Building resilience with digital twins and analytics: Strategies and cases from pharma supply chains

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Resilience is considered a key success factor for supply chain management in the coming years. This article provides an overview of resilience strategies pursued in pharmaceutical supply chains based on a synthesis of observed industry practices and scientific literature. We also discuss the focal role of data and analytics for successfully identifying risks and building resilience into supply chains. We outline some of the drawbacks of traditional methods for risk analysis and critically review the potential of modern supply chain analytics. We provide managerial insights from the application of digital twins and prescriptive analytics – two modern approaches for risk management – to a case of a global pharmaceutical supply chain. We show how analytics can enable a data-driven stress test that provides visibility into where and how a supply chain will be impacted during a major disruption. Furthermore, our results demonstrate how to design risk mitigation strategies that reduce the financial and operational impact of disruptions.

1 Resilience strategies for pharmaceutical supply chains

Over the past two decades, an increasing number of drug shortages have been reported (Fox et al., 2014; Pauwels et al., 2014; Bogaert et al., 2015). The consolidation of production sites and the relocation of production to Asia have shaped the design of global supply chains (Richman et al., 2017; Stricker et al., 2019). While these adoptions helped to lower supply chain costs, they may have reduced the ability to withstand disruptions (Schweitzer, 2013). These past developments and today's Covid-19 era have increased Pharma leaders' focus on risk management considerably (Kelleher et al. 2020). For example, Novartis states their "success depends on [the] ability to manage risk" (Novartis, 2020). Likewise, Roche "seek[s] to build a resilient supply chain" (Roche, 2020). Studies by Camelot Management Consultants have identified risk management as crucial element of successful operating models for biotech supply chains (Ebel and Hild, 2020).

In this section, we provide an overview of strategies for pharmaceutical companies to increase resilience and robustness. Following Brandon-Jones et al. (2014), we define supply chain resilience as "the ability of a supply chain to return to normal operating performance, within an acceptable period of time, after being disturbed", and supply chain robustness as "the ability of the supply chain to maintain its function despite internal or external disruptions". Both dimensions are interlinked to each other (Wieland and Wallenburg, 2013).

Figure 1 summarizes key elements for building and maintaining resilience in pharmaceutical supply chains, including some design principles found in theory and practice. Risk strategies are proactive or reactive. Proactive mitigation measures create certain protection before a disruption occurs. In contrast, reactive measures such as contingency plans focus on an effective response to disruptive events (Ivanov et al. 2014). Supportive measures enable the effective deployment of risk strategies.

Key proactive mitigation measures are risk inventory, dual sourcing, and reserve capacity (Lücker and Seifert, 2017; CheManager, 2020). Risk inventory refers to extra inventory held as a buffer or protection at a manufacturing stage in the event of a supply disruption. Reserve capacity is kept at another reliable manufacturing site. In the event of a disruption at the primary production site, reserve capacity can be used to produce output to supply the next

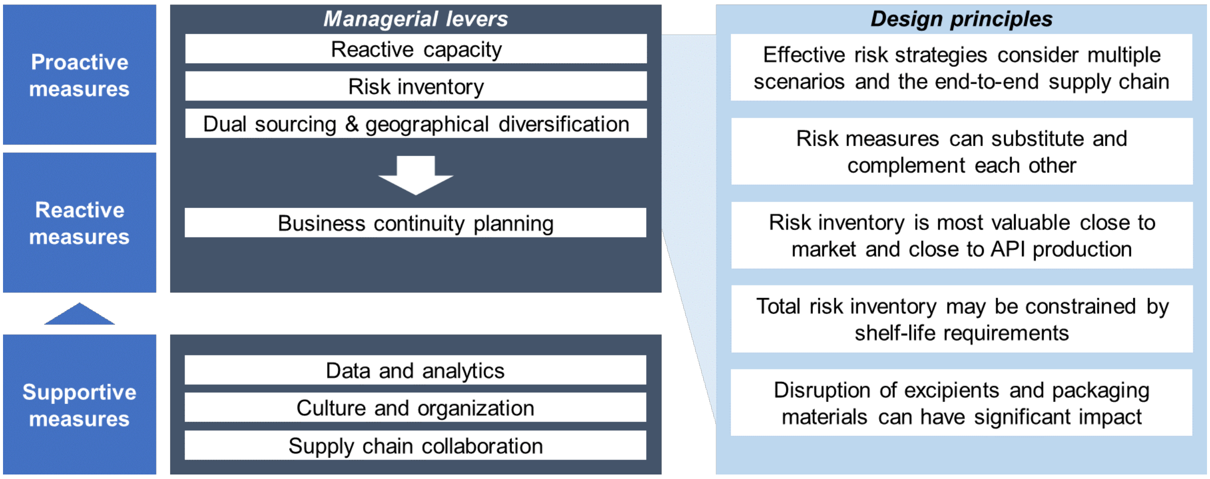

Figure 1: *Key elements for building and maintaining resilience in pharmaceutical supply chains (source: author)*

downstream site (Lücker et al., 2020). Dual (multi) sourcing refers to establishing two (multiple) supply sources for the same raw material (API) or intermediates. Further considerations may include geographic diversification. In particular, the high concentration of API manufacturing in Asia has sparked a debate to diversify supply locations (Kelleher et al., 2020; CheManager, 2020).

When building resilience into a multi-tier supply chain, a key challenge is to identify the optimal location and type of risk mitigation measures. For example, a firm may add risk inventory more upstream (closer to API production) or more downstream (closer to patients). Furthermore, either inventory or dual sourcing might mitigate disruptions at the supplier-level. Based on academic literature, own model-based analyses, and industry experience, we outline some design considerations for risk measures in Figure 1 (see Lücker et al., 2020; Eidam, 2020; Francas, 2018; Lücker and Seifert, 2017). These principles can provide general guidelines, but the complexity of supply chains typically demands a complementing in-depth analysis. In the following, we focus on the role of data and analytics for analyzing risks and building resilience.

2 Data and analytics: Avoiding pitfalls and building resilience

Industry reports see a rapidly growing demand for supply chain analytics that create transparency and support developing risk mitigation strategies (Kelleher et al., 2020; Payne, 2019). We refer to Hosseini et al. (2019) for a general overview of analytics for risk and resilience and to Sheng et al. (2020) for a review of such analytics in the context of life sciences and Covid-19. In the following, we outline the benefits of modern analytics and discuss the limitations of traditional methods for risk analysis.

The common approach for supply chain risk management is event-based. It focuses on an event-by-event analysis and tries to determine the consequences of an initial triggering event (Heckmann and Nickel, 2017). Traditional methods also rely on knowing the likelihood of occurrence and the magnitude of impact for every potential event that could disrupt a supply chain. Experience shows that for common supply-chain disruptions— forecast errors, lead-time fluctuations, varying yield factors, and so on—those methods often work well. Such known unknowns can appropriately be quantified using historical data risk (Simchi-Levi et al., 2014).

Whereas known unknowns are still measurable, it is a different story for low-probability, high-impact events. Mega disasters like the 2019 Corona outbreak and the 2011 Earthquake and Tsunami in Japan or major outages due to unforeseen events such as factory fires and supplier failures are difficult to anticipate. Historical data on these rare events – also called “black swans” – are limited or non-existent. Consequently, traditional models for risk analysis tend to fail and many companies struggle to adequately prepare for them (Heckmann and Nickel, 2017; Simchi-Levi et al., 2014). Using predictive analytics does not resolve this issue either: Even advanced machine learning models fail to detect low-probability, high-impact disruptions well and long enough ahead of time. The systematic failure to foresee Covid-19 and its impact confirmed this dramatically (Ioannidis et al., 2020).

Therefore, new supply chain risk management approaches focus on managing and limiting the impact

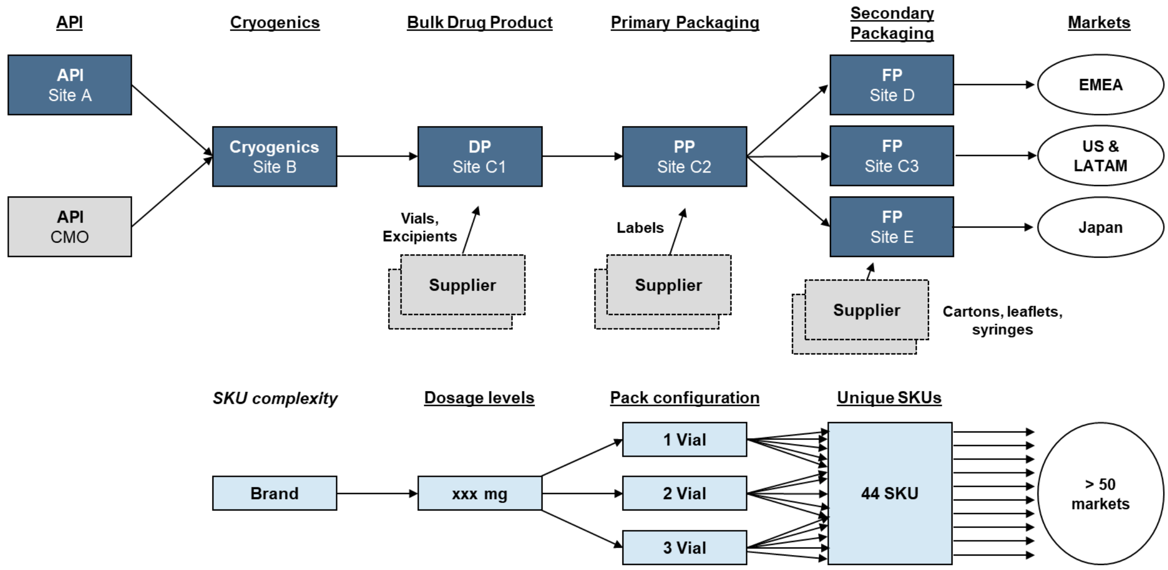

Figure 2: *Modelled pharmaceutical supply chain (source: author)*

of potential disruptions. Instead of trying to identify each and every possible disruptive event and estimating its impact and probability, they aim to analyze a supply chain's vulnerability. Simchi-Levi (2015) proposes to shift attention to the impact of potential failures at points along the supply chain (such as the breakdown of a supplier), rather than the cause of the disruption. In line with our experience, Simchi-Levi argues that this type of analysis obviates the need to estimate the probability that any specific risk will occur; this is a valid approach since the mitigation strategies for disruptions are equally effective regardless of their causes. Modern supply chain analytics play a prominent role in implementing this type of risk analysis. Digital twins – computerized models of a supply chain – provide the means to assess supply chain vulnerability and risk exposure. They allow studying the impact of disruptions on the end-to-end supply chain in real-time (see Ivanov, 2019 for a review of digital twins). Furthermore, it is possible to embed optimization algorithms in a digital twin. Such prescriptive analytics provide the means to identify the most suitable risk mitigation strategies automatically. We illustrate the application of digital twins and prescriptive analytics in a case study in the following section.

3 Analyzing risk and resilience in pharmaceutical supply chains: A case study

In this section, we demonstrate the application of digital twins and prescriptive analytics to a pharma supply chain. Our analysis utilizes the "E2E Risk Guru", a software for analyzing risks and optimizing resilience in supply chains (www.building-resilience.de). It is inspired by methods and metrics developed at the Massachusetts Institute of Technology (MIT), which were implemented at Ford, Cisco, and the United Nations, among others (Gao et al., 2019). The E2E Risk Guru uses the "OPTANO" platform - a technology and cloud platform for prescriptive analytics and artificial intelligence.

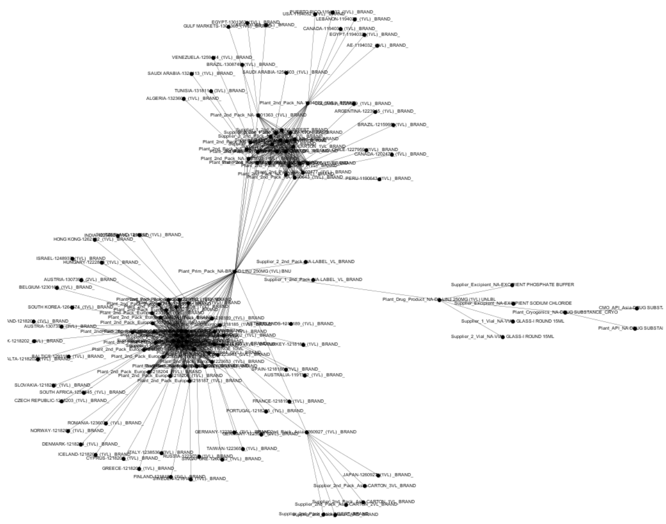

Figure 3: *Graph representation of the digital twin (source: author)*

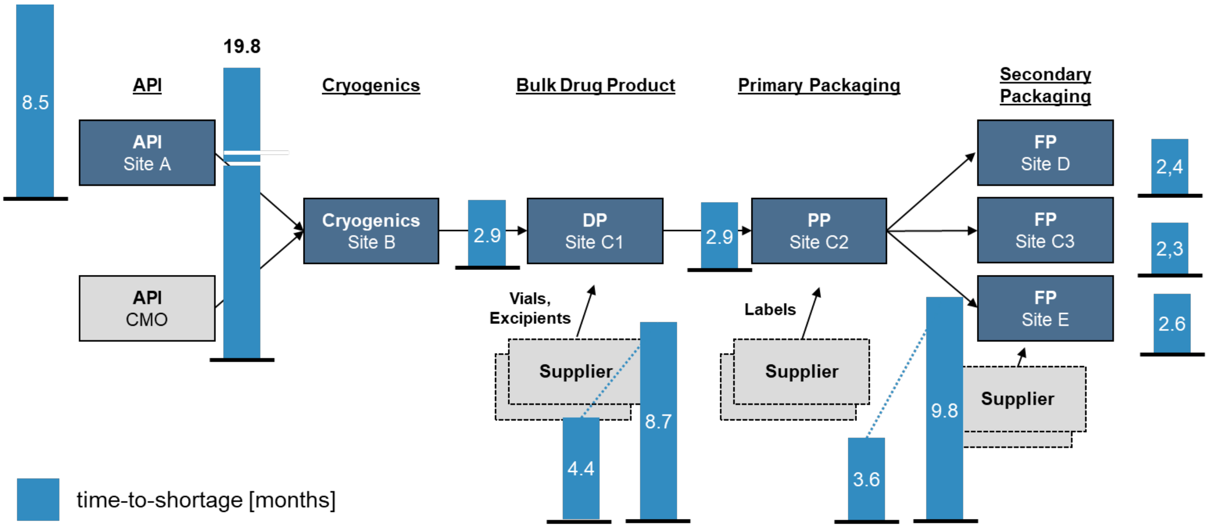

Figure 4: *Time-to-Shortage values for supply chain (source: author)*

3.1 Creating supply chain transparency with digital twins

We model a global end-to-end supply chain, including all supply links between sites, CMOs, and key suppliers (excipients, primary and secondary packaging) for 44 final SKUs sold in more than 50 markets (see Figure 2).

To avoid the pitfalls mentioned above of traditional risk analysis – the need for highly subjective judgment (the type and the probability of risk) – the modeling approach primarily relies on data commonly available in Enterprise-Resource-Planning (ERP) and supply chain systems. Based on the supply chain data, a digital twin is created that represents the entire supply chain network with its interdependencies, volumes, and capacities. The graph representation of the digital twin with all modeled entities is shown in Figure 3.

3.2 Identifying risks and vulnerabilities

Digital twins allow for end-to-end supply chain visibility to improve resilience and test recovery plans (Ivanov et al., 2019). Without the further specification of probabilities or risk scenarios, the digital twin can determine the risk exposure of each site (plant, contract manufacturing organization (CMO) or supplier) by calculating the Time-to-Shortage metric. This metric shows the maximum duration that the supply chain can match supply with demand after a node disruption. If this value is small for a specific node in the supply chain or less than the expected time until the node is restored to full functionality after a disruption, the node is at risk. Otherwise, the node is sufficiently protected.

Figure 4 shows the Time-to-Shortage of our analyzed supply chain in months. The most vulnerable sites in the network are the secondary packaging plants close to the market and the dedicated sites for drug production and primary packaging. Furthermore, the analysis identified some of the suppliers as vulnerable, too. This example confirms anecdotal evidence emerging during the Covid-19 pandemic that disturbed supplies of excipients and packaging material can become a serious threat to supply chains. By using these values, it is possible to segment the supply chain based on risk exposure.

3.3 Quantifying the impact of disruptions

A digital twin can also evaluate the financial and optional impact of a disruption. In our digital twin, a company can choose different measures of performance impact: lost units of production, service-level, revenue, or profit margin, for instance. In Figure 5, we show the results of a stress test for the overall supply chain. For each site, a four-month disruption is considered (duration of disruption and ramp-up time afterward). A specification of the cause is not required. We evaluate the impact of disruptions based on average service-levels and sales at risk. In line with the results from the Time-to-Shortage analysis shown in Figure 4, all sites are negatively affected that exhibit a time-to-shortage value smaller than four months.

The highest impact on revenues (sales at risk due to interrupted supply) results from disruptions at the dedicated sites for drug production and primary packaging and the secondary packaging site in North America that serves a significant share of market

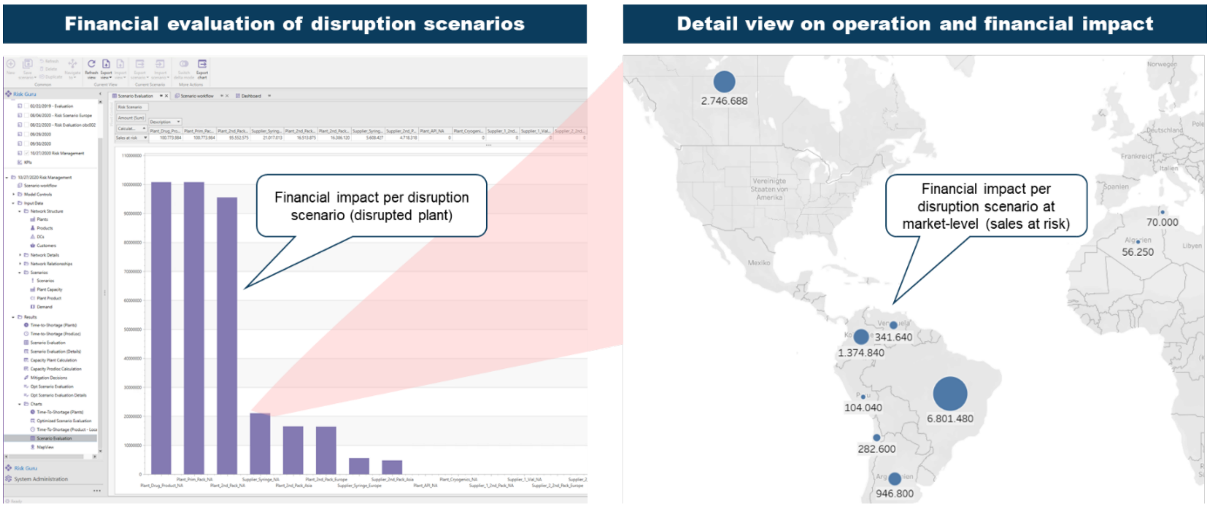

Figure 5: *Financial and operational evaluation of supply chain disruptions. Left part: sales at risk per disruption scenario (4-month disruption per site). Right part: Detail evaluation of disrupted supplier (source: author, www.building-resilience.de)*

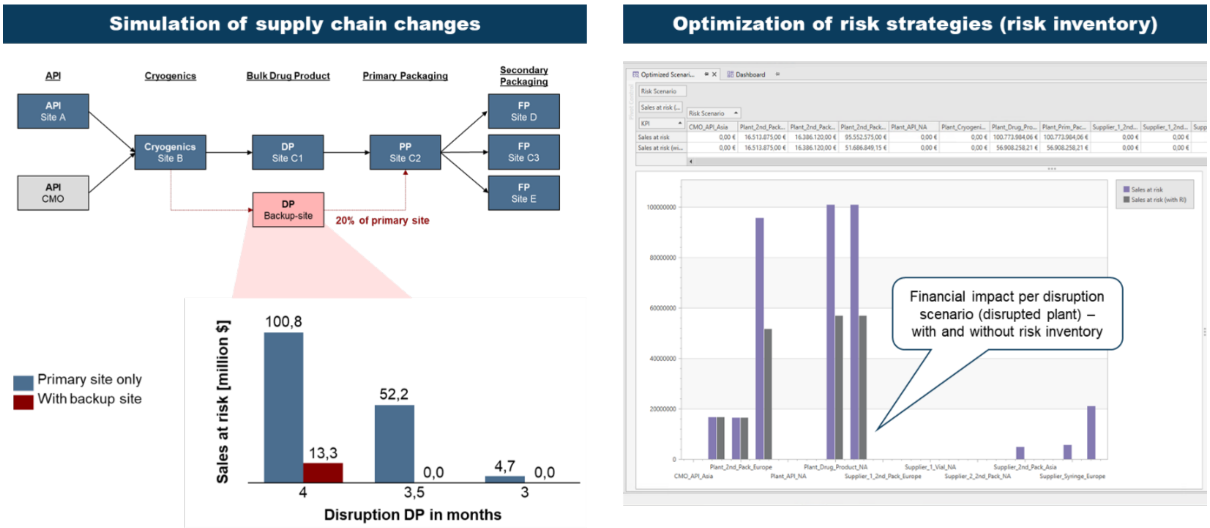

Figure 6: *Simulation and optimization of structural changes and risk mitigation strategies (financial impact measured in sales at risk). Left part: Simulation of installing reserve capacity at drug production-level. Right part: Comparing risk scenarios without and without 10% additional risk inventory, measured in cost of goods sold (source: author, www.building-resilience.de)*

sales. The digital twin allows drill-down into details. For example, it is possible to assess how an upstream disruption (e.g., disrupted API supply) affects the availability of finished products (drugs) at the market and SKU-level (see right part of Figure 5). Such an analysis is also beneficial in the recovery-phase after a disruption. It helps the supply chain organization to quickly create transparency on how patients might be affected through the disruption of operations.

3.4 Simulating and optimizing risk strategies

Once the supply chain is modeled in a digital twin, it is possible to evaluate the risk-mitigation potential of alternate supply chain configurations. For example, the above analysis has shown that the dedicated drug production site is particularly prone to disruptions. We simulate the benefit of introducing reserve capacity to the network (see left part of Figure 6). Based on our experience, installing reserve capacity (e.g., kept at a CMO) is frequently discussed for supply chains of high-value blockbuster drugs.

Setting risk inventory is a complex task in pharmaceutical supply chains (Eidam, 2020). We use an optimization algorithm to identify the right size and location of risk inventory across the supply chain. The algorithm considers multiple risk scenarios (disruption scenarios) simultaneously and can put emphasis on mitigating high-impact disruptions. We find that it is optimal to keep risk inventory close to the patient. Despite higher holding costs, risk inventory held downstream protects against failures of all upstream sites. Furthermore, risk inventory is built up to protect critical suppliers. Overall, risk inventory – if optimally positioned – provides effective means to reduce or even eliminate the vulnerability to disruptions (right part of Figure 6).

Summary

Risk management and proactively building resilience will be key priorities for the pharmaceutical supply chain in the coming years. In the wake of the disturbances caused by the Covid-19 pandemic, there is even a growing belief that governments should consider establishing a stress test for supply chains that provide critical goods and services (Tinglong et al., 2020; Simchi-Levi and Simchi-Levi, 2020). To create more visibility into the end-to-end supply chain, companies can benefit from using digital twins. Such computerized models allow for more effectively analyzing a supply chain's risk exposure as well as systematically testing the benefit of structural changes. By additionally embedding prescriptive analytics into a digital twin, and automatic optimization of risk mitigation strategies is possible.

About the E2E Risk Guru

The E2E Risk Guru is available as a professional software solution. It employs linear and robust optimization to calculate time-to-shortage metrics, evaluate the financial and operational cost impact of risk scenarios, and simulate and optimize risk mitigation measures. Unlike a discrete-event simulation, the model does not require the specification of detailed business rules for the case of a disruption. The data model used to build the digital twin (model) uses standard ERP data fields as input. Further details can be found on www.building-resilience.de.

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