pay a fee for the audit*

As the above citation reveals, especially in Western countries, getting more than one audit day may be impossible, especially with active substance manufacturers. With finish product supplier's, getting more than two audit dates was told to be challenging to almost all of the

companies. Again, the challenge was bigger in Western countries than for example in Asia. Available time can be extended by adding more auditors, but this will also increase needed resources and costs, and will only be beneficial to a certain point.

There was a clear, partly formal and partly informal, risk assessment made when allocating resources to audits or, in other words, deciding how many days the audit should last and the members to be included in the audit team. Formal as some basic principles were described by written procedures, and informal as the specifics were decided case-by-case. Written principles might for example require allocating more audit resources to suppliers located in third countries than in Western countries, suffering from bad authority inspection history, or manufacturing sterile products compared to non-sterile products. Case-by case considerations could include the exact number of days and auditors, as well as experience and expertise areas of the auditors. Audit teams consisted of a lead auditor, meaning a person having more experience on auditing and leading the audit team, and subject matter experts, meaning a person having specific experience and knowledge on one specific subject, such as microbiological laboratory practices.

### 6.4.3 Qualification decision

The audit step was followed by a supplier qualification decision or, in other words, a decision of whether the supplier achieves required GMP-compliance level and can be accepted to the company's supplier pool. Three of the six companies made this decision directly based on the audit result, meaning that if the audit was acceptable, the supplier could be qualified. One of the informants described this process as follows:

> *The outcome of the audit is a last step. For the selection, it is the project leader from the manufacturing that will decide with a quality manager in charge of this project and they will decide if they will want to work with the supplier or not. If the audit is positive, then it is ok to work with them. If the audit is negative, as a head of quality, I will have to jump in and ensure changes at the supplier, or we take some other measures to improve the GMP-compliance of the supplier*

Three of the six companies conducted some additional means before qualifying the supplier, one of them conducting stability testing on the materials. Only two remaining companies conducted a formal GMP-compliance risk assessment after the audit before qualifying the supplier, one of them making this assessment only to suppliers located outside Europe. The purpose of this risk assessment was to fully evaluate the supplier compliance risks and the actions needed to manage them, and it followed the normal risk assessment principles: gathering all the relevant information from previous steps, evaluating risk factors and assigning risk points to them, and evaluating which risks are acceptable and which demand further risk mitigation actions.

## 6.5 Existing supplier management

When supplier had been qualified through the above process, it entered company's supplier pool and could be used for further projects as well. There was no initial supplier or similar status to indicate that there might not yet be much experience with the supplier, nor did any of the companies have a process where they would test the supplier with smaller projects before granting bigger ones. It was emphasized many times during the interviews, that the suppliers could not be seen as generic, but were usually picked for a certain project based on their specific capabilities. Once qualified, they could also be used for other projects. Again, quality department had the responsibility and mandate for managing GMP-compliance of existing suppliers, whereas other supplier management activities were overseen by procurement (or an equivalent department). There were three main tools that were the backbone of existing supplier GMP-compliance management: quality agreement, risk assessment and follow-up audits. All these three means are also required by the EU-GMP.

### 6.5.1 Quality agreement

Before starting the operations, a separate quality agreement has to be signed with the supplier to agree on the GMP-related activities and responsibilities. This agreement was described by one of the companies as the foundation of the supplier GMP-compliance management, a tool to set the principles and nature of the supplier relationship.

### 6.5.2 Risk assessment

For existing qualified suppliers, all companies performed a risk assessment. Its purpose in five of the six companies was not to fully list the risks prevalent to a certain supplier, but rather to build an outline on the supplier risk profile. One of the informants describes the risk assessment as follows:

> *...risk assessment is done on a regular basis to define how often we have to repeat the audit. So after the supplier is selected, we start to work with them and after one year we have some KPIs [key performance indicators] and we evaluate, make a risk assessment, on these KPIs and depending on the outcome of the risk assessment, we define if we make an audit after one year or two and so on*

This step didn't thus follow the three risk assessment phases presented in Figure 2.1, but comprised of giving risk points to a certain supplier in pre-defined risk factors and assessing the risk level of a certain supplier through the sum these points. Examples of the evaluated risk factors includes criticality of the product dosage form (topical, oral, intramuscular, intravenous etc.), scale of different dosage forms manufactured, geographical location, business effect, authority inspection history, GMP-compliance history and certain GMP-compliance key performance indicators, such as number of customer complaints proportional to sales. This risk level was then used in defining frequency for the supplier follow-up GMP audits. The risk assessment was updated on a yearly basis to evaluate the follow-up GMP audit frequency. Only one of the companies performed a supplier specific risk assessment, that followed the traditional risk assessment phases. This risk assessment was initially conducted already in the supplier qualification decision phase and updated yearly for the existing suppliers.

### 6.5.3 Follow-up audits

The main purposes of follow-up audits were to oversee and enforce issues agreed in the quality agreement, evaluate the manufacturing process against existing product marketing authorization, verify that the supplier has implemented corrective actions for concerns raised

in previous audits, and that the supplier's GMP-compliance level has overall remained above the required threshold. Same challenges and limitations exist as in the initial audit. The minimum frequency for follow-up audits required by EU-GMP is 3 years, but with the risk assessment it could be raised to one or even half year. Audit result was first approved in the quality, and if major issues were discovered, they could be elevated within the quality department or to cross-functional teams.

### 6.5.4 Other supplier and risk management tools

As described in earlier chapters, EMA and FDA are keeping public databases of their inspection history and issuing reports of supplier non-compliance (EMA) and critical GMP-violations (FDA). Several companies were actively following these databases to be alerted of possible supplier problems with authorities. Finding one's supplier to be rejected by either of EU or U.S. authorities would naturally be a signal that company's own GMP-compliance management process has failed and following these databases by its nature a rather retroactive tool for GMP-compliance management.

This incidence of finding authorities lifting an import ban or placing other restrictions to a company's supplier, as well as discovering supplier critical GMP-compliance by any other ways, would call for urgent actions to secure company's supply, or at least minimize the caused shortages. A bit surprisingly, only two of the six companies had a clear process to follow in case of supplier critical GMP-violations were recognized, either from internal or external sources. This process included calling up a cross-functional director meeting, evaluating the case and needed actions, contacting the supplier in regards of corrective actions and supplier termination in case the problems could not be solved.

As acknowledged in the literature review part of this thesis, back-up suppliers are a common way of controlling the risk of supply chain disruptions. This was also true for the companies in case of active substance suppliers: all companies except one had back-up suppliers at least for the most critical active substances. With drug product suppliers, however, the picture is

quite different. As described by one of the informants, having back-up suppliers would mean "one should transfer manufacturing to another manufacturer, go through changes in manufacturing authorization, [manufacturing] process should be validated, so the transfer becomes too expensive…". In general, the interviewees described the costs and resources needed for qualifying and maintaining a back-up supplier to be so significant that it has been considered impossible to maintain one, even when taking into consideration the risks related to keeping only one source of products. These costs include for instance transferring manufacturing capability, conducting separate process validations and updating product MAs for two different sites. Only one company of the six had back-up suppliers for drug products, and only for the most critical products. It should be pointed out that none of the companies measured costs related to supplier GMP-compliance violations that caused supply chain disruptions or other negative impacts on the company's economic performance.

### 6.6 Links to traditional supplier management

All the companies had quarterly or half-yearly cross-departmental internal meetings to review individual supplier performance, including also GMP-compliance issues. These meetings were organized to have a holistic view on the supplier performance and were the main link between traditional supplier management and GMP-compliance management processes. To measure this performance, companies used different key performance indicators, such as number of customer complaints proportional to sales, number of rejected batches and number of manufacturing-related deviations. Some of these key performance indicators were the same as in the yearly risk assessment. These internal meetings were usually followed by meeting with the supplier to discuss topics raised in the internal meetings. Only one of the six companies had launched a GMP-compliance related supplier development program, meaning in this case sending their own employees to the supplier's premises to train and develop supplier GMP-performance.

It is quite obvious, that there is also other, informal interaction between the traditional and GMP-compliance management processes, and that these two don't work in isolation of each other outside the formal linkages. One type of these informal interactions discovered was elevating topics from the GMP-compliance management process to the traditional supplier management process to get a better or quicker response from the supplier. It is also given that the purchasing department usually having the overall supplier responsibility cannot manage the supplier relationship without being also aware of the supplier's GMP-compliance status and possible risks and problems. When examining Figure 6.1, it should thus be kept in mind that it is an illustration depicted based on the companies' formal processes and responsibilities.

One final note to be made is that the traditional supplier management process varied in the companies depending on the relative importance of the supplier to the company, minor suppliers having a reduced process compared to more important ones. The GMP-compliance management process, however, remained the same for all suppliers, be they minor or important. This feature can be traced to the EU GMP requirements, which do not make any separations between important and minor suppliers.

# 7. CONCLUSIONS AND DISCUSSION

This chapter will assess research findings through the research questions, and reflect these findings to the reviewed literature on SCM, supplier selection, evaluation and qualification process, SSCM and SCRM. For the sake of clarity, it is beneficial to start this assessment from the lower-level context of GMP-compliance management in pharmaceutical industry and then draw connections to the higher-level contexts of supply chain, sustainability and risk management.

## 7.1 Significance and nature of GMP-compliance risk

The first of the three research question to be addressed is: *what is the significance and nature of GMP-compliance risk?* This thesis started by claiming that GMP-compliance must be of relevance to pharmaceutical companies – it is one of the very basic conjectures of the companies' and their supply chain's business. Without compliance, the companies are simply not allowed to sell drug products. As presented in chapter five, the GMP-regulations are strongly monitored and enforced by different authorities, making GMP-compliance risk a continuous threat to company's existence if it is not managed appropriately.

This claim was supported by the interviews: all companies had established a process for managing their supply chain GMP-compliance, and expressed that not complying to the regulations is not an option. GMP-compliance was also brought up as one of the biggest risks in their supply chain by several interviewees. The significance of GMP-compliance risk is thus clearly established.

The nature of GMP-compliance risk can be approached from two angles - through perceived consequences and through perceived challenges. Immediate consequences are similar to those of any quality-related risks: if the drug products are not safe to consume or lacking the effect they should, companies may need to withdraw products from markets, causing financial losses and usually short-term shortages. On the other hand, if a supplier loses its ability to supply due to import restrictions or refusal of licenses, the consequences are similar to those of supply chain disruptions (product stock-outs), but may also lead to product recalls. Besides the immediate consequences, product shortages, market actions and especially product-related adverse reactions or patient deaths may also cause severe reputational damages to companies, extending the financial losses from concerning individual products to the overall business. The GMP-compliance risk can thus clearly be classified as belonging to supply risks, but it can also be considered to bear similarities to man-made macro risks and being more significant than supply risks: even though not comparable to war or political

tremor, a non-compliance report from the European authorities or a warning letter from FDA may well destroy supplier's business if it is banned from selling its products.

From challenges point of view, supply chain GMP-compliance bears similarities to the challenges of governing supply chain sustainability that were presented in Table 3.2, with some differences. Informational & knowledge and communication challenges are the most apparent commonalities that were also highlighted by the interviewees: retrieving reliable, comprehensive and credible information from suppliers was described to be challenging in terms of GMP-compliance, as well as establishing effective communication routes. Even though compliance and power challenges were not directly mentioned by the interviewees, it is nonetheless obvious that these are applicable to GMP-compliance management. Here, finding complimentary ways to govern compliance besides audit programs and finding common ways to interpret and implement GMP-guidelines can be considered the main points for overcoming these challenges. Legitimacy challenges are also apparent to exist in GMP-compliance management. Finally, geographical challenges may be the only one of the gaps presented by Boström *et al.* (2015) that is not directly applicable to GMP-compliance management: where in terms of sustainability, effects of violations can be ignored by buyers due to the geographical distances, the violations in GMP-compliance usually affect the product end consumers and are thus much closer and may cause a much bigger negative effect to the business of the buyer organization. Overall, from the challenges point of view, GMP-compliance risk can be considered to be similar to sustainability risk in its nature.

### 7.2 Supplier and risk management in a highly regulated and enforced environment

Let us next turn our attention to the second research question: *how is supplier and risk management constructed in a highly regulated and enforced environment?* As presented in chapter 4, the EU GMP already withholds and requires a certain framework for supplier GMP-compliance management: API and drug product manufacturers have to be audited with a minimum of three-year cycle, companies have to perform a yearly risk profile assessment for individual suppliers and it has to be the quality department, who manages the overall

process. None of the interviewees had questioned these basic principles or tried to modify them, rather these principles had been used as the focal point to the management processes. With some companies, it seemed that the supplier GMP-compliance management process was a direct copy of the requirements, without any or very little further development. Even with the companies having more elements than the minimum in their process, the basic elements were clearly observable: audit, qualification decision, quality agreement, yearly supplier risk profile assessment and follow-up audits.

Even though present with every company, pre-evaluation and qualification steps differed the most between companies. With some, GMP-compliance aspects were already thoroughly considered during overall candidate assessment and in the initial site visits, whereas with some companies the pre-evaluation was done solely by quality assurance with a questionnaire. Same division existed in the supplier qualification phase, some of the companies considering a supplier to be qualified after it had passed an audit, whereas others concluded a holistic GMP-compliance risk assessment including risk mitigation actions, for which supplier audit was only one of the aspects. This study did not go as far to details as mapping the contents of quality agreements, specific points included in the formal risk assessments or supplier audit agendas, but differences must exist between companies, some of the companies doing the different steps more thoroughly and rigorously than others.

EU-GMP does not require any certain type of organization for GMP-compliance management process within the quality department, which leaves the companies open hands for allocating responsibilities to different levels and departments inside the quality function. Organization is perhaps where the companies differed the most from each other, on two aspects: having supplier GMP-compliance on a corporate level versus manufacturing site level, and having a separate “GMP-compliance” team managing centrally the overall process versus dividing the responsibility of different process steps to different quality functions and having thus a decentralized process.

One interesting aspect of the supplier GMP-compliance management is its connection to the traditional supplier management process. It was deductible from the interviews that these two processes have in past been almost totally isolated from each other, connecting only at the beginning (supplier candidate is fed to the GMP-compliance management process) and end (supplier is qualified and allowed to the company's supplier pool or rejected and deterred from supplying to the company). As seen in Figure 6.1, many of the companies have implemented integrative elements between the two processes: GMP-compliance evaluation is already started at the "traditional" candidate assessment stage, concerns related to GMP-compliance are shared in cross-functional meetings and cooperation between the quality and purchasing departments overall is encouraged.

When moving away from the research context, it is clear that many of the ground assumptions do not exist outside the pharmaceutical industry, and the framework presented in Figure 6.1 is not directly applicable to other industries. Especially two of these assumptions should be highlighted: mandate given for the quality department, admitting independent authority in decision making and basing these decisions solely on quality aspects (and excluding for instance economic aspects), and the rigorous authority enforcement through inspections, controlling that the individual process steps are in line with established requirements (rather than evaluating effectiveness of the overall process).

This acknowledgement leads to the main conclusion in regards to the outlying research question: in an environment of strong regulation and enforcement, supplier and risk management is constructed starting with the established regulations and building these processes on them, rather taking generally acknowledged or "best practice" processes as a starting point and adjusting them to the regulations. That said, the study results showed that even though the processes were established on grounds of regulations, there was a tendency of developing them towards these general practices and integration. The next chapter will continue from this conclusion.

## 7.3 The effects of strong regulation and authority enforcement

In this last chapter, I will address the third research question: *what are the impacts that strong regulation and authority enforcement impose to supplier and risk management practices?* As presented by Johnson & Flynn (2015; Table 2.1), traditional supplier selection begins with organization's strategic requirements and then continues into assessing supplier risks versus expected returns, possible purchasing strategies and evaluating supplier performance in regards of quality, price, sustainability and other factors. As with the traditional supply chain management, also sustainable supply chain management places organization's strategic values to the very core of supplier selection and management process. As presented in the Figure 6.1, candidate assessment lied in the traditional supplier management process and even though most of the companies included GMP-compliance partially to the assessment phase, it was evident that the main focus on supplier GMP-compliance level was only after the supplier candidate(s) had already been chosen. Since supplier candidates are assessed without a full GMP-compliance evaluation, and rather fed to the GMP-compliance management process after the assessment to verify that the minimum GMP-level is achieved, there is a clear gap between the company's strategy and supplier GMP-compliance management. Proposing that EU-GMP regulations have alone caused this gap would probably be over-exaggerating, but as will be presented below, it is obvious that they have influenced the way companies have built their processes.

The study of Luzzini *et al.* (2014; Table 2.2) showed, that supplier evaluation is normally conducted through three distinctive steps – collecting first preliminary general information about the supplier, then gathering more in-depth information on supplier capabilities to produce the actual product and allowing the supplier to organization's supplier pool, and assessing the supplier performance through different key performance indicators. The main insight from the traditional supplier management for the purpose of this thesis is that supplier requirements arise from organization's strategy and there are no separate processes for managing areas such as quality or sustainability, but these are integrated to the overall

process. This doesn't mean that traditional SCM wouldn't consider these areas important, but it has clearly been beneficial to integrate them to the overall process.

As concluded in the previous chapter, the approach companies had taken in regards of GMP-compliance management was not as simple: companies had built their GMP-compliance management process on the grounds of regulations and requirements, separate from the co-existent traditional supplier management process. One of the ground reasons for this approach is traceable to the GMP-regulations, that place the responsibility of supply chain GMP-compliance to quality department and grant them a mandate of independent decision making. As quality department has its focus mainly on product quality (and patient safety) instead of the overall supplier relationship, this setting can easily create departmental silos and even conflicts within an organization. This may especially occur between quality department responsible from GMP-compliance and purchasing department responsible from the overall supplier relationship. This leads to the first conclusion concerning the impacts of regulations: strong regulation, especially if granting independent authority to one department over the others, contributes to creating departmental and process-specific silos within an organization and reduces integration.

Another implication for building processes according to regulations is that the regulations don't consider variance between companies that is sure to exist, and thus the processes may not be optimal for a given company's business model. This can lead to inefficiencies and even contradictions between what is required and what would be the best solution. Furthermore, strong regulations coupled with strong enforcement through authority inspections can shift the focus from supplier management to complying to regulations. GMP-audits serve as a good illustration on this: whereas supplier on-site audits are normally considered a quite extreme tool and conducted only for the riskiest suppliers, the companies performed them by default for every supplier as required by the EU-GMP. As audits are to be performed in any case, most of the companies omitted supplier risk assessment, perhaps the most important phase in traditional and sustainable supplier selection, evaluation and

qualification process, and qualified the supplier solely based on audit. Taking into consideration limitations of supplier audits, this leaves companies without a holistic view of the supplier and the related risks. The third conclusion is as follows: strong regulation and authority enforcement on the other hand reduces flexibility and shifts the focus from effectiveness of supplier management process to the compliance of the process itself, and on the other, may lead to omitting critical process steps if the consecutive steps are already defined by the regulations.

The literature review section on managing supply chain sustainability introduced a link between SSCM and dynamic capabilities and some specific dynamic capability categories, such as knowledge assessment, supply chain partner development and co-evolving. According to the reviewed literature, dynamic capabilities are an extension of more traditional SSCM capabilities, a next step, and for a company to be able to develop dynamic capabilities, it must have the traditional SSCM practices in place. Both traditional SSCM and dynamic capability categories build on supply chain partnership and integration. This study did not specifically address dynamic capabilities, but the results strongly imply that the base for building dynamic capabilities related to supply chain GMP-compliance management process is missing: supplier relationships remain more transactional than collaborative in their nature. Actions towards supply chain integration would most certainly create similar benefits in the research context as with traditional SCM and SSCM, but they are seemingly hard to take as the GMP-compliance management process is not even internally an integral part of the overall supplier management process.

In the literature review section, Table 2.3 listed some commonly used risk management strategies for overcoming macro risks. Most of these strategies focused on stock and logistics management or commercial or marketing aspects and are thus not directly applicable to managing GMP-compliance risk. Two strategies are relevant in this manner: flexible supply base and make-and-buy. Both of these strategies rely on having an alternative source for products, in case the main supplier is for some reason unable to supply its products. This

strategy was followed by most of the companies in case of active substances, but due to EU GMP-regulations on manufacturing and supplier management, maintaining a back-up supply for drug products was deemed so expensive and resource-demanding that only few of the companies had pursued this strategy, and only for the most critical drug products. Based on the above, I present the following conclusion: regulations can drive costs and resources needed for maintaining back-up supply and possibly other risk management strategies so high that companies might omit these strategies.

Both strategies managing supply risks presented in literature (see Table 2.4) and the framework presented for SSCM by Beske & Seuring (2014; see Figure 3.2) build on strategic rather than transactional supplier relationship, supplier development and integration, reducing supply chain complexity and choosing carefully the kind of right suppliers and monitoring them through pre-defined key performance indicators. Supplier relationship in terms of GMP-compliance management in the companies, on the other hand, did not have many integrative or strategic elements: supplier development activities were virtually missing, early supplier involvement and long-term relationship were not brought up in the interviews and learning from and enhancing innovation through suppliers were absent. It is true that these elements may exist in the traditional supplier management process, but nevertheless they were scarce in GMP-compliance management.

One interesting area bearing similarities between the traditional supplier risk management, SSCM and supply chain GMP-compliance management is controlling suppliers through pre-defined standards: establishing quality management program, standards and supplier certification are common themes for all the three practices. In the research context, standards were established by authorities instead of NGOs or companies themselves. Similarly, in the research context, certification can be seen to be conducted by the authorities through GMP-inspections after which, if passed, suppliers were granted a GMP-certificate that are disclosed publicly. Likewise, if the inspection was not passed, authorities issued a public non-compliance certificate. This certification program is a natural way for a company to evaluate

the GMP-compliance risk of its supplier: if there is a recent GMP-certificate, the risk is considerably lower than if the supplier has not been inspected by authorities. Suppliers not passing an inspection can be banned from supplying products before appropriate corrective actions and a re-inspection. Even though the EU-GMP requires companies to audit their AS and drug product suppliers, as presented in the results section, companies enhance authority inspections in their supplier evaluation and risk assessment processes. Thus the following conclusion about the effects of authority enforcement is drawn: strong authority enforcement and certification schemes transfers responsibility of supplier management and related risks partially towards the authorities.

## 8. MANAGERIAL IMPLICATIONS AND SUGGESTIONS FOR FURTHER RESEARCH

The findings presented above have implications on both private and public sector. Perhaps the most valuable insight from this study is that setting industry-specific regulations and system for enforcing them may not be as straight-forward as many think. This can have some major impacts on how companies operate and create significant inefficiencies as well as unintentional shifts of responsibility from companies to authorities. However, as many regrettable incidences such as the thalidomide crisis demonstrate, strict regulations are necessary to protect health of the masses. It is thus of upmost importance to understand the implications of high authority regulation and enforcement. This study was conducted in the pharmaceutical industry, which can without doubt be described as one of the strictest industry in terms of regulatory demands and control and thus gives an accentuated view of these implications. I will first discuss the effects for companies and on an industry-level and then proceed to implications for authorities and the society.

As was concluded in the previous chapter, supply chain GMP-compliance management processes were designed to comply with the prevalent regulations and there was in several cases no or only little tendency to develop these processes beyond compliance to these

regulations. It is obvious that from company or business perspective, this causes unnecessary inefficiencies and rigidity. Following the recent developments in supplier, risk and sustainability management, a better integration of supply chain GMP-compliance management to the overall supplier management process would create clear benefits for a given company in terms of efficiency and transparency, reduce unnecessary silos within a company and encourages cooperation between departments. Designing the GMP-compliance management processes as an integral part of holistic supplier management process, not only a mere necessity arising from regulations, would most definitely support supplier risk management, eliminating weak suppliers at earlier phases, elevating and reacting to problems more efficiently et cetera. Furthermore, this would encourage companies to refine the meaning and purpose of each process step and introduce complementary steps, rather than conducting the steps defined in regulations without considering their relevance.

This is not to say that companies should ignore the regulations or try to shift the responsibility assigned in this case to the quality department and risk facing sanctions or other regulatory actions, rather they should build the processes first as a fit to company strategy and business model and secondary as a fit to regulations. Regulations will most probably require adjusting the established processes, but it is the principle of linking the process to company's strategy from the beginning that matters.

From authority and societal perspective, two of the conclusions presented in the previous chapter are of considerable significance: partial shift of responsibility towards authorities and arising costs of risk management strategies. The shift of responsibility applies especially in connection with high regulatory enforcement and oversight, where the authorities themselves use the power to interpret whether a specific supplier is approvable or not and also use this power in practice. Companies will enhance the available information on authority inspection history in their supplier evaluation and risk assessment processes, which leads to favoring suppliers with strong inspection history over the ones with no or limited history and the

companies that have failed an authority inspection. I will not go on arguing whether this phenomenon itself is good or bad (or both), but it is nevertheless something that should be acknowledged.

Raising the costs of maintaining back-up supply of a certain product in specific and other risk management strategies in general, on the other hand, may have more immediate and far reaching consequences. Having no or limited contingency planning for keeping a certain drug product on markets makes the supply chain seemingly vulnerable for macro risks, both man-made and natural, and thus long-lasting disruptions. In case of pharmaceuticals, this may evidently mean shortages of life-saving or maintaining drugs and patient deaths. Even though the consequences would not be as devastating, they may still have a negative effect to society and individual patients. This is something that the regulators must take into account and concerns especially health-related industries where the regulations are by default stricter than in other industries.

This study was one of the first ones to address the impacts of high authority regulation and enforcement, thus it contains many assumptions and the conclusions made remain to be challenged. As mentioned in the method chapter, the purpose of this study was not to capture a holistic view but rather give a directional overview on the studied phenomenon. To validate the conclusions made, it would be beneficial to examine other highly regulated industries to see if they bear similarities. The actual effects of the implications raised in this chapter should also be addressed in more detail. Finally, given the scope and limitations of this study, there might be a need to refine some of the presented results and frameworks to better represent the general approaches and decisions made by different companies after gathering more data and, due to a rather limited number of samples, some relevant insights could have been omitted. This calls for further research.

## 9. REFERENCES


Ahi, P., Searcy, C. (2013): “A comparative literature analysis of definitions for green and sustainable supply chain management”, *Journal of Cleaner Production,* Vol. 52, pp. 329-341

Beamon, B. M. (1999): “Designing the green supply chain”, *Logistics Information Management,* Vol. 12 (4), pp. 332-342.

Beske, P. (2012): "Dynamic capabilities and sustainable supply chain management", *International Journal of Physical Distribution & Logistics Management*, Vol. 42 (4) pp. 372 – 387

Beske, P., Land, A., Seuring, S. (2014): “Sustainable supply chain management practices and dynamic capabilities in the food industry: A critical analysis of the literature”, *International Journal of Production Economics*, Vol. 152, pp. 131-143

Beske, P., Seuring, S. (2014): "Putting sustainability into supply chain management", *Supply Chain Management: An International Journal*, Vol. 19 (3), pp. 322 - 331

Biddles, F. M. (1998, 4. Nov.): “Dole Food, Chiquita Feel Effect of Hurricane Mitch”, *The Wall Street Journal,* Available from: http://www.wsj.com/articles/SB910108968672819500 [accessed on 5 August 2016]

Boström, A.; Jönsson, A. M.; Lockie, S.; Mol, A. P. J., Oosterveer, P. (2015): “Sustainable and responsible supply chain governance: challenges and Opportunities”, *Journal of Cleaner Production,* Vol. 107, pp. 1-7

Bryman, A., Bell, E. (2003): “*Business Research Methods*”. 2nd ed. Oxford: Oxford University Press

Burgess, K., Singh, P., J., Koroglu, R. (2006): "Supply chain management: a structured literature review and implications for future research", *International Journal of Operations & Production Management,* Vol. 26 (7), pp. 703-729

Börjeson, N., Gilek, M., Karlsson, M. (2015): "Knowledge challenges for responsible supply chain management of chemicals in textiles - as experienced by procuring organisations", *Journal of Cleaner Production,* Vol. 107, pp. 130-136

Carr, A. S., Pearson, J. N. (1999): "Strategically managed buyer–supplier relationships and performance outcomes", *Journal of Operations Management,* Vol. 17 (5), pp. 497-519

Carter, C. R., Rogers, D. S. (2008): "A framework of sustainable supply chain management: moving toward new theory", *International Journal of Physical Distribution & Logistics Management,* Vol. 38 (5) pp. 360-87

Chkanikova, O., Lehner, M. (2015): "Private eco-brands and green market development: towards new forms of sustainability governance in the food retailing", *Journal of Cleaner Production,* Vol. 107, pp. 74-84

Choi, T. Y., Krause, D. R. (2006): "The supply base and its complexity: Implications for transaction costs, risks, responsiveness, and innovation", *Journal of Operations Management,* Vol. 24 (5), pp.637-652

Chopra, S., Sodhi. M., S. (2004): "Managing Risk to Avoid Supply-chain Breakdown", *MIT Sloan Management Review,* Vol. 46 (1), pp. 53–62

Colicchia, C., Dallari, F., Melacini, M. (2010): "Increasing supply chain resilience in a global sourcing context", *Production Planning & Control,* Vol. 21 (7), pp. 680-694

Croom, S., Romano, P., Giannakis, M. (2000): "Supply chain management: an analytical framework for critical literature review", *European Journal of Purchasing & Supply Management,* Vol. 6, pp. 67-83

Diehl, D., Spinler, S. (2013): "Defining a Common Ground for Supply Chain Risk Management – A Case Study in the Fast-moving Consumer Goods Industry", *International Journal of Logistics: Research and Applications,* Vol. 16 (4), pp. 311–327

Dubois, A., Gadde, L. E. (2002): "Systematic combining: an abductive approach to case research", *Journal of business research,* Vol.55, pp. 553-560

Drakulich, A., Van Arnum, P. (2009): "Evaluating the pieces of the pharma supply chain", *Pharmaceutical Technology Europe,* Vol. 21 (3), pp. 42-44

Edney, A. (2016, 21. Jan.): "Chinese Pharmaceutical Firm Hisoar Added to U.S. Import Ban", *Reuters,* Available from: http://www.bloomberg.com/news/articles/2016-01-20/chinese-pharmaceutical-company-hisoar-added-to-u-s-import-ban [accessed on 29 March 2016]

Eisenhardt, K. (1989): "Building Theories from Case Study Research", *Academy of Management Review,* Vol. 14 (4), pp. 532-550

Eisenhardt, K. 1989. Building Theories from Case Study Research. Academy of Management Review 14(4): 532-550

Eisenhardt, K. M., Martin, J. A. (2000): "Dynamic Capabilities: What Are They?", *Strategic Management Journal,* Vol. 21, pp. 1150-1121

Ellram, L. M., Carr, A. S. (1994): "Strategic purchasing: a history and review of the literature", *International journal of purchasing and materials management,* Vol. 30 (2), pp.10–18

Elkington, J. (1998): "*Cannibals with Forks: The Triple Bottom Line of 21st Century Business",* Gabriola Island: New Society Publishers

Eriksson, P. & Kovalainen, A., 2008. *Qualitative methods in business research,* London, UK: Sage

European Medicines Agency (2005): "*Guidance on the occasions when it is appropriate for Competent Authorities to conduct inspections at the premises of Manufacturers of Active Substances used as starting materials",* London: EMEA

Foerstl, K., Reuter, C., Hartmann, E., Blome, C. (2010): "Managing supplier sustainability risks in a dynamically changing environment—Sustainable supplier management in the chemical industry", *Journal of Purchasing and Supply Management*, Vol. 16 (2), pp. 118-130

Gelderman, C. J., Van Weele, A. J. (2003): "Handling measurement issues and strategic directions in Kraljic's purchasing portfolio model", *Journal of Purchasing and Supply Management*, Vol. 9 (5-6), pp. 207-216

Ghauri, P. & Gronhaug, K., (2005): *Research methods in business studies. A practical guide*. London, UK: Prentice Hall

Gimenez, C., Tachizawa, E. M. (2012) "Extending sustainability to suppliers: a systematic literature review", *Supply Chain Management: An International Journal*, Vol. 17 (5), pp.531 - 543

Harris, G. (2009, 19. Jan.): “Drug Making’s Move Abroad Stirs Concerns”, *New York Times*, pp. D.1

Grimm, C., Knemeyer, M., Polyviou, M., Ren, X. (2015): “Supply chain management research in management journals: a review of recent literature (2004-2013)”, *International Journal of Physical Distribution & Logistics Management,* Vol. 45 (5), pp. 404-458

Hahn, C. K., Kim, K. H., Kim, J. S. (1986): “Costs of competition: implications for purchasing strategy”, *Journal of Purchasing and Materials Management,* Vol. 22 (3), pp. 2-7

Hammami, R., Temponi, C., Frein, Y. (2014): “A scenario-based stochastic model for supplier selection in global context with multiple buyers, currency fluctuation uncertainties, and price discounts”, *European Journal of Operational Research*, Vol. 233 (1), pp. 159-170

Harris, G. (2014, 15. Feb.): “Medicines Made in India Set Off Safety Worries”, *New York Times*, pp. A.1

Helin, S., Babri, M. (2015): “Travelling with a code of ethics: a contextual study of a Swedish MNC auditing a Chinese supplier”, *Journal of Cleaner Production,* Vol. 107, pp. 41-53

Ho, W., Zheng, T., Yildiz, H. & Talluri, S. (2015): “Supply chain risk management: a literature review”, *International Journal of Production Research,* Vol. 53 (16), pp. 5031-5069

Johnson, P. F., Flynn, A. E. (2015): “*Purchasing and Supply Management”*. New York: McGraw-Hill Education

Kannan, V. R., Tan, K. C. (2000): “Buyer-supplier relationships: The impact of supplier selection and buyer-supplier engagement on relationship and firm performance”, *International Journal of Physical Distribution & Logistics Management,* Vol. 36 (10), pp. 755-775

Lawton. C., Dade, C. (2006, 15. Aug.): “Dell to Recall 4 Million Notebook-PC Batteries”, *The Wall Street Journal*, Available from: http://www.wsj.com/articles/SB115559142481135423 [accessed on 5 August 2016]

Lee, H. L. (2004): “ The triple-A supply chain”, *Harward Business review*, Vol. 82 (10), pp. 102-112

Li, S. H., Ragu-Nathan, B., Ragu-Nathan, T. S. (2006): “The impact of supply chain management practices on competitive advantage and organizational performance”, *Omega*, Vol. 34 (2), pp. 107-124

Luzzini, D., Caniato, F., Spina, G. (2014): “Designing vendor evaluation systems: An empirical analysis”, *Journal of Purchasing & Supply Management*, Vol. 20, pp. 113-129

Manuj, I., Mentzer, J. T. (2008): “Global supply chain risk management strategies”, *International Journal of Physical Distribution & Logistics Management,* 38 (3), pp. 192–223

Marschan-Piekkari, R., Welch, C. (2004): “*Handbook of Qualitative Research Methods for International Business”.* First edition. Cheltenham: Edward Elgar Publishing Ltd.

Miemczyk, J., Johnsen, T. E., Macquet, M. (2012): "Sustainable purchasing and supply management: a structured literature review of definitions and measures at the dyad, chain and network levels", *Supply Chain Management: An International Journal*, Vol. 17 (5), pp.478 - 496

Miller, A. M. M., Bush, S. R. (2015): "Authority without credibility? Competition and conflict between ecolabels in tuna fisheries", *Journal of Cleaner Production*, Vol. 107, pp. 137-145

Mol, A. P. J. (2015): "Transparency and value chain sustainability", *Journal of Cleaner Production,* Vol. 107, pp. 154-161

Patton, M. Q., (1990): "*Qualitative evaluation and research methods".* Second Edition. Newbury Park, CA: Sage

Porter, M. E. (1975): "Note on the Structural Analysis of Industries", *Harvard Business School Background Note*, pp. 376-054

Rosania, L. (2010): "Heparin crisis 2008: a tipping point for increased FDA enforcement in the pharma sector?", *Food and drug law journal*, Vol. 65 (3), pp. 489-502

Sarkis, J., Qinghua, Z., Kee-hung, L. (2011): "An organizational theoretic review of green supply chain management literature", *International journal of production economics*, Vol. 130 (1), pp. 1-15

Saunders, M., Lewis, P., Thornhill, A. (2000): "*Research Methods for Business Students*". Second edition. Harlow. Pearson Education Limited. Edinburgh Gate Harlow, U.K.

Seuring, S., Muller, M. (2008): "From a literature review to a conceptual framework for sustainable supply chain management", *Journal of Cleaner Production,* Vol. 16 pp. 1699–1710

Sheffi, Y. (2005): "*The Resilient Enterprise: Overcoming Vulnerability for Competitive Advantage*", Boston, USA: The MIT Press

Siddiqui, Z. (2016, 1. Feb.): FDA warns IPCA Labs on manufacturing lapses at 3 plants, *Reuters*, Available from: http://in.reuters.com/article/ipca-labs-warning-fda-idINKCN0VA1RB [accessed on 29 March 2016]

Siddiqui, Z.; Chatterjee, S. (2014, 13. Mar.): "Sun Pharma hit by FDA ban on Gujarat plant, shares fall", *Reuters*, Available from: http://in.reuters.com/article/sun-pharma-india-fda-idINDEEA2C03K20140313 [accessed on 29 March 2016]

Soni, G., Kodali, R. (2013): "A critical review of supply chain management frameworks: proposed framework", *Benchmarking: An International Journal*, Vol. 20 (2), pp. 263-298

Storey, J., Emberson, C., Godsell, J., Harrison, A. (206): "Supply chain management: theory, practice and future challenges", *International Journal of Operations & Production Management*, Vol. 26 (7), pp. 754-774

Story, L., Barboza, D. (2007, 15. Aug.): Mattel recalls 19 million toys sent from China, *The New York Times*, Available from: http://www.nytimes.com/2007/08/15/business/worldbusiness/15imports.html?_r=0 [accessed on 5 August 2016]

Svensson, G. (2007): "Aspects of sustainable supply chain management (SSCM): conceptual framework and empirical example", *Supply Chain Management: An International Journal*, Vol. 12 (4), pp. 262-266

Tang, C. S. (2006a): "Perspectives in Supply Chain Risk Management", *International Journal of Production Economics*, Vol. 103 (2), pp. 451–488

Tang, C. S. (2006b): "Robust strategies for mitigating supply chain disruptions", *International Journal of Logistics: Research and Applications*, Vol. 9 (1), pp. 33-45

Teece D. J., Pisano, A. (1997): ”Dynamic capabilities and strategic management”, *Strategic Management Journal*, Vol. 18 (7), pp. 509–533

Vellema, S., van Wijk, J. (2015): “Partnerships intervening in global food chains: the emergence of co-creation in standard-setting and certification”, *Journal of Cleaner Production,* Vol. 107, pp. 105-113

Walker, H., Lucio, Di Sisto, L., McBain, D. (2008): “Drivers and barriers to environmental supply chain management practices: Lessons from the public and private sectors”, *Journal of Purchasing and Supply Management*, Vol. 14 (1), pp. 69-85

Yadav, V., Sharma, M. P. (2016): Multi-criteria supplier selection model using the analytic hierarchy process approach, *Journal of Modelling in Management*, Vol. 11 (1)

Yin, R. K. (2003): “*Case Study Research: Design and Methods*”. Third edition. Thousand Oaks, California: Sage

Zimmer, K., Fröhling, M., Schultmann, F. (2016): “Sustainable supplier management - a review of models supporting sustainable supplier selection, monitoring and development”, *International Journal of Production Research*, Vol. 54 (5), pp. 1412-1442

Zsidis, G. A. (2003): “A grounded definition of supply risk”, *Journal of Purchasing & Supply Management*, Vol 9 (5/6), pp. 217-224

Zsidis, G. A., Ellaram, L. M. (2003): “An agency theory investigation of supply risk management”, *Journal of Supply Chain Management*, Vol. 39 (3), pp. 15-27

Zsidis, G. A., Smith, M. E. (2005): “Managing supply risk with early supplier involvement: a case study and research proposition”, *Journal of Supply Chain Management*, Vol. 41 (4), pp. 44-57