Scenario-based supply chain risk management to avoid drug shortages caused by external threats to the pharmaceutical supply chain

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Executive Summary

The aim of the pharmaceutical supply chain (PSC) is to provide sufficient drugs for the population. One of the threats to drug availability is the characteristic of the PSC itself: Being lean and highly complex, the PSC is increasingly vulnerable to any disturbances which lead to drug shortages. However, the special characteristics of the PSC are not appropriately integrated in the literature about supply chain risk management yet. Therefore, this paper mainly discusses the development of scenarios leading to a dysfunction of the PSC and focuses on the risk management of external threats to the PSC.

Keywords: Operations Risk Management and Resilience, Supply Chain Management

Drug shortages and the need for action

Supply chains are networks, which fulfill a business task more efficient than a single enterprise by concentrating on the core competences of every supply chain partner (see Chopra/Meindl, 2010). The aim of the pharmaceutical supply chain (PSC) is to provide sufficient drugs for the population. This purpose includes two main aspects: drug safety and drug service security.

Drug safety focuses on the quality, effectiveness and integrity of drugs. Therefore numerous national and international administrations supervise the approval of drugs and oblige pharmaceutical manufactures to implement several guidelines, e.g. “Good Manufacturing Practices” (GMP). However, the drug service security guaranteeing the availability of drugs everywhere and at every time gets more and more crucial.

The European Medicines Agency has set up an implementation plan in order to improve awareness of drug shortages in pharmaceutical enterprises and the general public (see European Medicines Agency, 2012).

In the United States the Drug Information Service at the University of Utah Hospitals and Clinics (UUHC) started in 1996 to systematically observe drug shortages and reported the information to the American Society of Health-System Pharmacists (ASHP) since 2001. Since that point in time there has been an overall number of 1.400 reported drug shortages in the U.S.

Descriptive analyses of the data provided by UUHC shows a rising frequency of shortages in the past years (see Figure 1) with an average duration of 256 days. In 2011 ten percent of all registered pharmaceutical ingredients were unavailable (see Le et al., 2011). This causes negative consequences both on patient care and health care costs, as reported by multiple empirical studies (see Griffith et al., 2012 or Kaakeh et al. 2011). The problem is not restricted to the U.S. In summer 2012 it reached Germany as well. First signs are shortages of the beta-blocker "*Metoprololsuccinat*" or various antibiotics.

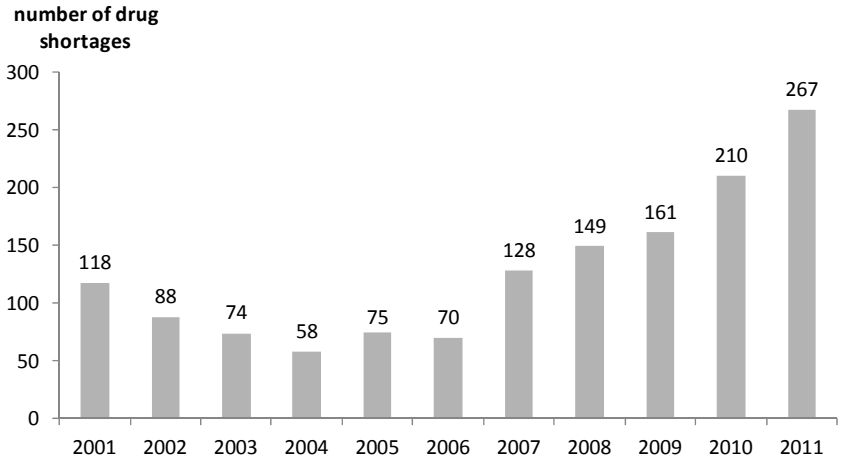

Figure 1: Number of shortages reported by ASHP per year

There are several reasons for drug shortages. As shown in Figure 2 highest importance have manufacturing problems followed by business decisions and the mismatch of supply and demand. Other reasons are the unavailability of raw material, regulatory problems or the occurrence of natural disasters.

The consequences of accidental events, as manufacturing or delivery problems of raw material are more crucial due to the characteristic of the PSC itself. In fact of rising customer claims regarding cost, quality and availability of products and an increasing competitive pressure the PSC as well as other Supply Chains has become lean and highly complex. Characteristics of these Supply Chains are optimized flow of goods, liquidity and information, high capacity utilization and minimized total lead times (see Ewers/Mohr, 2010 for the PSC or Blackhurst et al., 2005 or Christopher/Peck, 2004 general supply chains).

Signs of this development are globalization of the supply chain, reduction of suppliers or minimization of working capital. Also outsourcing of business processes

and centralization of production and distribution facilities are obtainable (see Jüttner et al., 2005).

Being lean and highly complex, the time- and functional dependencies between activities of supply chain partners and the vulnerability of the whole supply chain is increasing. The more vulnerable a supply chain is, the higher the probability of disturbances and the worse their negative consequences are (see Svensson, 2002). In view of these conditions failures of business activities of supply chain partners may have higher impacts of the whole supply chain. Risks of single companies may influence the supply chain and evolve to supply chain risks (see Kersten et al., 2007). Therefore supply chain risk management (SCRM) has become a critical success factor (see Pfohl et al., 2010). As for risk management in general this includes the identification, assessment, treatment and monitoring of risks.

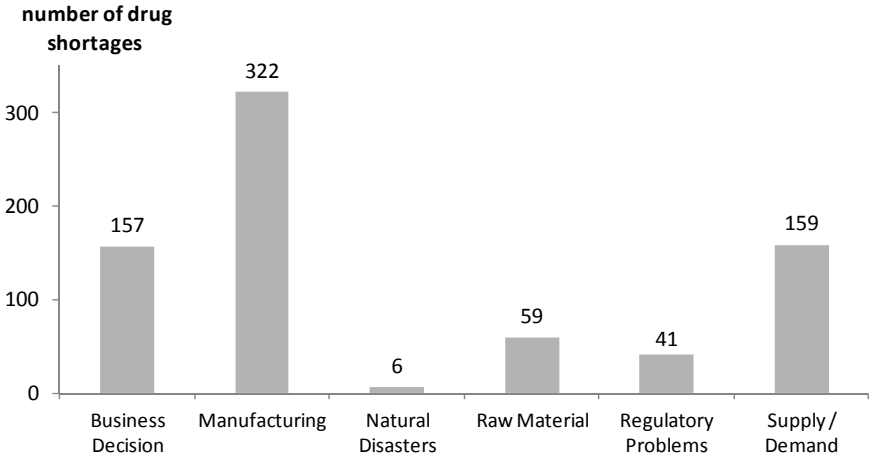

Figure 2: Reasons for drug Shortages reported by ASHP

Despite frequent research on SCRM, the special characteristics of the PSC are not appropriately reflected in the literature yet. This is unsatisfactory since the PSC significantly contributes to public health (see Breen, 2008).

The research project "SafeMed - System Design for Efficient Protection of Pharmaceutical Supply Chain" attempts to improve the supply chain risk management focusing especially on drug service security. In particular the project will address the following research questions:

- Which external threats cause a dysfunction of the PSC concerning drug service security?
- Which operational, institutional and systemic measures can prevent a dysfunction or provide guidance in case of occurred disturbances?
- How can the risks and the potential measures be evaluated from a managerial and economical perspective?

SafeMed places emphasis on the development of solutions supporting actors of the PSC and the respective authorities in avoiding or managing drug shortages caused by external threats in particular. Dysfunctions of the PSC having their origin in the highly regulated processes of manufacturing and distribution itself are not being considered.

This paper is addressing the first of the mentioned research questions. Therefore the following description of the methodological approach in chapter 2 will be limited to the identification of scenarios describing external threats to which the PSC can be exposed. The scenarios are described in chapter 3. A short outlook with respect to further steps in the research project is given at the end of this paper (chapter 4).

2. The methodological approach for development of external threat scenarios

For the development of external threat scenarios several methodological approaches were combined (see Figure 3):

1. An analysis of the PSC, which identifies the main impact factors on its supply function,
2. a Cross-Impact Balance Analysis (CIB) in order to construct consistent images of the network behavior,
3. the identification of trends challenging the PSC, the pharmaceutical industry and health care in general,
4. the Group-Delphi Method for obtaining expert judgments on the Probability of Failure (PoF) and the Consequence of Failure (CoF) with respect to different external threats. The judges are based on the identified main impact factors.

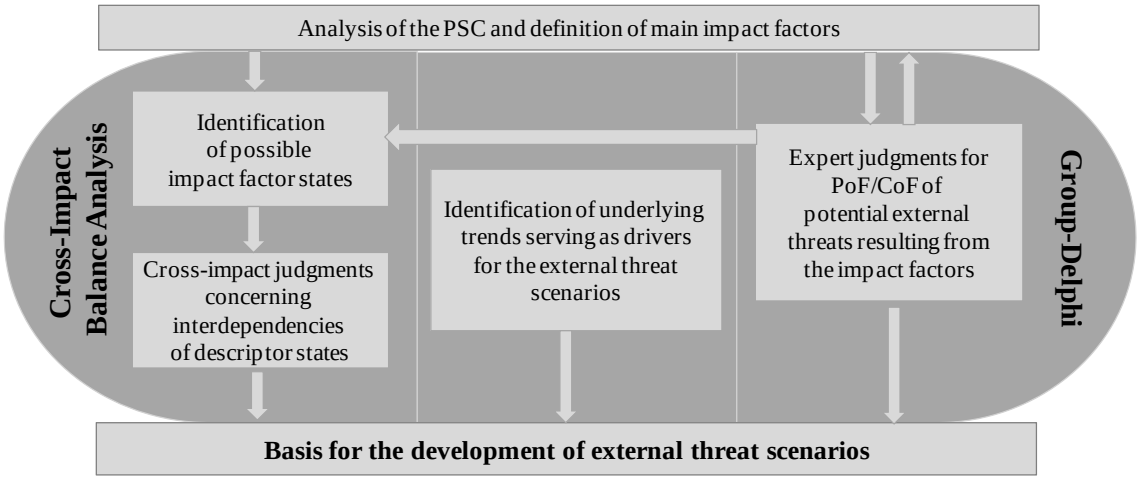

Figure 3: Methodological approach for scenario development applied in SafeMed

2.1 Analysis of the PSC and definition of main impact factors

In order to capture the complexity and specifics of the PSC, a first step of the methodological approach was a morphological analysis (see Zwicky, 1969) of the complete system. This includes processes and actors involved up-stream and down-stream the PSC. By means of this technique, which was initially designed for problem-solving, main relevant impact factors ("descriptors") have been identified, which are to be considered as crucial for the drug service security of the PSC. These descriptors can be clustered in three groups (Table 1): (1) internal descriptors, (2) external descriptors and (3) contextual descriptors. Adding a core descriptor "*drug service security*" with the states "impaired" and "unimpaired" allows filtering for threat scenarios fulfilling the core descriptor´s state "drug service security impaired".

2.2 Cross-Impact Balance Analysis

According to Weimer-Jehle (2009),

- the descriptors have to find themselves always in one of the identified states
- the identified states have present all possible alternative states of the descriptor
- the identified states have to be mutually exclusive.

The above requirements for each descriptor state are to be respected for the applied Cross-Impact Balance Analysis (CIB), using the descriptors and their states as input. The CIB offers a structured procedure for the derivation of plausible future developments of rough scenarios. It is based on qualitative judgments concerning cross-impact relations between fundamental system elements: the defined descriptors (see Weimer-Jehle, 2009). These relations are described by a network of influences.

For each descriptor state expert judgments have been obtained, providing information on what the impact on state x of descriptor X would be if descriptor Y were in state y. The experts are specifying only direct influences during the subsequent analysis. The result of this step is a cross-impact matrix.

Table 1: PSC Descriptors identified by SafeMed

Internal Descriptors	Basic supply of resources (energy, IT, etc.)
	Personnel / Staff
	Active pharmaceutical ingredients and auxiliary supplies for production of drugs
	Production of drugs
	Transport of active pharmaceutical ingredients and auxiliary supplies
	Storage of drugs and active pharmaceutical ingredients
	Medical dispensing (Point of care / Point of Sale)
External Descriptors	Regulatory framework
	Economic framework
	(national / international) Political framework
	Nature-/weather-related impacts (local/global)
	Demand for drugs
Contextual Descriptors	Health expenditures
	Faith in the supply function of the PSC
Supply Function (core descriptor)	Drug service Security impaired or unimpaired

The developed matrix is used for a systematical scan of all possible scenarios. This is done by calculating the impact balances for each scenario, which leads to a restriction of the scope of possibilities and to the selection of those scenarios that are considered as consistent. Excluded are all scenarios containing contradicting cross-impact judgments.

Using the CIB method, 17 rough scenarios have been identified and used as input for further refinement of the final external threat scenarios.

2.3 Underlying trends within the PSC

The identification of underlying trends within the PSC, the pharmaceutical industry and health care in general served as further input for the development of external threat scenarios. The trends have been derived from literature review and expert interviews and were consolidated by interdisciplinary working groups, consisting of experts in risk management, natural science, social science and medicine. The trends are to be considered as the driving forces providing explanation and justification for the selected rough scenarios. For that purpose, the identified trends were assigned to the respective rough scenarios based on their specific set of descriptor states. The underlying trends identified in SafeMed are shown in Table 2.

Table 2: Underlying trends within the PSC, the pharmaceutical industry and health care in general

T1	Globalization of the supply chain - exposed to international political and economic risks.
T2	Increase in chronic (persistent) drug therapy - exposing larger groups of patients to shortages on patented drugs from exclusive providers.
T3	Production of specific drugs (especially for rarer indications) in discontinuous cycles - possibly causing supply relevant production losses at relatively short failure of operational infrastructure and resource.
T4	Objective increase in major weather events - endangering regional / national parts of the infrastructure (e.g. roads).
T5	Rapid spread of infectious epidemics, inter alia by intense international and regional mobility of the population.
T6	Rapid and systematic manipulation of public opinion through media reports.
T7	Budget crises of public budgets can unexpectedly lead to government intervention in the business processes along the PSC.
T8	Increasing risk of getting into the focus of international terrorist activities.
T9	Integration/Interdependence of international finance - particularly vulnerable to political and economic risks.
T10	Increasing public debt in European countries with cash loss - can cause lack of medical supplies from manufacturers.
T11	An aging population with increasing health costs and declining revenues.
T12	Regulatory requirements increasing financial risks for the research-based pharmaceutical industry by facing always shorter maturities of patents on the other hand.

2.4 Group Delphi Method for estimating PoF and CoF

Another input was the result of a group-delphi workshop. Experts estimated probabilities of occurrence and consequences of occurrence for each of the descriptors potentially leading to a dysfunction of the PSC. The group-delphi method was applied due to the lack of available statistical data (see Webler et al., 1991).

The Group Delphi is a discursive method designed for developing policy guidelines and has already been used in practice (see Schulz/Renn, 2009). With this approach, the lack of contextual reasoning for differing judgments, which is a problem of the classical Delphi approach, can be eliminated by group discussions in, e.g., face-to-face workshops. Consequently, the anonymity of the classical Delphi approach (see Dalkey/Helmer, 1963) has to be given up, so interference from status or seniority during the discussions at the workshop has to be expected. This puts the role of the moderator at the workshop very much in focus: The moderator not only leads the discussion and

obtains experts´ judgments by consensus or consensus on dissent in the given time, the moderator also has to deal with social interferences by limiting their influence on the outcome of the discussion as much as possible.

The iterative procedure of the Group Delphi foresees eight steps (see Renn/Webler 1998), in which the participants discuss answers to a questionnaire in split-up group and plenary sessions until consensus or consensus about dissent has been achieved.

The result of the Group Delphi Workshop in SafeMed with participation of experts representing all actors of the PSC was a consens-based estimation on the Probability of Failure (PoF) and the Consequence of Failure (CoF) for each of the descriptors (see Table 1) in failure state. These estimations are reflected in “Risk Profiles” for each of the descriptor clusters (see the example for external descriptors/factors in Figure 4).

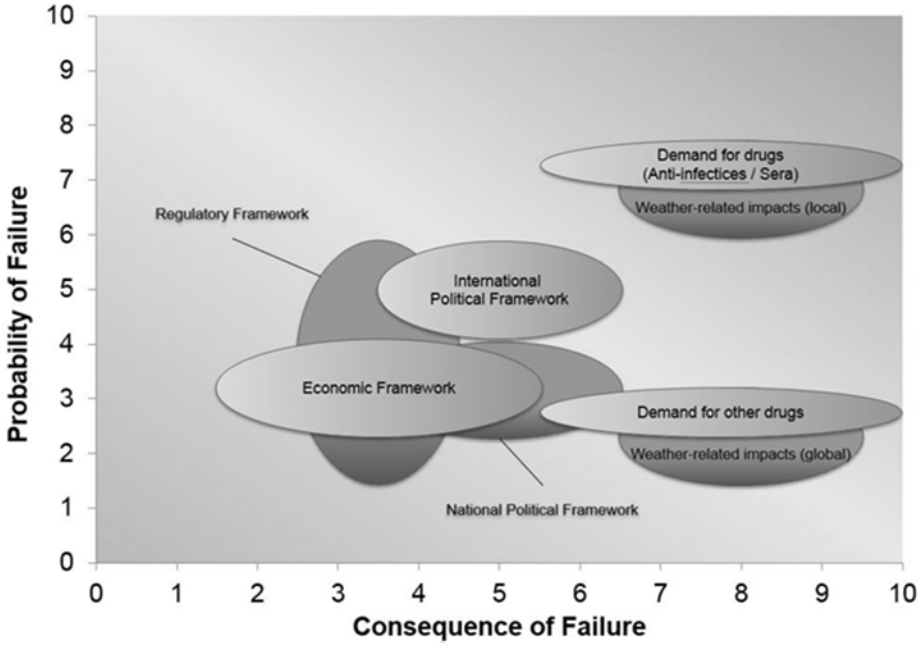

Figure 4: "Risk Profile" for external descriptors in failure state

The nine external threat scenarios developed in SafeMed are the result of the above described approach and will be presented in the following chapter.

3. The external threat scenarios in SafeMed

The first threat scenario captures production losses of medicines due to ad hoc changes of the legal and political framework. Those changes lead to shortages of active pharmaceutical ingredients and operational resources, which render the production of affected medicines impossible. This is even more problematic if active pharmaceutical ingredients are produced by a solely supplier or in one geographical region only. The expected damage for patients is manifested in suspended medical treatments of certain patient groups, which requires alternative treatments and, should the occasion arise, hospitalization.

The second threat scenario deals with production cuts of patented medicines due to natural disasters and severe weather events. If such locally destructive events hinder both the transport and the production (facilities) of patented medicines, the lacking drug

delivery to patients causes similar damages to patients than the first scenario. Here again, the exclusiveness of manufacturers increases the likelihood of occurrence and worsens the consequences.

If in addition to the second scenario a short-dated regional strike of pharmacists occurs due to governmental regulation of prices for prescription drugs the drug availability is hampered. The same applies if a drop out of single pharmacies in regions with low density of pharmacies takes places, as the third scenario describes.

The fourth threat scenario adds additional hazards to the second scenario: a sharp increase in the demand of vaccines and drugs to treat infections encounters the lack or shortage of active pharmaceutical ingredients that are offered by sole-source suppliers. An Epidemic might cause this increased demand. Although the according drug shortage might be geographically restricted to certain regions, the consequences concern the whole population in this scenario, namely a rapid spreading of epidemics.

This includes the staff of sole-source suppliers of raw or bulk materials. Staffing shortage due to an epidemic hampers the production, which becomes problematic in the fifth scenario, since reserves in the PSC cannot compensate the increased demand.

The sixth scenario takes account of the fact that underproduction of monopolistically supplied vaccines and drugs to treat infections can be due to geopolitical risks if the production depends on the import of a particular raw or bulk material only growing in exclusive geographic regions. Political upheaval or armed conflicts are some of the geopolitical risks disrupting the import of raw or bulk materials (see Fox et al., 2009).

In the seventh scenario the criminally motivated contamination of raw material used for the production of numerous generic drugs causes a major recall and thus unavailability of drugs. Comprehensive decontamination measures to be implemented by producers and suppliers can interrupt the production process for several weeks. Despite national regulations and guidelines targeting at the product safety, the PSC may not be protected entirely against criminal and terroristic actions.

There are countless factors influencing “business decisions” of enterprises operating in the PSC (see Fox et al., 2009), but the current Eurozone crisis demonstrates that instable macroeconomic framework conditions in particular may lead to drug shortages. The eighth scenario regards, for instance, countries being on the brink of insolvency and stopping payments of drugs, but also aggravated bank lending or turbulences in the financial markets in general. These macroeconomic conditions may deteriorate the economic situation of manufacturers and suppliers in the PSC, right up to their disappearance from the market.

The ninth scenario finally models disruptions in the supply of patented or exclusively supplied medicines due to lacking reimbursement in health care systems. Increasing public health expenditures often put pressure on policymakers to implement legal mechanisms which dilute the exclusive supply and control the pricing of costly patented drugs. If primary or sole manufacturers withdraw from the national market, drug shortages are bound to occur.

A consolidated view of all scenarios indicates that it is only the parallel occurrence of multiple disturbances that leads to fundamental threat scenarios suspending the functionality of the PSC. The relevance of the nine fundamental threat scenarios results from the lacking capability of actors inside and outside the PSC to compensate the dysfunction in the short and medium term. The variety of disturbances furthermore implies that there is no gold standard answering to all of them. Practical, preventive and

reactive measures have to refer to every stage of the PSC, but also to the PSC as a whole, including institutional, political or other actors. The methodological approach allows for deriving these measures from the threat scenarios.

4. Future Research

Appropriate actions for improving the overall resilience and robustness of the PSC against external threats are being suggested and used to develop a self-assessment questionnaire (safety-audit), which supports companies and authorities to check their preparedness against external threats. In a further step, an approach to assess risks and actions concerning their costs and benefits from a micro- and macroeconomic perspective is going to be developed. The results target at improving the firm risk management and the supply chain risk management of the PSC in Germany.

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