Hamburg University of Applied Sciences
Faculty of Life Sciences

# Changes in the Dynamics of the German pharmaceutical market due to the Corona pandemic:

# Supply bottlenecks, increased demand and the development of vaccines

**Master Thesis**
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**Submitted by**

Leon Stephan
Matriculation number: [redacted]

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1. Reviewer: Prof. Dr. York Francis Zöllner (HAW Hamburg)

2. Reviewer: Dr. Klaus-Jürgen Preuß (EPC HealthCare GmbH)

## Abstract

**Background:** The current Corona pandemic shaped the year 2020. In spring 2020 the dynamic development of infections led to national and international changes worldwide. So-called ‘lockdowns’ were the consequence in several countries containing the virus. This has had considerable implications for the international economy. International global supply chains have been disrupted. In the field of pharmaceuticals there was concern about new supply bottlenecks. To enable the continued nationwide supply of pharmaceuticals in Germany, new regulations that facilitated dispensation of pharmaceuticals were introduced.

**Methods:** A secondary data analysis of the supply bottlenecks that have occurred from January to June 2020 of the database of the BfArM was performed in order to identify and characterize the shortages by using descriptive statistics. This was followed by an exploratory trend analysis to analyse the changes of the prescriptions of most affected pharmaceutical groups by supply bottlenecks from July 2019 to June 2020. To supplement the quantitative data, expert interviews were conducted, mainly to find out whether a supply bottleneck led to a supply shortage during the first peak or not. To examine the development of vaccines against COVID-19 referring literature was reviewed.

**Results:** Analysis part 1 and 2: In March and April 2020 an increased number of supply bottlenecks were reported. A relatively homogeneous picture from February to May 2020 can be seen in the analysis of medical prescriptions. In March compared to February more pharmaceuticals were prescribed. Prescriptions then recorded a large decrease until May 2020. Two main causes of the supply bottlenecks could be identified: ‘The interrupted or restricted production of API and their interrupted supply chain’ and ‘increased demand’. According to the experts an ‘overall’ supply shortage of pharmaceuticals did not occur in the population. Analysis part 3: Worldwide 260 COVID-19 vaccines are in development. Four vaccines are already authorised in Germany.

**Discussion:** The results show that supply bottlenecks, which had been a problem for some time, were exacerbated by the Corona pandemic. Results also show that there is a necessity for action in order to cope better with future pandemics in the area of safe and nationwide supply of pharmaceuticals. With the ‘Pharmaceutical Strategy for Europe’, the EU has already initiated a goal to concretely counteract supply bottlenecks. The relocation of production of supply relevant active pharmaceutical ingredients and finished pharmaceuticals should be considered to be able to act more flexibly in future pandemics.

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## List of abbreviations

| | |
|---|---|
| ABDA | Bundesvereinigung Deutscher Apothekerverbände e. V. |
| AkdÄ | Drug Commission of the German Medical Association |
| AMG | German pharmaceutical law |
| AMK | Drug Commission of German Pharmacists |
| AMNOG | Law on the reorganisation of the pharmaceutical market |
| AMVSG | Pharmaceutical supply strengthening law |
| API | Active pharmaceutical ingredient |
| ApoG | Pharmacy law |
| ATC | Anatomical therapeutic chemical |
| AVWG | Pharmaceutical supply economic efficiency law |
| BAuA | Federal Institute for Occupational Safety and Health |
| BfArM | Federal Institute for Drugs and Medical Devices |
| BMBF | Federal Ministry of Education and Research |
| BMG | Federal Ministry of Health |
| BPI | Federal Association of the Pharmaceutical Industry |
| CEP | Certificates of Suitability |
| CEPI | Coalition for Epidemic Preparedness Innovations |
| CHMP | Committee for Medicinal Products for Human Use |
| COVAX | Covid-19 Vaccines Global Access |
| EDQM | European Directorate for the Quality of Medicines |
| EMA | European Medicines Agency |
| EU | European Union |
| GKV-FKG | Law for fair competition between health insurance funds in the statutory health insurance |
| GKV-WSG | Law to strengthen competition in the statutory health |

| | |
|---|---|
| | insurance system |
| GSAV | Law for more safety in the supply of pharmaceuticals |
| HO.P | Hospital pharmacist |
| HS.P | High street pharmacist |
| IfSG | Infection Protection Law |
| MedBVSV | Medical needs Health Care Insurance Regulation |
| MERS-CoV | Middle East Respiratory Syndrome coronavirus |
| NVI-KT | Statutory Health Insurance billing data |
| OTC | Over-the-Counter |
| PZN | Central pharmaceutical number |
| Rx | Prescription-only |
| SARS-CoV | Severe Acute Respiratory Syndrome Coronavirus |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome Coronavirus 2 |
| SGB V | Social security code V |
| SHI | Statutory health insurance |
| STIKO | Ständige Impfkommission |
| WHO | World Health Organization |
| W1 | Wholesaler 1 |
| W2 | Wholesaler 2 |

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# 1 Introduction

The year 2020 is marked by the current Corona pandemic which has led to national and international changes worldwide. In several countries, contact restrictions up to so-called ‘lockdowns’ were imposed at the beginning of the Corona pandemic in spring 2020. This was a reaction to the dynamic development of the increasing number of cases infected with Severe Acute Respiratory Syndrome Coronavirus type 2 (SARS-CoV-2) in order to contain the virus and to protect public health (1–3). Due to these lockdowns and border closures the Corona pandemic has had considerable implications for the international economy and division of labour. International global supply chains have been disrupted, affecting all sectors of industry (4).

Regarding to the pharmaceutical market, Health Minister Jens Spahn already warned on 13 February 2020 of possible new supply bottlenecks of pharmaceuticals, because of failure of production in China for relevant active pharmaceutical ingredients (API) (5).

Pharmaceuticals are essential for high quality health care (6) and represent the third largest expenditure share of the statutory health insurance (SHI) in Germany (7). Because of this public health relevance of pharmaceuticals, this research focuses on the dynamic changes of the German pharmaceutical market at the time of the first peak of the Corona pandemic in spring 2020. The focus concentrates on the changes in the German Rx-pharmaceutical (prescription-only pharmaceuticals) market of finished products. Especially, the supply bottlenecks that occurred during the Corona pandemic, are examined and analysed in more detail. On the other hand, this master’s thesis aims not only to analyse the supply bottlenecks of existing pharmaceuticals caused by the Corona pandemic, but also focuses on the development of new pharmaceuticals, namely the development of COVID-19 vaccines, to combat the Corona pandemic.

In Chapter 2, the Coronavirus is explained in more detail and the dynamic global and national developments that have occurred due to the Corona pandemic are shown. In Chapter 3, the German pharmaceutical market is first explained in more detail to provide an understanding of the regulatory environment and ongoing new regulations in the German pharmaceutical market. It also explains what exactly supply bottlenecks are. An important part of this chapter is the presentation of regulatory changes in the German pharmaceutical market that have occurred due to COVID-19 to be able to

continue to guarantee nationwide coverage with pharmaceuticals.

After the presentation of the background information, Chapter 4 explains the objectives and research questions of this master's thesis in more detail. This is followed by a description of the methodology in Chapter 5, which is divided into three parts. Firstly, an exploratory data analysis is carried out, followed by expert interviews to supplement the quantitative analysis with reports on experiences by experts. The third part relates to the analysis of the development of COVID-19 vaccines. Chapters 6 to 8 present the results of these three analyses. Subsequently, in Chapter 9 these results are discussed and recommendations for actions are given to be able to better cope with future pandemics.

# 2 COVID-19

The novel coronavirus, SARS-CoV-2, a beta-coronavirus first appeared in the Chinese city of Wuhan in the Province Hubei at the end of December 2019. On 7 January 2020, SARS-CoV-2 was identified as the cause of the lung disease COVID-19 (8,9).

Coronaviruses are enveloped RNA viruses and widespread among birds and mammals, including humans. Like SARS-CoV (Severe acute respiratory syndrome coronavirus) and MERS-CoV (Middle East Respiratory Syndrome coronavirus), SARS-CoV-2 belongs to the Coronaviridae family. Due to their ability for homologous recombination, coronaviruses can relatively easily extend their host spectrum and cross the species barrier (9–11). SARS-CoV-2 uses the transmembrane enzyme ACE-2 as a receptor to enter host cells of humans (12).

The novel coronavirus SARS-CoV-2 spread rapidly internationally. On 11 March 2020, the virus was declared as a worldwide pandemic according to the World Health Organization (WHO) (13). SARS-CoV-2 appears to spread more efficiently than influenza. So far, the main transmission route has been the droplet infection spreading easily from person to person. People produce respiratory droplets while breathing, speaking, sneezing, and coughing. These droplets can differ in size, some of them are even visible. Consequently people, who are physically near to another person infected with SARS-CoV-2 or have direct contact with that person, are at greatest risk of infection

(14).

Another way of transmission is the airborne transmission (14). Larger respiratory particles sink to the ground, while aerosols can also float in the air for long periods of time and spread in closed indoor rooms. Whether and how quickly the droplets and aerosols sink or remain suspended in the air, depends not only on the size of the particles but also on several other factors, including humidity and temperature (15). One study detected, by experimentally producing aerosols enriched with SARS-CoV-2, viruses capable of replication in aerosol after three hours (16). Some studies also show temperature and UV resistance in SARS-CoV and SARS-CoV-2 to a certain extent (17–21).

A less common way of transmission seems to be the indirect contact (contact with a contaminated surface) (14,16). However, transmission through contaminated surfaces cannot be excluded, as replicable SARS-CoV-2 can remain infectious for some time on surfaces. It was found especially on various surfaces in the vicinity of COVID-19 patients (16,22,23).

Coronaviruses mainly cause mild colds, but can sometimes cause severe pneumonia, especially for elderly and immunocompromised people (9–11). COVID-19 range from no symptoms to mild and moderate, with more systematic symptoms and or severe radiological abnormalities seen at older patients (24).

According to the statistics of the Robert Koch-Institute (status: 30 June 2020), clinical information is available for 86% of the cases transmitted in Germany. Frequently mentioned symptoms were cough (48%), fever (41%) and rhinorrhoea (21%). 3.0% developed pneumonia. Since the 17th calendar week, ageusia and anosmia can also be reported as a symptom of COVID-19 cases. At least 15% reported one of these two symptoms. 3.0% suffered from pneumonia. Ultimately, COVID-19 can lead to death (25).

Hospitalisation was reported in 17% of the COVID-19 cases transmitted (25). As you can see in table 1, according to Robert Koch-Institute the median base reproduction number R0 is around 3,3 to 3,8, the Index of manifestation is 55 to 85 percent, the median length of the incubation period is 5 to 6 days. The mean length of a hospital

stay in Germany amounts 8 to 10 days (26).

Table 1: Overview of the main parameters of COVID-19

Own representation according to Robert Koch-Institute (26)

| Parameters | Value |
|---|---|
| Main Transmission Route | Droplet infection / aerosols |
| Frequent symptoms | Cough, fever, rhinitis, loss of smell and taste, pneumonia |
| Risk groups | Especially elderly, previously ill persons |
| Base reproduction number R0 (median) | 3,3–3,8 |
| Incubation period (median) | 5-6 days |
| Index of manifestation | 55-85% |
| Duration of hospital stay (median) | 8-10 days |

## 2.1 International and national dynamic of infections

By the end of January 2020, a first COVID-19 Case in Germany was reported in Bavaria (21). On 22 February 2020, Italy reported its first death due to COVD-19 (2). Chapter 2 shows stability, different ways of transmission and the resistance of SARS-CoV-2. This led to a pandemic, i.e., COVID-19 cases worldwide (13).

Shown in Figure 1, case numbers also increased exponentially from March to April 2020 throughout Europe and the SARS-CoV-2 virus continued to spread internationally, with increasing case numbers in especially America, South-East Asia, and the Eastern Mediterranean.

On 30 June 2020, 10.185.374 cumulated cases were counted worldwide, with a proportion of 4.95% COVID-19 related to deaths (21).

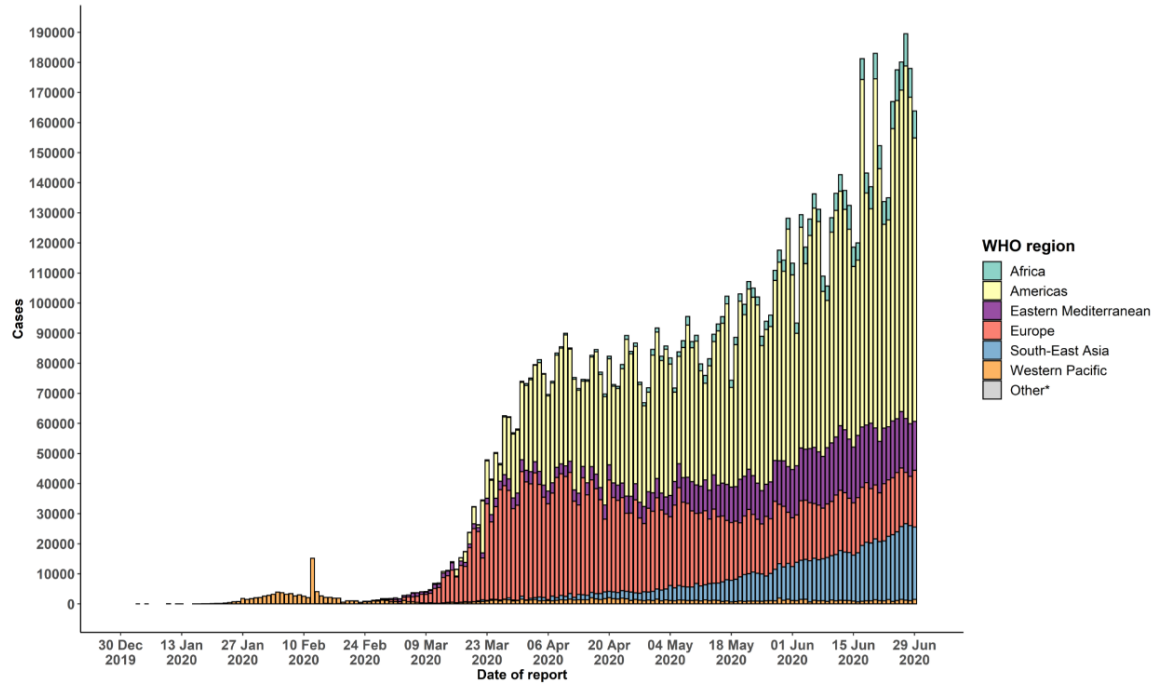


Figure 1: Number of confirmed COVID-19 cases, WHO region, December 30, 2019 through June 30, 2020

As shown in Figure 2, in Germany the incidence increased exponentially during March 2020 as well. At the same date (30 June 2020), Germany counted the 7th most confirmed cases in Europe. Furthermore, Germany counted 194.259 cumulated COVID-19 cases, 179.100 recovered. Of all reported cases until 30 June 2020, 52% of the cases were female and 48% male. Among all cases, for which data on gender were reported, under 10 years of age there was a proportion of 2.5%, children and teenagers aged 10 to 19 years 4.8%, in the age group 20 to 49 years 44%, in the ages 50 to 69 years 31%, in the age group 70 to 89 years 16% and persons aged 90 years and older 2.8%. The mean age of cases reported was 48 years (median age: 49 years) (19).

The proportion of deaths in confirmed cases of COVID-19 was 4.6% (in total: 8,973 deaths). The median age of COVID-19 related deaths was 82 years (19).

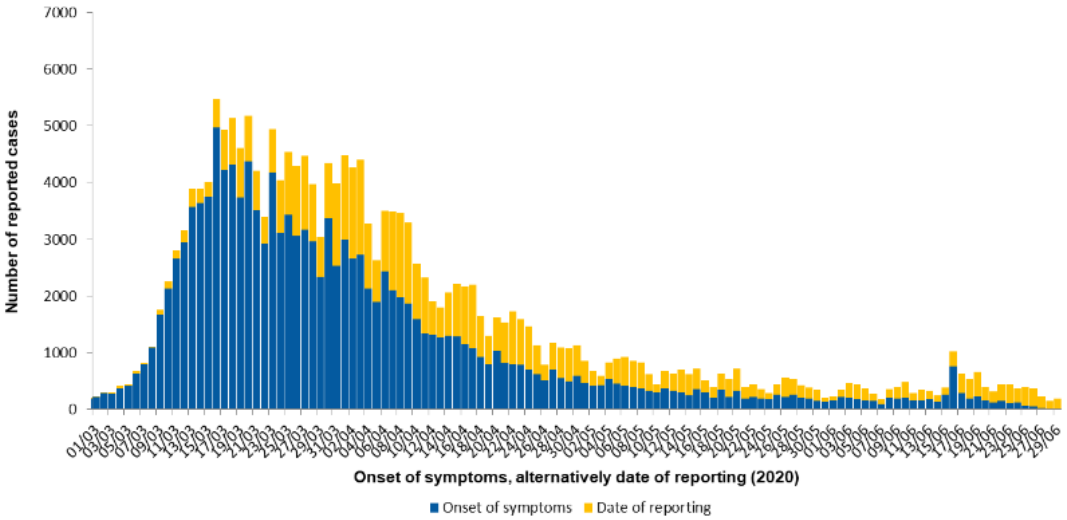


Figure 2: Number of COVID-19 cases in Germany electronically reported to the Robert Koch-Institute (19)

## 2.2 International and national restrictions and measures

During March 2020, the Coronavirus, coming from China, spread worldwide, leading to a worldwide ‘lockdown’. National borders were closed, and countries responded with contact restrictions and total ‘lockdowns’, the economy was shut down to contain the virus (1).

On 23 January 2020, the Chinese government took an unprecedented step to quarantine millions of people. All events for the new lunar year (starting on 25 January 2020) were cancelled. The Chinese government ordered travel restrictions for further cities in Hubei. The number of people affected by the quarantine measures on 25 January 2020 was already 56 million. (27).

According to the Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) of 16-24 February 2020, the strict quarantine measures in China were effective. According to the report, the pandemic in China peaked between 23 January and 2 February. Since then, the number of confirmed COVID-19 cases steadily decreased (28).

European states, with Italy as the initiator, began with restrictions and lockdowns in the middle of March including closing national borders (1).

On 22 March 2020, the federal and state governments agreed on exit and contact restrictions in Germany as well. Millions of Germans could no longer commute to work and had to work from home (3). Major events and public or private parties were forbidden. In public, only 2 persons from two households could meet with a minimum distance of 1,5 meters or with members of the own household (29). Visiting rules in nursing homes were also restricted to prevent the spread of the virus especially in risk groups (30). The retail trade (except grocery shops, pharmacies, and chemists), bars, restaurants, sports facilities, schools, universities, kindergartens and service companies in the field of personal care were closed. Moreover, national, and international travel and commuter traffic were largely suspended (29).

The infection protection law (Infektionsschutzgesetz - IfSG) came into force on 1 January 2001 and regulates which diseases in the event of suspicion, illness or death and which laboratory diagnostic evidence of pathogens must be reported (31). With the law on the protection of the population in case of an epidemic situation of national significance (Gesetz zum Schutz der Bevölkerung bei einer epidemischen Lage von nationaler Tragweite), which came into force on 28 March 2020 (32), the legislator took initial measures to ensure the functioning of the health care system in an epidemic situation affecting the whole of the Federal Republic of Germany and to mitigate the negative financial consequences associated with this special situation as well (33). On 23 May 2020, the second law for the protection of the population in case of an epidemic situation of national significance (Zweites Gesetz zum Schutz der Bevölkerung bei einer epidemischen Lage von nationaler Tragweite) came into force in order to ensure further measures in accordance with the epidemic situation (34). In particular, the IfSG was extended and specified.

Due to the development of the Corona pandemic, the German Bundestag identified an epidemic situation of national significance, which authorised the Federal Ministry of Health (Bundesministerium für Gesundheit - BMG) to take various measures by order without the approval of the Bundesrat. The BMG can thus, without the approval of the Bundesrat, take measures to reduce the risk of infection, i.e., to lay down regulations on contact tracing, to determine measures for the basic supply of pharmaceuticals and

aids, medical devices, personal protective equipment, and to take decisions to strengthen human resources in the health care system (32,34).

Also on 28 March 2020, the law on the compensation of COVID-19-related financial burdens of hospitals and other health care facilities (Gesetz zum Ausgleich COVID-19 bedingter finanzieller Belastungen der Krankenhäuser und weiterer Gesundheitseinrichtungen - COVID-19-Krankenhausentlastungsgesetz) came into force, in order to relieve hospitals of special financial burdens due to COVID-19 (35). In this context hospitals were supported in the procurement of ventilators, scheduled procedures were postponed, employees were specially trained for intensive care units and, to ensure an increased demand for personnel in the health sector, higher additional income was made possible in the pension scheme. Measures were taken to provide adequate protective equipment for specialist staff (30).

The overall aims of the German Federal Government were and still are to protect public health and maintain the efficiency of the health system, i.e., the infection process must be slowed down to provide the best possible care for severe COVID-19 cases. Furthermore, the health system should also be strengthened and has been strengthened to maintain health care and avoid excessive utilisation (30).

To ensure the secure and nationwide supply of pharmaceuticals in the pharmaceutical market new regulations were also adopted. These will be further explained in chapter 3.3.

## 2.3 International economy

The Corona pandemic has had considerable implications for the international economy and trade and division of labour. In particular, the supply of raw material originating abroad was no longer guaranteed. The absence of workers due to illness, quarantine, or the closure of production facilities due to the ‘lockdowns’ first in China in January and February, followed by other Asian and European countries, led to production losses (4). Also the production of important API of pharmaceuticals in China were stopped (5).

The pandemic and its restrictions and lockdowns to contain the spread of COVID-19 had a negative impact on the economy in general and on global value chains. In March 2020 China started to increase industrial production again. Nevertheless, such a decline in economic output and production of raw material in an important economic country like China necessarily has an impact on global value chains. Additionally, the subsequent lockdowns in the other countries worldwide had further implications for global value chains. This had effects in delays and interruption of the global value chain in several economic fields (4).

# 3 German pharmaceutical market

Pharmaceuticals are essential for high quality health care (6) and are therefore of high public health relevance, even in times of a pandemic, to provide basic health care for the entire population.

Moreover, the pharmaceutical sector is an important health care spending factor. Expenditure on pharmaceuticals is the third largest amount of expenditure of the SHI. In 2019 the expenditure for hospital treatment accounted for 80.34 billion euros, medical care for 41.08 billion euros, closely followed by pharmaceuticals with an expenditure of 41.04 billion euros (7).

## 3.1 Legal and regulatory framework

The German pharmaceutical law (Arzneimittelgesetz - AMG) in the version valid today applies to the corresponding law, which was passed in the Bundestag on 24 August 1976 with the approval of the Bundesrat and came into force on 01 January 1978. The AMG consists of 18 sections (36).

According to the AMG section 1 §2 “pharmaceuticals are API or preparations consisting of API which are intended for application in or on the human body and are intended to have properties for treating, alleviating or preventing human (or animals) disease or morbidity or applied to the human body or administered to a human being to restore, correct or modify physiological functions by exerting a pharmacological, immunological or metabolic action or to establish a medical diagnosis” (36).

The aim of the law according to §1 is “to ensure, in the interests of the proper supply of pharmaceutical products to humans and animals, safety in the marketing of pharmaceutical products, in particular the quality, efficacy and safety of pharmaceutical products in accordance with the following regulations” (36).

The AMG thus controls the regulatory provisions in the pharmaceutical market. This includes among others:

Requirements for pharmaceuticals (section 2), including special labelling, package leaflets and specialist information for pharmaceuticals. Clearly defined requirements for the manufacturing authorisation and manufacturer of pharmaceuticals are defined in chapter 3. It also includes the authorisation of pharmaceuticals (section 4), both national and international provisions of the European Union (EU). The protection of human beings during clinical trials (section 6) is also regulated, i.e., certain requirements must be met during clinical trials (36).

Furthermore, the dispensation of pharmaceuticals is regulated (section 7). In this section, §43 describes the pharmacy obligation. Pharmaceuticals, as described in §2, may only be dispensed through pharmacies (36). According to § 11a of the pharmacy law (Apothekengesetz - ApoG), which defines the more precise procedure for pharmacies, the mail order business of pharmaceuticals is also permitted under certain conditions with a special licence (37).

Similarly, § 48 AMG defines the obligation to prescribe pharmaceuticals which may only be dispensed in a pharmacy if a doctor prescribes them for the patient, because the use of such pharmaceuticals requires medical supervision (Rx-pharmaceuticals). These include pharmaceuticals which may endanger health if they are used without a doctor’s prescription even when used as intended. However, they also include pharmaceuticals which are frequently misused with a direct or indirect impact on health and pharmaceuticals containing API with effects not generally known in medical science to date (36). All other pharmaceuticals that are only available in pharmacies, but are not subject to prescription, are called Over-the-Counter pharmaceuticals (OTC-pharmaceuticals) (38). Not subject to prescription are pharmaceuticals which, due to an acceptable or known extent of possible side effects in medical science, may be used without medical supervision, but with pharmacist’s advice (39).

The AMG also regulates quality assurance and control (section 8), the monitoring, collection and evaluation of pharmaceutical risks (section 10), the supervision of companies producing pharmaceuticals (section 11), the import and export of pharmaceuticals (section 13), and liability for damage to pharmaceuticals (section 16) (36).

In recent years, the supply of pharmaceuticals has been the subject of numerous attempts to reform. These have focused on the objective of cost containment, but efforts have also been made to ensure high quality care, to improve safety of pharmaceuticals and to reduce supply bottlenecks/shortages (6).

### 3.1.1 Rebate contracts

With the pharmaceutical supply economic efficiency law (Arzneimittelversorgungs-Wirtschaftlichkeitsgesetz AVWG), which came into force on 1 May 2006, the health insurance funds can conclude a rebate contract with the pharmaceutical companies of pharmaceuticals, according to § 130a [8] rebate for pharmaceutical companies SGB V (Rabatt der pharmazeutischen Unternehmer) (40). By means of the rebate contracts, more economic efficiency in the prescription of pharmaceuticals should be ensured and the cost development of pharmaceuticals should be slowed down. By means of the law to strengthen competition in the statutory health insurance system (GKV-Wettbewerbsstärkungsgesetz - GKV-WSG), the rebate contracts have had a greater impact since 1 April 2007. According to these rebate contracts, pharmacies must observe the rebate contracts of a health insurance fund when exchanging pharmaceuticals with preparations containing the same API (41).

If a physician does not expressly exclude the exchange of pharmaceuticals, only packages of the rebate contract partners may be dispensed (42), which, according to § 130a [8] rebate for pharmaceutical companies SGB V concludes as follows: “The health insurance funds or their associations may agree rebates with pharmaceutical entrepreneurs for the pharmaceuticals dispensed at their expense. A volume-related graduation of the rebate, an annual sales volume with compensation for additional revenues or a reimbursement depending on measurable therapeutic success can be agreed. Contracts pursuant to the first sentence above for off-patent medicines must be agreed in such a way that the duty of the pharmaceutical entrepreneur to guarantee the

ability to supply begins at the earliest six months after the dispatch of the information pursuant to § 134 [1] of the law against restraints of competition (Gesetz gegen Wettbewerbsbeschränkungen) and at the earliest three months after the award of the contract" (43).

The AOK Baden-Württemberg was the first health insurance fund to make extensive use of rebate contracts and concluded contracts with 11 pharmaceutical companies for 43 API and combinations (44). Until now, all statutory health insurance funds negotiate with the pharmaceutical companies and conclude many rebate contracts. There are now more than 30.000 (status: September 2019: 30.400) rebate contracts existing, with overall 213 participating pharmaceutical companies (status: September 2019), specific to the statutory health insurance funds that stipulate which insured person can obtain which pharmaceutical product from which company. According to Bundesvereinigung Deutscher Apothekerverbände e. V. (ABDA) the SHI saved 4.9 billion euros in 2019 due to rebate contracts (45).

The statutory health insurance funds conclude the rebate contracts with the pharmaceutical companies in different ways. Pro Generika e. V. presents the common three different ways (46):

Open house model:
An unlimited number of pharmaceutical companies may provide care for all insured persons of a statutory health insurance fund. The companies can join the contract any time. The health insurance company selects the rebate itself, to enable to receive a high one. The advantage is that the supply of one API is distributed among several pharmaceutical companies.

1-partner-model:
In this exclusive model, only one pharmaceutical company may provide care for all insured persons of a statutory health insurance fund. The pharmaceutical company which assigns the highest rebate gets the rebate contract and therefore this company has a 'monopoly position'.

2-3-partner model:
This partner model is like the 1-partner model, but several companies may provide care

for all insured persons of a statutory health insurance fund. The model with the number of three partners is often chosen.

Criticism of the 1-partner model consists of the fact that the supply is outsourced to one contractual partner, i.e., if the only one contractual partner fails (e.g. loss of the production site), other companies often cannot manage the supply adequately and thus supply bottlenecks can arise in the entire pharmaceutical market. The diversity of suppliers is also weakened, and the other companies could become less interested in the market and may produce less of the API (46).

Despite the existing criticism of 1-partner contracts, the share of 1-partner contracts in the tendering models in 2019 (average values in 2019) amounts to 31.6%. The share of 2-3 partner contracts is 31.7% and the share of open house contracts is 36.7% high (46).

### 3.1.2 AMNOG

On 1 January 2011, the German law on the reorganisation of the pharmaceutical market (Arzneimittelmarktneuordnungsgesetz - AMNOG) came into force. The main aim of AMNOG is to contain the rapidly increasing expenditure on pharmaceuticals by the SHI. The law defines the way for fair competition and a stronger orientation towards the well-being of patients. AMNOG creates a balance between innovation and affordability of pharmaceuticals and the additional benefit of pharmaceuticals for patients determine the price of pharmaceuticals (47).

### 3.1.3 Jour Fixe and Advisory Board

In 2016, the German government decided that a regular ‘Jour Fixe’ specifically on the topic of supply bottlenecks and supply shortages (‘Jour Fixe’ zu Liefer- und Versorgungsengpässen’) should be held with the participation of federal authorities and organisations (overall: 14 institutions), for example institutions such as the Drug Commission of German Pharmacists (AMK), Drug Commission of the German Medical Association (AkdÄ), Federal Association of the Pharmaceutical Industry (BPI), Pro Generika e. V. and the Federal Institute for Drugs and Medical Devices (BfArM), in order

to monitor and evaluate the supply of pharmaceuticals. The pharmaceutical industry committed itself to contribute to an improvement in the supply situation by further optimising the processes and quality management. This also includes an early notification of the regulatory authorities about possible supply bottlenecks for supply-relevant API. On 22 July 2020 the meeting of the Advisory Board according to §52b [3b] AMG, due to the law for fair competition between health insurance funds in the statutory health insurance (Fairer-Kassenwettbewerb-Gesetz - GKV-FKG), the previous 'Jour Fixe' on supply bottlenecks and supply shortages are dissolved to the Advisory Board (48), which also consists of the above mentioned associations, organisations and authorities (overall: 19 institutions). The Advisory Board continuously monitors and evaluates the supply situation of the population with medicinal products. It is intended to support the higher federal authorities in assessing the relevance of a supply bottleneck, considering possible existing therapy alternatives, and finding recommendations for improving the general supply situations with pharmaceuticals (49).

### 3.1.4 AMVSG

On 13 May 2017, the pharmaceutical supply strengthening law (GKV-Arzneimittelversorgungsstärkungsgesetz - AMVSG) came into force.

The AMVSG created the basis for information about the availability of Rx-pharmaceuticals and the stockpiling of pharmaceuticals in hospitals. The AMG was amended in § 52b [3b] as follows: "Pharmaceutical companies are obliged to inform hospitals immediately, in the scope of their responsibility, if they become aware of supply bottlenecks of Rx-pharmaceuticals for inpatient care" (50). Additionally, "within the scope of their responsibility, this means in this context that pharmaceutical companies are obliged to inform their contractual partners in hospitals or hospital-supplying pharmacies with which they have supply contracts for the direct purchase of hospital preparations about supply bottlenecks. Immediately means without undue delay within 3 days after a supply bottleneck situation becomes known to the pharmaceutical company" (51).

§ 73 [3] of the AMG is extended according to hospitals which will be able to stockpile with special finished pharmaceuticals in accordance with § 73 (3) of the AMG within

certain limits in future (50,51).

§ 29 [1d] emphasised that the higher federal authority can demand all data in connection with the sales volume of the pharmaceutical from the manufacturer in particular for reasons of pharmaceutical safety and all data available in connection with the prescription volume (50,51).

### 3.1.5 GSAV

On 16 August 2019, the law for more safety in the supply of pharmaceuticals (Gesetz für mehr Sicherheit in der Arzneimittelversorgung - GSAV) came into force. The aim of this law is to improve the quality and safety of the supply of pharmaceuticals. Pharmacies and manufacturers should be more controlled, i.e., the Federal Government is to be given extended powers to ensure safety of pharmaceuticals. Information about the manufacturers of the API in pharmaceuticals will be made publicly available in the future (52,53).

The statutory health insurance funds will be obliged to consider the diversity of pharmaceutical companies in rebate contracts in order to counteract supply bottlenecks and supply shortage in the population (52,53).

### 3.1.6 GKV-FKG

On 01 April 2020, the law for fair competition between health insurance funds in the statutory health insurance (Fairer-Kassenwettbewerb-Gesetz - GKV-FKG) came into force, which became law by the Bundestag on 13 February 2020 (54). On 25 March 2019, the Federal Ministry of Health had already developed a draft bill for the GKV-FKG (55). The aim of the law is to promote fair competition between health insurance and to counteract supply bottlenecks. Regarding to supply bottlenecks, changes have been made as to reporting requirements, storage, labelling and rebate pharmaceuticals (56).

Pharmaceutical companies and wholesalers of pharmaceuticals will be obliged to report BfArM on supply relevant pharmaceuticals, requested by the BfArM. Information on available stocks, production and sales volumes helps the BfArM to better assess the

supply situation for certain pharmaceuticals and to react adequately in certain emergency situations (§52b [3e], AMG) (56).

For supply critical and supply relevant pharmaceuticals, federal authorities can issue storage requirements for pharmaceutical companies and wholesalers (§52b [3d], AMG) (56).

In exceptional cases, supply relevant pharmaceuticals (for reasons of pharmaceuticals safety only supply relevant pharmaceuticals), which are labelled in another language, may also be used in the future (§10 [1a], §11 [1c], AMG) (56).

In case of rebate contracts between health insurance funds and pharmaceutical manufacturers, these particularly low-priced pharmaceuticals must be dispensed as already described in chapter 3.1.1. If these rebate pharmaceuticals are not available in the pharmacy, pharmacists will be immediately allowed to dispense a pharmaceutical containing the same API in future and substitute the rebate contract pharmaceuticals in accordance with § 129 [1 Set 2] SGB V. If the comparable pharmaceutical is more expensive than the fixed price, it is not the insured person who bears the additional costs but the statutory health insurance fund (§129 [4c], SGB V) (56).

## 3.2 Supply bottlenecks

Across the globe there are several different definitions of supply bottlenecks. In Germany, the BfArM defines a ‘supply bottleneck’ (BfArM uses the German word ‘Lieferengpass’) “as an interruption of delivery to the usual extent, probably exceeding 2 weeks, or a significant increase in demand which cannot be adequately met” (57).

Supply bottlenecks of pharmaceuticals can have hugely different causes. Global supply chains with a concentration on a few manufacturing sites for pharmaceuticals and API can be a reason for supply bottlenecks. Also export stops for certain API imposed by a government, quality defects and contamination in manufacturing, delays in production and delivery of raw materials, increased market demand, decisions by manufacturers such as stopping production or withdrawing pharmaceuticals from the market for various reasons and negative effects due to parallel trade, could be other reasons for a supply bottleneck (58–60).

According to the BfArM a supply bottleneck does not always lead to a therapeutically relevant ‘supply shortage’ for patients in Germany (BfArM use the German word ‘Versorgungsengpass’). Alternative pharmaceuticals are often available, i.e., a supply bottleneck does not necessarily lead to a supply shortage. A supply shortage first occurs when there is no alternative or comparable preparation available which can be substituted (57,59).

The BfArM as well distinguishes between supply relevant and not supply relevant API. Based on the proposals of the medical societies and the WHO list of essential medicines, the BfArM established a ‘list of active substances which are essential for supply (excluding vaccines) (Liste der versorgungsrelevanten Wirkstoffe (ohne Impfstoffe))’ (61). Currently 535 API or combinations of API are classified by the BfArM as relevant for health care of the general population (62).

According to BfArM, it is a fundamental prerequisite to define an API as supply relevant, that the pharmaceuticals are subjects to prescription, i.e., they must be Rx-pharmaceuticals. On the other hand, the API needs to be relevant for the total population. The list is regularly reviewed in the ‘Jour Fixe’ on supply bottlenecks and supply shortage’ and adjusted when necessary, last updated on 30 June 2020 (61).

Germany has been facing an increasing number of supply bottlenecks for pharmaceuticals for several years, there have been acute problems since 2012. In 2015 there were 40 notification (including 18 notifications with supply relevant API) of supply bottlenecks, 81 notifications (including 29 notifications with supply relevant API) in 2016, 108 notifications (including 57 notifications with supply relevant API) in 2017, 268 notifications (including 139 notifications with supply relevant API) in 2018 and 216 notifications (including 127 notifications with supply relevant API) until October 2019 (status: 08 October 2020) (59). During the first peak phase of the Corona pandemic in spring 2020, Germany experienced increased supply bottlenecks for pharmaceuticals, especially in March, April, and May 2020 (58). This topic is further analysed and presented in chapter 6 Results of the exploratory data analysis.

Stella Kyriakides, European Commissioner for Health and Food Safety highlighted the importance of a supply bottleneck: „Shortages result in patients not receiving their treatments in a timely manner and they can lead to a worsening of symptoms and

negative outcomes. Shortages generate anxiety and significant emotional distress for patients and their families: delays in treatment of life-threatening diseases such as cancer can be particularly traumatic. Patients often then search for treatments from unreliable sources out of desperation" (Kyriakides is using the word 'shortage' for a supply bottleneck) (63). This statement underlines the importance of the effect on the population of ever-increasing supply bottlenecks.

## 3.3 Changes and regulations in the German pharmaceutical market due to COVID-19

Supply bottlenecks increased during the first peak of the Corona pandemic. Therefore it was necessary to adapt laws and regulations to counteract these supply bottlenecks and to continue to guarantee a nationwide supply of pharmaceuticals.

Already at the beginning of February 2020 the BfArM was concerned that the outbreak of the Corona virus could lead to new supply bottlenecks and shortages in Germany as well. As a result of the Corona virus outbreak and the lockdown measures, there were fears that interruptions in supply routes could lead to new supply bottlenecks. Following a search by the BfArM, it was found that an API manufacturer for 19 pharmaceuticals was registered in the city of Wuhan. 17 API were supply relevant. For Hubei province, a total of 136 pharmaceuticals with an API manufacturer in that province is listed, 48 of which are supply relevant in Germany (64). Germany's Health Minister Jens Spahn also warned on 13 February 2020 of possible new supply bottlenecks. Production stops in China for important API could lead to supply bottleneck and supply shortages in Europe (5). Furthermore, EU health ministers were calling on the EU Commission to develop measures within six months to counter any possible supply bottlenecks for pharmaceuticals (65). In chapter 6 Results of the exploratory data analysis and chapter 7 Results of the interviews, the supply bottlenecks in the first peak phase in spring 2020 will be analysed and presented in more detail.

On 4 March 2020, the Federal Institute for Occupational Safety and Health (Bundesanstalt für Arbeitsschutz und Arbeitsmedizin - BAuA) announced an exemption concerning the provision on the market and the use of biocidal products containing 2-propanol in disinfectants. As the Corona virus has posed a risk to public health,

disinfectants were in great demand in the first peak of the Corona pandemic and were hardly available in pharmacies. At that time, the infection rate was still at a low level, but disinfectants were already in short supply in Germany and demand was higher than supply. As a result, this derogation allowed pharmacists to produce and distribute hand disinfectants by themselves (65,66).

### 3.3.1 COVID-19 agreement on the framework agreement according to § 129 (2) SGB V

On 31 March 2020, the GKV-Spitzenverband and the Deutscher Apothekerverband e.V. (DAV) decided to reach an agreement on the already existing framework agreement on the supply of pharmaceuticals (Rahmenvertrag über die Arzneimittelversorgung according to §129 [2] SGB V). This agreement was adopted corresponding the COVID-19 pandemic, in which the rebate contracts (see chapter 3.1.1) were restricted nationwide. This agreement was valid until 30 April 2020 (67).

The agreement ensures the supply of the population with pharmaceuticals during the pandemic, with the aim of avoiding patient contact in pharmacies. It was agreed that if the pharmaceutical, which is not available via a rebate contract according to §11 of the framework agreement with the statutory health insurance fund and/or no low-priced finished pharmaceutical according to §12 of the framework agreement is available, pharmacies may dispense another pharmaceutical according to the substitution regulations of §9 of the framework agreement. This was previously not possible without penalties of the statutory health insurance fund. Similarly, pharmacies were free to select the size of the package in order to minimise patient contacts in pharmacies and thus contain the spread of the virus (67).

### 3.3.2 SARS-CoV-2 Pharmaceutical Supply Regulation

On 21 April 2020, a regulation on deviations of the provisions of the social security code (SGB V), the pharmacy law, the pharmacy operating regulations, the pharmaceutical price regulation, the narcotics law and the narcotics prescription regulation as a result of the SARS-CoV-2 epidemic (SARS-CoV-2 Arzneimittelversorgungsverordnung) came into force and expired on 30 September 2020. This regulation is based on the law on

the protection of the population in the event of an epidemic situation of national significance (68).

With the SARS-CoV-2 pharmaceutical supply regulation, the BMG is taking further measures established by law to ensure that patients continue to be supplied with supply relevant pharmaceuticals and medical devices during the corona pandemic. It regulates temporary payment for the courier service for pharmacies and, as in the described agreement in chapter 3.3.1, facilitated more substitution possibilities when dispensing pharmaceuticals. The aim is to ensure the care of the chronically ill, of patients in quarantine and domestic isolation. Moreover, the BMG will be given the opportunity to control the sale of products of medical need (69).

According to §1 [3] of this regulation, contrary to SGB V and the framework agreement on the supply of pharmaceuticals, if the prescribed pharmaceutical is not available, pharmacies may directly dispense pharmaceuticals containing the same API. If a pharmaceutical with the same API is not available, pharmacies may, after consultation with the prescribing doctor, dispense a pharmacologically and therapeutically comparable pharmaceutical product to the insured person (68). According to the agreement (chapter 3.3.1), pharmacists may, without consulting the doctor, deviate from the package size and number of packages if the prescribed total quantity is not exceeded. If necessary, partial quantities of a package may also be supplied. The strength of the API may also vary if there are no pharmaceutical concerns. The facilitated exchange of pharmaceuticals cannot be objected to by the statutory health insurance funds. (68). This is permitted in order to supply patients with the necessary pharmaceuticals without additional contacts with doctors, even in the event of supply bottlenecks (69).

According to §2 of this regulation, in order to be able to continue to ensure the supply of pharmaceuticals to the population, hospitals may, in individual cases, derogate from the provisions of the ApoG on the management of pharmacies and the dispensation of pharmaceuticals within the framework of statutory discharge management, if permitted by the responsible authorities (68).

Furthermore, the courier service of pharmacies is subsidised with a one-off subsidy of 250 euros per pharmacy to purchase protective equipment for the couriers. Each

delivery is remunerated at 5 Euro per delivery point (§4) (69).
Pharmacies may also supply narcotics to other pharmacies to ensure the distribution of narcotics more widely (§5) (68,69).

BMG and bodies notified by it can demand information from manufacturers and distributors of supply relevant products of medical needs about stocks, storage location, production, distribution, and prices. Likewise, manufacturers and distributors of supply relevant products of medical needs must ensure an adequate and continuous supply of the products and no additional prices may be charged (§7) (68,69).

### 3.3.3 Medical needs Health Care Insurance Regulation - MedBVSV

On 26 May 2020, the Regulation to Secure the Supply of the Population with Products of Medical Need in the Epidemic Caused by the Coronavirus SARS-CoV-2 (Medizinischer Bedarf Versorgungssicherstellungsverordnung - MedBVSV) came into force (70).

If a pharmaceutical is not authorised within the scope of the AMG, the manufacturer submits all documents containing information on quality, efficacy and safety of the pharmaceutical required for authorisation to the responsible higher federal authority. The Federal Ministry must include the evaluation of the decision on the procurement and marketing of the medicinal product. This will speed up the authorisation of important pharmaceuticals in the pandemic (§3 [2] MedBVSV). The higher federal authority may order in individual cases that, by the way of deviation of §10 and §11 of the AMG pharmaceuticals may be placed into the market without a label and package leaflet if necessary, to ensure the supply of pharmaceuticals (§4 [1] MedBVSV). Likewise, a pharmaceutical whose expiry date has expired or which has been manufactured in derogation from the regulation on the manufacture of pharmaceuticals and API (Arzneimittel- und Wirkstoffherstellungsverordnung - AMWHV) may be put into the market if necessary to ensure the supply of pharmaceuticals and if it has been ascertained that the quality, efficacy and safety of these pharmaceuticals are not substantially impaired (70).

### 3.3.4 OTC-market

In addition to the legal regulations, there have also been changes in purchasing behaviour of OTC-pharmaceuticals in the pharmaceutical market.

SEMPORA Consulting analysed the OTC market using the INSIGHT Health DatamedIQ database (71–73). A data week always starts on Wednesday of a calendar week until the following Tuesday. In the 9th to 12th data week (DW) in 2020 (26 February 2020 to 24 March 2020) the sales of mail order and public pharmacies increased significantly and recorded a 28% increase in sales compared to the same period of the previous year. Compared to the previous year, as you can see in table 2, antiseptics, and disinfectants (sales increase: 307%), preparations for the immune system and vitamin C (sales increase: 236%), vitamins A and D, etc. (sales increase: 85%), analgesics (sales increase: 73%), were highly affected by the increase in sales. After the federal government decided to restrict contacts on 22 March, the high street pharmacy recorded sales losses. The OTC-market then slowly returned to normal. The increase in sales of antiseptics and disinfectants remained at a high relative level in contrast to the previous year and returned to relatively normal from mid-May onwards. Influenza preparations and expectorants also recorded a 41% and 47% increase of sales in the 9th to 12th calendar week compared to the previous year, but then recorded a 72% drop in sales compared to the previous year due to the agreed contact restrictions (72).

Table 2: Increase sales in real pharmacy retail price in relation to the previous year in the OTC-market

Own representation according to SEMPORA Consulting (72)

| OTC-Category (ATC 3) | DW 9 - DW12 (26.02. -24.03.) | DW 13 - DW16 (25.03. -21.04.) | DW 17 - DW20 (22.04. -19.05.) | DW 21 - DW24 (20.05. -16.06.) |
|---|---|---|---|---|
| Antiseptics, and disinfectants | +307% | +85% | +98 | +55% |
| Immune system and vitamin C | +236% | +80% | +14% | -2% |
| Vitamins A and D, etc. | +85% | +27% | +14% | +17% |
| Analgesics | +73% | -18% | -22% | -17% |
| Expectorants, etc. | +47% | -33% | -60% | -63% |
| Influenza preparations | +41% | -50% | -71% | -72% |

### 3.3.5 Subsidization of vaccines

To overcome the COVID-19 pandemic, vaccine development is underway worldwide and, according to the WHO 78, candidate vaccines are in clinical evaluation. To advance vaccine development in Germany, the Federal Ministry of Education and Research (BMBF) launched a special programme for vaccine development. The Federal Government is funding three vaccine developers with a total of 750 million Euros to accelerate the research and development of urgently needed vaccines against SARS-CoV-2. The prime goals of the special programme for accelerating the development of vaccines against SARS-CoV-2 are to promote clinical trials, expand study capacities and increase production capacities for the vaccine candidates to be tested. The programme enables inclusion of special risk groups in Germany in clinical trials on a larger scale.

Three German vaccine developers whose projects are at an advanced stage are currently being funded:

- BioNTech with approximately 375 million euros
- CureVac with approximately 252 million euros
- IDT Biologika GmbH with approximately 114 million euros (74)

Chapter 8 Development of vaccines takes a closer look at the status of vaccine development.

# 4 Objectives and research questions

This master thesis aims to analyse the changes in the German Rx-pharmaceutical market of finished products due to the Corona pandemic. The development of vaccines against COVID-19 will be analysed as well.

The four following research questions will be answered in this thesis:

1) What kind of changes occurred in the German Rx-pharmaceutical market in the cause of the Corona pandemic from January 2020 until June 2020?
2) Which types of Rx-pharmaceuticals were affected by the supply bottlenecks and how did the prescription numbers develop over the months?
3) Did the supply bottlenecks that arose lead to a supply shortage for the population?
4) What is the status of the development of COVID-19 vaccines?

More specific, the objectives to answer the research questions are:

1. To investigate and analyse the supply bottlenecks from January 2020 until June 2020

2. To find out a possible supply shortage of the German population with Rx-pharmaceuticals

3. To identify difficulties and changes encountered in the German Rx-pharmaceutical market

4. To suggest recommendations for action to avoid future supply bottlenecks/shortages

5. To summarize the status of the development of vaccines against COVID-19

# 5 Methodology

To answer the research questions, the methods are divided into three parts.

1. A quantitative method, using secondary data analysis, is used to analyse the supply bottlenecks in Germany during the first peak phase of the Corona pandemic. Also, an exploratory prescription trend analysis of supply bottlenecks is done. The quantitative methods will help to answer research questions 1 and 2 and serve objective 1.

2. Expert interviews are used, as a qualitative method, to supplement the analysed quantitative data on supply bottlenecks in the context of the Corona pandemic with qualitative expert knowledge and practice-oriented reports. In this way, it was possible to explore which changes played a major role in the Corona pandemic and whether a supply bottleneck led to a supply shortage. Finally, the qualitative data obtained, will be used to develop recommendations for action for future pandemics. Subsequently, the qualitative method will also help to answer research question 1 and 3 and serves objectives 2, 3 and 4.

3. To examine the development of vaccines against COVID-19 and its significance for geopolitical power and to answer research question 4 and serve objective 5, the current literature is reviewed.

## 5.1 Exploratory data analysis

To analyse the supply bottlenecks in Germany during the first peak of the Corona pandemic reported supply bottlenecks from January to June 2020 were reviewed.

The database ‘supply bottlenecks of pharmaceuticals for human use in Germany (excluding vaccines)’ (‘Lieferengpässe für Humanarzneimittel in Deutschland (ohne Impfstoffe’)) of the BfArM is used to identify the occurring supply bottlenecks of Rx-pharmaceuticals in time of the Corona pandemic in the first half of the year 2020. BfArM receives supply bottleneck reports from the pharmaceutical companies, based on a voluntary obligation to report supply bottlenecks for supply relevant API declared in the Pharma Dialogue. Supply bottlenecks not relevant to supply can also be reported. According to the BfArM, a notification is required if the number of authorisation holders, the end-releasing manufacturers or manufacturers for a certain API falls below a critical limit. In addition, the voluntary obligation of manufacturers to report supply bottlenecks applies to all API for which a supply bottleneck already existed in the past. The BfArM publishes the data shortly after the pharmaceutical companies submitted a corresponding notification and updates the database continuously (57).

Pharmaceutical companies are requested to report a foreseeable supply bottleneck at least 6 months in advance and to notify BfArM immediately of any sudden unforeseen supply bottlenecks (57). The database contains information on the affected central pharmaceutical number (PZN), start and expected end date of the supply bottleneck, the pharmaceutical name, the ATC (Anatomical therapeutic chemical) Code, the API, if the pharmaceutical is relevant for the supply in hospitals, on marketability and whether an alternative preparation to the pharmaceutical affected by the supply bottleneck is known. The causes of the supply bottlenecks are also included. In addition, it is important to note that the indication of the causes for supply bottlenecks is also voluntary and represents sometimes additional qualitative data collected. The database contains also the notification type of supply bottlenecks. When a supply bottleneck is reported for the first time, it is a ‘first notification’. ‘First notification’ does not mean that this PZN has never been affected by a supply bottleneck in the past, but it does mean that a new supply bottleneck of this pharmaceutical occurred. If changes to a current supply bottleneck (e.g.: extension of duration) are notified, the status ‘change notification’ is given. When a manufacturer reports that the supply bottleneck is over, the notification contains the status ‘delete notification’ (58).

The appearing supply bottlenecks are chosen to analyse the changes in the pharmaceutical market in the period from January 2020 (start of the Corona pandemic in China) until June 2020 (relaxation of contact restrictions in Germany). Additionally to the database of BfArM the *'Gelbe Liste website'* (commercial) was used to gain additional information like the causes of supply bottlenecks or available alternatives for some pharmaceuticals, which sometimes are not available in the BfArM data base (75).

For a comprehensive analysis, all 'first notifications', 'change notifications' and all 'delete notifications' entered the database from 1 January 2020 to 30 June 2020, regardless of the expected end date of the supply bottlenecks, are included. It might have happened that a supply bottleneck was still reported in June but did not start before July 2020. The 'delete notifications' were particularly important because the analysis of the supply bottlenecks first started in June 2020, but for a comprehensive analysis all notified supply bottlenecks in the period from January to June 2020 should be included. Thus, for example, supply bottlenecks which were reported for the first time in March but were already deleted in May are included.

A flowchart presents the detailed search and evaluation strategy of the analysis of the supply bottlenecks (Figure 3). 912 PZN were identified. All notifications were then divided into 'first notifications' and 'change notifications'. All supply bottlenecks whose 'first notification' took place in 2020 were grouped together and supply bottlenecks that were accompanied by a 'change notification' but were first reported before 2020, were separated. 640 PZN (359 products) were identified as 'first notification' and 272 PZN (130 products) were identified which were already reported before 2020 but were subject to a 'change notification' of any kind. The identified supply bottlenecks were then further processed using Microsoft Excel to perform a descriptive analysis of the supply bottlenecks. The supply bottlenecks were systematically characterised according to the duration and causes of the supply bottlenecks. Whereas the supply bottlenecks of the 'change notifications' were only included to compare the causes for supply bottlenecks. For further analyses, only the 'first notifications' were used, as they have occurred during the period of the Corona pandemic.

The database 'SHI billing data' ('GKV-Abrechnungsdaten - NVI-KT') of the INSIGHT Health Galaxy NG platform was used for further analysis of the supply bottlenecks regarding ATC groups 1 and 2, API, and to present the monthly changes in the

prescriptions of the supply bottlenecks in an exploratory trend analysis. The NVI-KT database contains selling out data for prescription pharmaceuticals of the SHI funds. Prescriptions of the private health insurance are not part of the database (73). The data were collected by the pharmacy computer centres according to §300 SGB V (76). It is counted as a census, but no online-pharmacy or mail-order business is included in this database. Furthermore, data from hospital pharmacies are not included in the NVI-KT database (73). To show the changes of prescriptions during the first peak of the Corona pandemic, as the period of interest, prescription data from July 2019 to June 2020 were chosen, to see whether substantial changes in prescription numbers occurred during the period of the Corona pandemic. No analysis was carried out for groups of API whose prescription numbers were continuously below 5000 in the period under review.

The NVI-KT database was also used to analyse the whole Rx-pharmaceutical market from July 2019 to June 2020 to compare the prescriptions with those of the supply bottlenecks. This was also done for the ATC 1 groups. For 39 PZN, which were identified as a ‘first notification’ in the BfArM database, no data was available, i.e., were excluded for further analysis (see Figure 3).

Subsequently to the exploratory trend analysis of the prescription of selected API, the database for information on Certificates of Suitability of Monographs of the European Pharmacopoeia (CEP) granted by the EDQM was used to find out in which countries manufacturers hold the CEP of a certain API (77). The CEP is issued by the European Directorate for the Quality of Medicines (EDQM) and proves that the API is of the required quality (78,79). This database is the only publicly accessible database that lists the production sites and countries for a specific API. However, where the manufacturers get their API from, is not published.

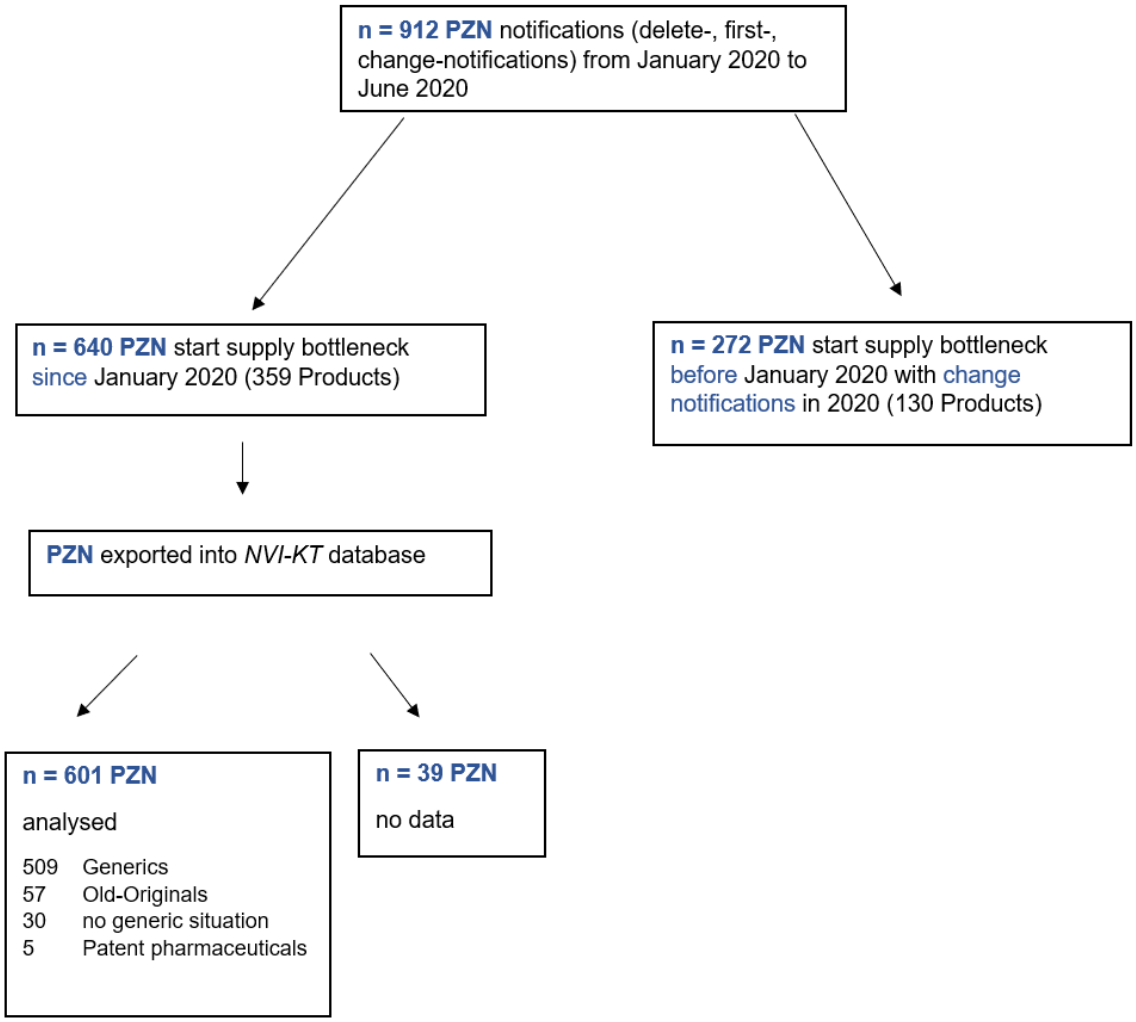


Figure 3: Flowchart of detailed search and evaluation strategy of supply bottlenecks

## 5.2 Expert interviews

The purpose of the expert interviews is to supplement the quantitative data with actual practical experience in the pharmaceutical market.

In the social sciences "'Experts' are commonly referred to as experts, connoisseurs, or professionals, i.e., people who have special knowledge. Thus, the expert interview is characterised by the fact that it is aimed at an exposed group of people who have specific knowledge with regard to the respective research interest" (80).
Since, as already described in chapter 3.2, a supply bottleneck does not necessarily lead to a supply shortage, it is important to ask experts whether the supply bottlenecks that have occurred have also led to supply shortages. The opinion of the experts on the

origin of the supply bottlenecks at the first peak of the Corona pandemic is also important to compare the analysed data with expert knowledge. Another aim of the expert interviews is to find out, from their observations, which API, ATC groups and pharmaceuticals were heavily affected by the supply bottlenecks. The opinion on measures and recommendations for action is also important to see the experts' opinions on how future crises can be better managed.

With the method semi-structured interviews, the interviewer develops an interview topic guide with open questions. The interviewer is flexible and does not refer exactly to the questions from the topic guide in order to gain rich and detailed data (81).
The developed German semi-structured interview topic guides (see APPENDIX E) consist of three main topics with open questions:

1. Structural changes in the pharmaceutical market
2. Supply bottlenecks / supply shortages
3. Future changes

Three different interview topic guides were developed, because three different expert groups were interviewed.

### 5.2.1 Sampling and target group

Experts from three different professional groups were selected to cover the ambulant and hospital German pharmaceutical market to gain as much information as possible and to cover all areas of the supply chain:

1. High street pharmacists (HS.P)
2. Hospital pharmacists (HO.P)
3. Wholesalers (sales department) (W1 and W2)

The 'convenience method of snowball sampling' is used as the sampling strategy (82). The interviewees were recruited in a convenient manner. The interviewer has contacts in the pharmaceutical sector and was also passed on to potentially relevant experts through additional contacts. Possible interviewees were contacted by mail or telephone

and were asked if they were willing to participate in an expert interview. The interviewees did not have to meet any specific requirements, they only had to belong to one of the three selected professional groups. All interviewees come from Northern Germany. A total of four experts were interviewed, a high street pharmacist, a hospital pharmacist and two wholesalers (wholesaler 1, wholesaler 2) working in sales departments.

### 5.2.2 Data Collection

The participation of the interviewees was completely voluntary. All study participants have been appropriately and sufficiently informed about the content and the purpose of the interview by using the participant information sheet (see APPENDIX B). The participation was based on a written informed consent obtained by all participants (see APPENDIX C) and confidentiality and anonymity regarding their personal data was guaranteed (see APPENDIX D). The interviews were conducted in German.

As the times of the Corona pandemic call for sensitivity, the interviews were conducted as to the requirements of the interviewee. The interviews with the high street pharmacist and Wholesaler 1 were conducted face-to-face with a ‘corona-distance’, with no third person present. The interview with the hospital pharmacist took place via video conference. The interview with Wholesaler 2 took place on telephone.

The interview procedure was identical for all interviews. The interviewer introduced himself personally, the participants were informed about the data processing procedure and signed the written informed consent (see APPENDIX C). The two interview partners whose interview did not take place face-to-face signed the written consent in advance. The aim of the Master thesis was also presented, and it was thoroughly explained what the expert interviews are used for. The interviewer started to ask questions using the interview topic guide (see APPENDIX E). The interview was also recorded.

### 5.2.3 Transcription and data analysis

All four interviews are transcribed in a table by key points in German (see APPENDIX G). Breaks, non-relevant topics, and words like 'mmh' or 'ehh' are not transcribed.

The framework analysis method was used to analyse the data collected. Therefore a set of categories was developed by analysing all conducted interviews to create a new framework of the collected data (83). Eight main categories were created by the researcher. The most important statements of the experts were translated from the transcripts into English and assigned to the eight main categories (APPENDIX F).

## 5.3 Development of vaccines

To examine the development of vaccines against COVID-19 a literature search was done. The main sources are sources from the WHO, the Paul-Ehrlich-Institute, Federal Institute for Vaccines and Biomedicines, from Federal Ministry of Education and Research (BMBF), from the European Medicines Agency (EMA) and European Commission.

# 6 Results of the exploratory data analysis

In this chapter the results of the exploratory data analysis will be shown. First the main characteristics of identified supply bottlenecks from January to June 2020 will be displayed, from coarser (ATC 1 group) to smaller (API). This is followed by a prescription trend analysis of the whole pharmaceutical market compared to all supply bottlenecks with ‘first notification’ in 2020 to get an overview of the dynamics of the prescriptions. Finally, a detailed prescription trend analysis of the supply bottlenecks with ‘first notification’ will be presented, likewise from coarser (ATC 1 group) to smaller (API).

## 6.1 Characteristics of supply bottlenecks from January to June 2020

As already shown in Figure 3, 640 PZN (359 products) were identified, which were reported for the first time in 2020. Of the 601 PZN analysed, 509 PZN are generics, 57 are old-originals (old pharmaceuticals where patent is unknown), 30 PZN there is no generic situation (no patent anymore, but no generics available) and 5 PZN of patent pharmaceuticals. Of them 199 PZN have package size N1, 180 PZN package size N2, 172 package size N3 and 50 PZN have no standard package size. For 417 PZN it was stated that no alternative preparation was available. For 223 PZN an alternative preparation is known. 436 are hospital relevant, 204 are not stated as relevant for the supply in hospitals.

272 PZN (130 Products) were identified, which were reported before January 2020, but a ‘change notification’ in 2020 has occurred.

Shown in Figure 4, March is the main start month of supply bottlenecks with ‘first notifiations’ in 2020. In March supply bottlenecks of 231 PZN started. In January and February below 100 supply bottlenecks, in May and June under 50 supply bottlenecks started. Figure 5 presents the average expected month duration of supply bottlenecks. The most expected duration of supply bottlenecks is 5 months (n=110). The second most duration is 6 months (n=88), the third most is 4 months at (n=76). The mean length counts 167,64 days (5-6 months), with a minimum length of 29 days (1 month) and a maximum of 638 days (21 months). In contrast, the average expected duration of supply bottlenecks with change notifications is 641,574 days (22-23 months), with a minimum of 212 days (7 months) and a maximum of 2221 days (74 months).

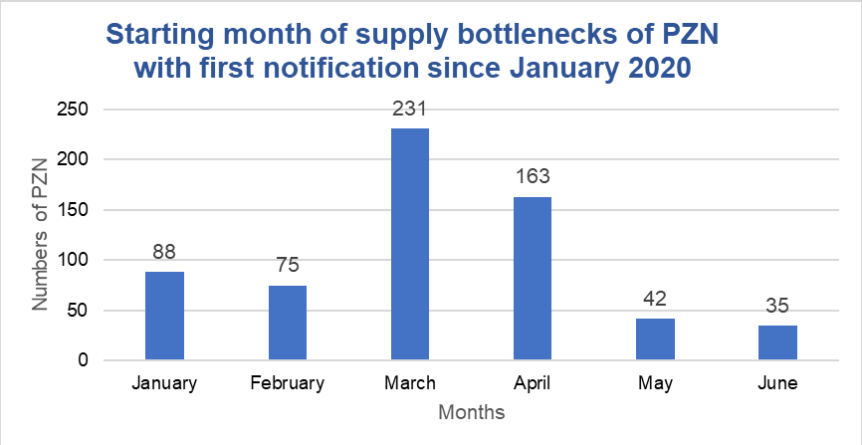


Figure 4: Starting month of supply bottlenecks of PZN with first notification since January 2020

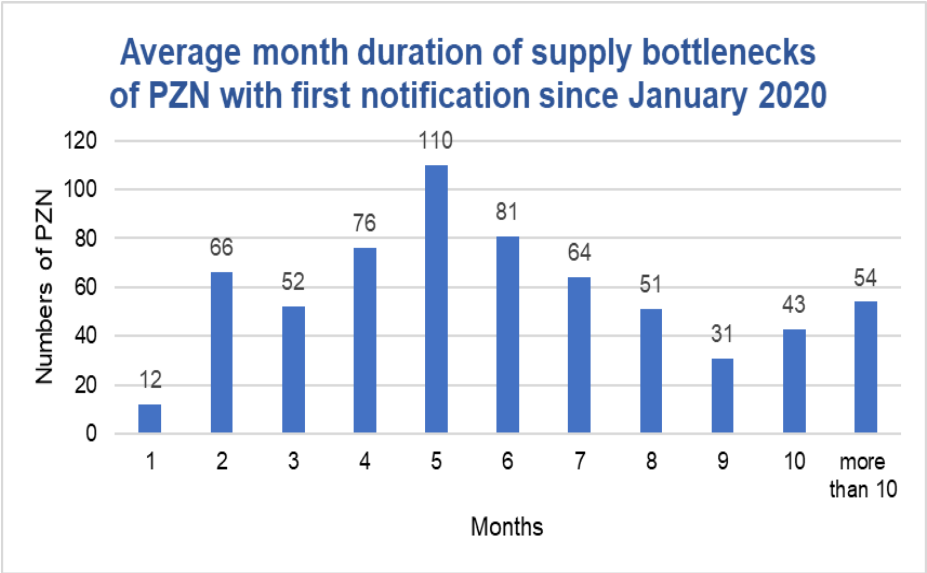


Figure 5: Average month duration of supply bottlenecks with first notification since January 2020

### 6.1.1 Causes of supply bottlenecks – change notification

Pharmaceutical companies can, but do not have to, give detailed causes for a supply bottleneck. For supply bottlenecks with a change notification in 2020, reasons were given for 91 PZN of the 272 PZN. The most common reason (n=47) for a supply bottleneck is 'quality issues / product contamination'. This includes for example the EU-wide recall of Valsartan by itself 26 PZN. The 2nd most frequent reason for supply bottlenecks is non-deliverability of a competitor, resulting in higher sales in the market (n=21). Also causes given are 'increased demand/sales in the market', 'a tense market situation' and 'delay within the production process'.

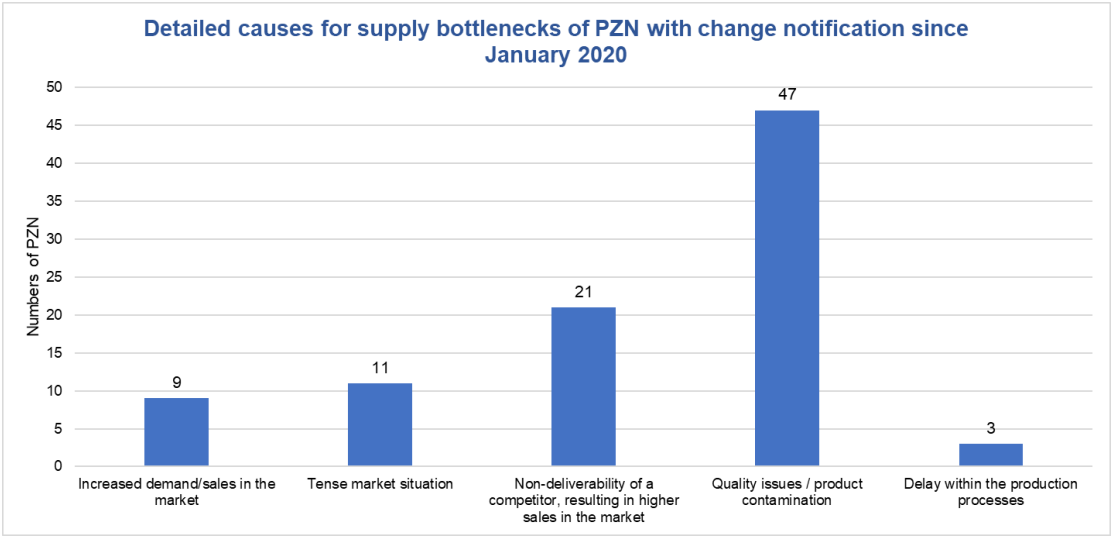


Figure 6: Detailed causes for supply bottlenecks with change notification since January 2020

### 6.1.2 Causes of supply bottlenecks – first notification

For the supply bottlenecks occurred until June 2020, detailed causes have been given for 289 PZN of 640, which are slightly different from the supply bottlenecks with change notifications. For 186 PZN, the stated cause for a supply bottleneck was an ‘increased demand/sales in the market’. For 36 PZN, some manufacturers made it more precise and attributed the increased sales due to the Corona pandemic. For two PZN, the increased demand was supplemented by a limited availability of raw material. 14 PZN were affected according to quality issues. The ‘non-deliverability of a competitor, resulting in higher sales in the market’, was stated for 12 PZN. Also, the ‘interrupted supply chain’ (n=12) was mentioned, this was also specified for 7 PZN and attributed to the Corona pandemic (n=7). For six PZN the changes in rebate contracts were specified and for five PZN packaging size problems were identified. For one PZN, for the API Hydroxychloroquine, it was indicated that the Indian government imposed an export stop on this API. For Hydroxychloroquine it was first indicated as a useful treatment of patients with COVID-19, but then in May the EMA warned against the use of Chloroquine and Hydroxychloroquine (84).

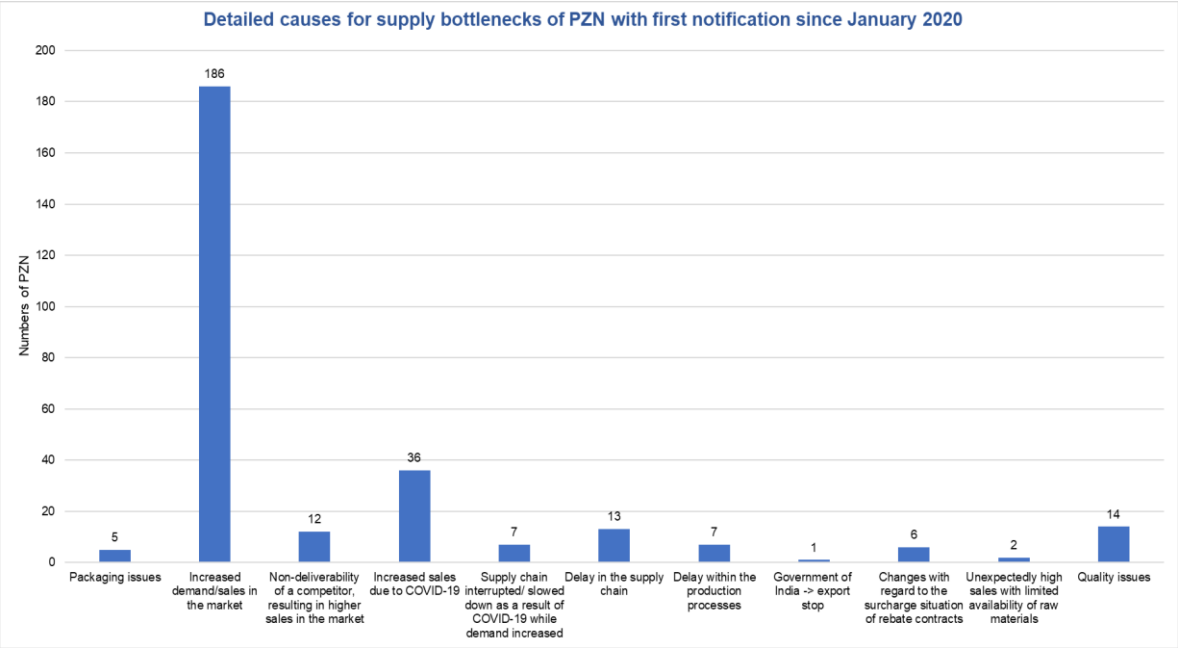


Figure 7: Detailed causes for supply bottlenecks with first notification since January 2020

### 6.1.3 Distribution of supply bottlenecks (first notification) – ATC 1 group

As seen in Figure 8, the most affected ATC 1 group of supply bottlenecks is the N Nervous System (n=204). Followed by J Antiinfectives, systemic (n=141), C Cardiovascular system (n=67), L Antineoplastic and immunomodulators (n=44), G Urogenital tract and sex hormones (n=28).

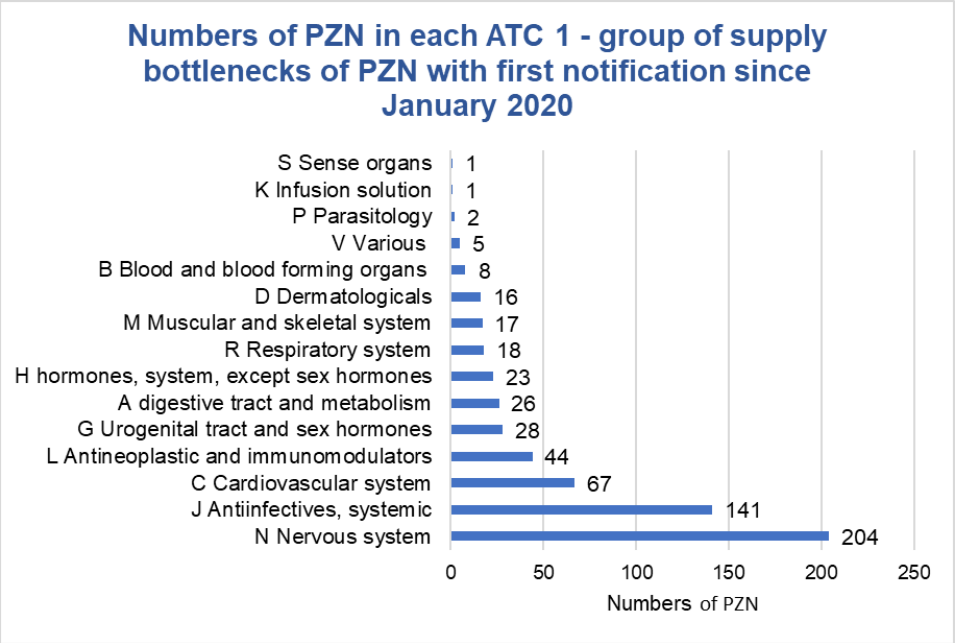


Figure 8: Numbers of PZN in each ATC 1 - group of supply bottlenecks with first notification since January 2020

### 6.1.4 Distribution of supply bottlenecks (first notification) – ATC 2 - group

In the ATC 2 group, the J01 Antibiotics, systemic (n=105) are the most affected. Followed by N03 Antiepileptic pharmaceuticals (n=72), N01 Anaesthetics and narcotics (n=44), N02 Analgesics (n=44) and L01 Antineoplastic agents (n=38).

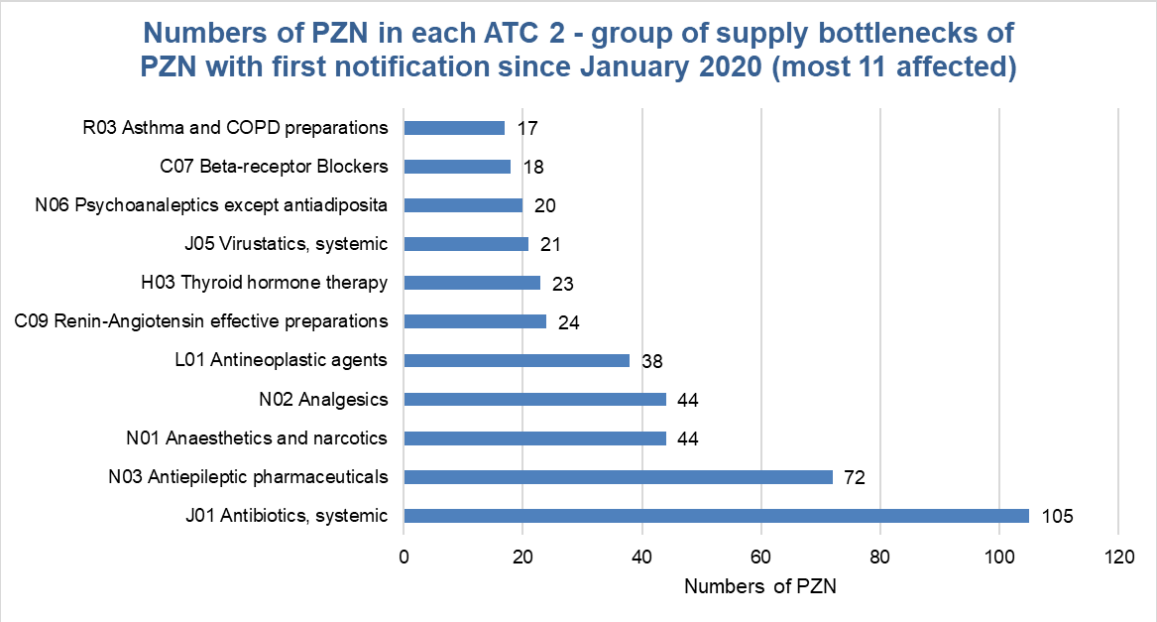


Figure 9: Numbers PZN in each ATC 2 - group of supply bottlenecks with first notification since January 2020

### 6.1.5 Numbers of most affected API (first notification)

According to the 'list of active substances which are essential for supply (excluding vaccines)' (62) the API of supply bottlenecks were divided into supply relevant and not supply relevant. In total 99 API are supply relevant and 53 API are not relevant to supply. This corresponds to 440 supply relevant PZN and 164 PZN not relevant to supply. Of this 440 PZN only 170 of them (38,64%) had an alternative pharmaceutical available, 284 PZN are relevant for the supply in hospitals. Most API have been analysed in terms of the most affected PZN and the most affected products (one product may contain several PZN). Several supply bottlenecks of products also indicate that several manufacturers are affected by the supply bottleneck. Only those API were analysed which are relevant to supply.

The most affected API by PZN are Pregabalin (n=22), Amoxicillin (n=18), Midazolam (n=18), Propofol (n=17), Lamotrigine (n=17), Levothyroxine (n=17), Topiramate (n=14), Metoprolol (n=12) and Venlafaxine (n=12) (see Table 3). After products are also Paracetamol (n=5), Metronidazole (n=4), Morphine (n=4), Ibuprofen (n=4), Aciclovir (n=3), Azithromycin (n=3) and Salbutamol (n=3) most affected (see Table 4). For a closer view, in Appendix A there is a detailed overview of the product names and manufacturers of the most affected supply relevant API.

Table 3: Most 9 API (supply relevant) of supply bottlenecks of PZN with first notification since January 2020

| Numbers of PZN | API | ATC 1 | ATC 2 |
|---|---|---|---|
| 22 | Pregabalin | N Nervous system | N03 Antiepileptic pharmaceuticals |
| 18 | Amoxicillin | J Antiinfectives, systemic | J01 Antibiotics, systemic |
| 18 | Midazolam | N Nervous system | N03 Antiepileptic pharmaceuticals/N01 Anaesthetics and narcotics |
| 17 | Propofol | N Nervous system | N01 Anaesthetics and narcotics |
| 17 | Lamotrigine | N Nervous system | N03 Antiepileptic pharmaceuticals |
| 17 | Levothyroxine | H Hormones, system, except sex hormones | H03 Thyroid hormone therapy |
| 14 | Topiramate | N Nervous system | N03 Antiepileptic pharmaceuticals/N02 Analgesics |
| 12 | Metoprolol | C Cardiovascular system | C07 Beta-receptor blockers |
| 12 | Venlafaxine | N Nervous system | N06 Psych analeptics except anti-obesity pharmaceuticals |

Table 4: Most 12 API (supply relevant) of supply bottlenecks of products with first notification since January 2020

| Numbers of products | API | ATC 1 | ATC 2 |
|---|---|---|---|
| 5 | Midazolam | N Nervous system | N01 Anaesthetics and narcotics |
| 5 | Paracetamol | N Nervous system | N02 Analgesics |
| 4 | Metronidazole | G Urogenital Tract and Sex Hormones | G01 Urogenital tract and sex hormones |
| 4 | Morphine | N Nervous system | N02 Analgesics |
| 4 | Ibuprofen | N Nervous system | N02 Analgesics |
| 3 | Aciclovir | J Antiinfectives, systemic | J05 Virustatics, systemic |
| 3 | Amoxicillin | J Antiinfectives, systemic | J01 Antibiotics, systemic |
| 3 | Azithromycin | J Antiinfectives, systemic | J01 Antibiotics, systemic |
| 3 | Lamotrigine | N Nervous system | N03 Antiepileptic pharmaceuticals |
| 3 | Levothyroxine | H Hormones, system, except sex hormones | H03 Thyroid hormone therapy |
| 3 | Propofol | N Nervous system | N01 Anaesthetics and narcotics |
| 3 | Salbutamol | R Respiratory system | R03 Asthma and COPD preparations |

## 6.2 Prescription trend analysis of supply bottlenecks (first notification) and whole pharmaceutical market

In this chapter the prescription numbers of the whole Rx-pharmaceutical market and all supply bottlenecks with a first notification in 2020, from July 2019 to June 2020 are analysed to view the development of the prescription numbers in times of the corona pandemic.

As shown in figure 10, the selling out data of the whole Rx-pharmaceutical market of finished products in the statutory health insurance between July 2019 and February 2020 vary between 54,415,762 (2019.08) and 63,913,536 (2020.01) prescriptions in a pattern that cannot be precisely identified. In March, the number of prescriptions peaked at 69,199,408, after which the number of prescriptions fell to 52,261,550 in April and 50,798,701 in May. In June 2020, the number of prescriptions increased again to 54,757,356.

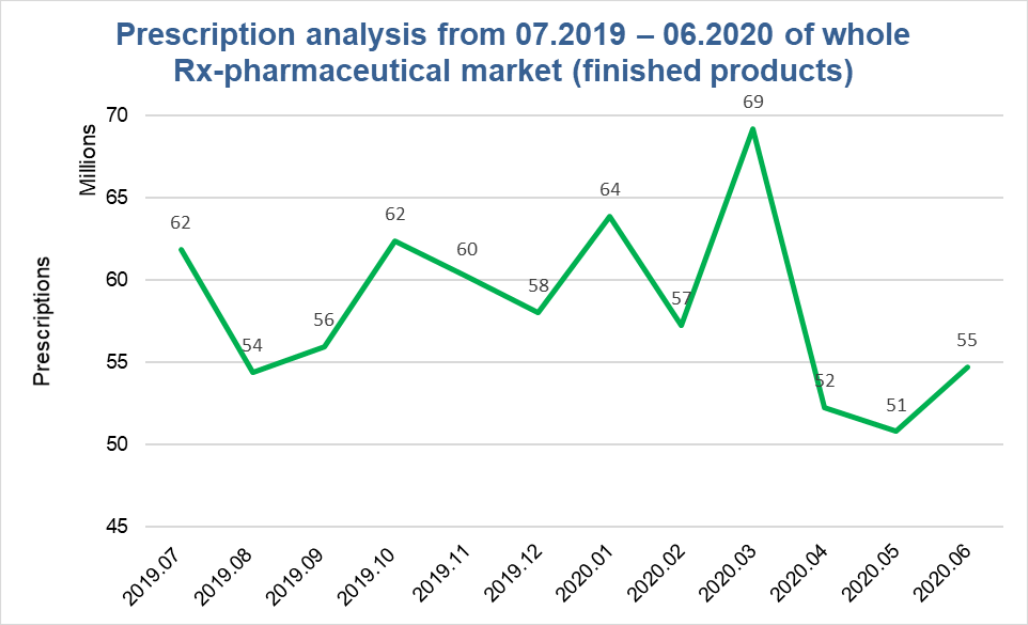


Figure 10: Prescription analysis of whole Rx-pharmaceutical market (finished products)

As presented in Figure 11, in August 2019, the prescription numbers for identified supply bottlenecks are at a relatively low level (2,044,313). The increase reaches the highest prescription value in March 2020 (2,869,569). In contrast to the previous month,

the number of regulations rose by 13.92% in March (Figure 12). In April, the prescription numbers fall by -38.23% compared to March. From April to May, they also decrease by a further 3.21%. A slight increase of 5.99% is recorded for June. Figure 12 also shows the percentage development of the prescription numbers for the whole Rx-pharmaceuticals market, compared to the supply bottlenecks with first notification in 2020. The whole market shows a similar pattern to the occurred supply bottlenecks. From February to March 2020, the selling out of the whole Rx-pharmaceutical market increased by 20.87%, a higher increase than that of supply bottlenecks. From March to April, however, the number of prescriptions did not decrease (-24.48%) as much as for the supply bottlenecks.

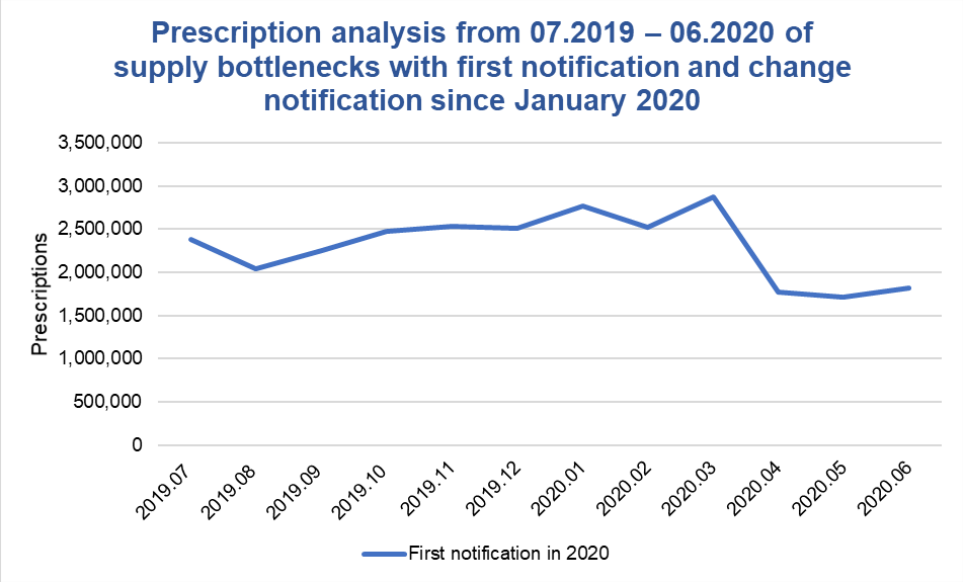


Figure 11: Prescription analysis of supply bottlenecks with first and change notification since January 2020

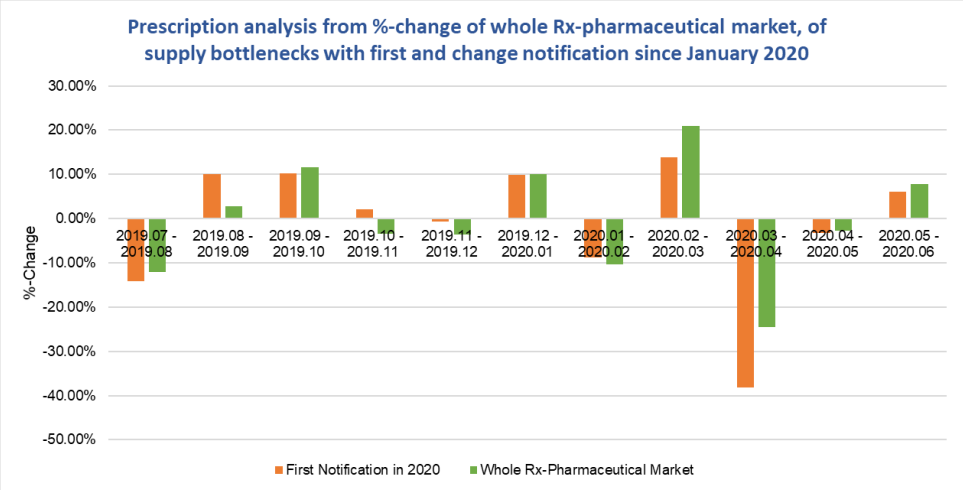


Figure 12: Prescription analysis from %-change of whole Rx-pharmaceutical market, of supply bottlenecks with first and change notification since January 2020

Figure 13 shows the percentage changes of one month compared to the previous month from February to May 2020 according to the three package sizes N1, N2, N3. The changes in the prescriptions from February to March are similar for all three package sizes of both groups. The N1 prescriptions show a minimal decrease. The medium N2 sizes show an increase of 17.47% for pharmaceuticals with supply bottlenecks and an increase of 12.53% for the whole market. The largest N3 packages show a prescription increase of over 30% for both groups. The change from March to April shows that the N1 packs were prescribed even less. However, the other two package sizes also show a significant decrease in prescriptions. This decline continues to a small extent for all packages as of May. Only the N3 package size prescriptions have increased again.

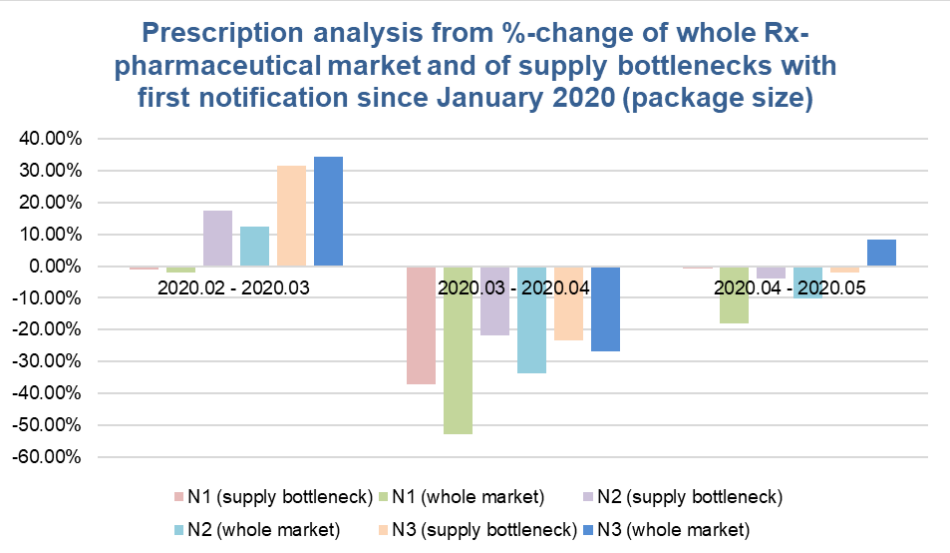


Figure 13: Prescription analysis from %-change of whole Rx-pharmaceutical market and of supply bottlenecks with first notification since January 2020 (package size)

### 6.2.1 ATC 1 group

A detailed look at the whole Rx-pharmaceutical market (including all prescription pharmaceuticals) for 11 selected ATC 1 groups most affected by the supply bottlenecks shows that of the ATC 1 groups presented, eight had their highest prescription value in March 2020: C Cardiovascular system (19,350,172), N Nervous System (12,485,032), A Digestive tract and metabolism (8,347,548), M Muscular and skeletal system (4,228,862), H Hormones, system, expect sex hormones (4,112,145), R Respiratory System (5,407,521), B Blood and blood forming organs (2,844,761) and L Antineoplastic and immunomodulators 605,273. L Antineoplastic and

immunomodulators and M Muscular and skeletal system recorded their lowest prescription numbers in the following month of April. The others recorded their lowest prescription numbers in May, although April was also at a low level. For these ATC 1 - groups, no noticeable fluctuations are visible in 2019 (see Figures 14 and 15).

3 groups, however, had their highest prescriptions in January 2020 in the period under review: J Antiinfectives, systemic (3,910,885), D Dermatologicals (2,194,574) and G Urogenital tract and sex hormones (1,940,392) (see Figures 14 and 15). The month with the lowest prescription number of J Antiinfectives, systemic was April. In this ATC 1 group, no substantial fluctuations were visible in 2019 to 2020, except in April when the prescription value dropped to its lowest level. D Dermatologicals and G Urogenital tract and sex hormones recorded their lowest prescription numbers in December 2019. In these two groups, no substantial changes in the number of prescriptions can be seen. It should be added that all ATC-1 groups were at a low prescription level in August 2019 (see Figure 15).

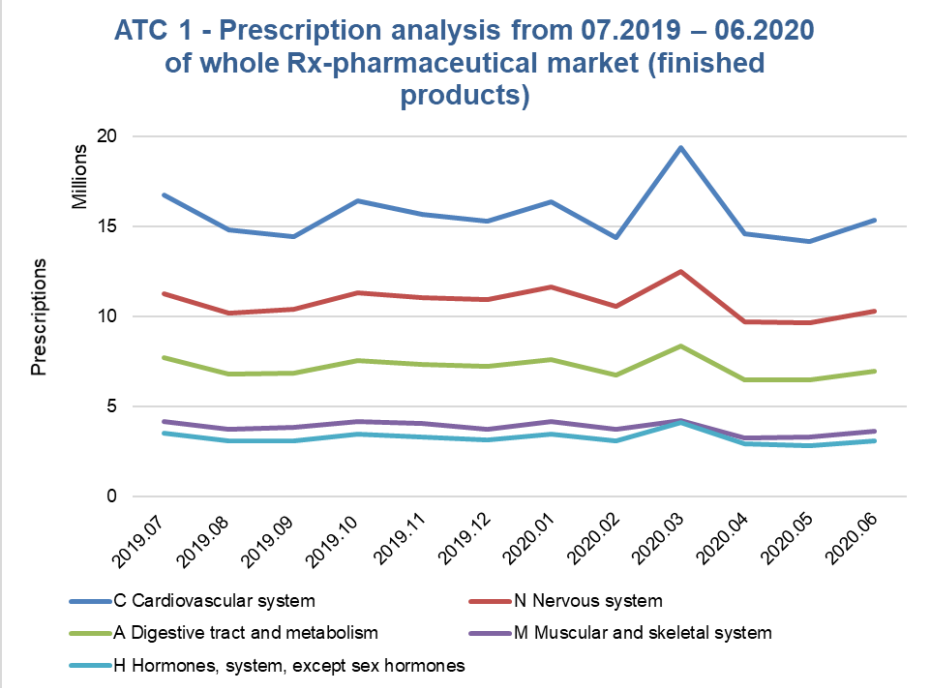


Figure 14: Prescription analysis of whole Rx-pharmaceutical market (finished products) - part 1

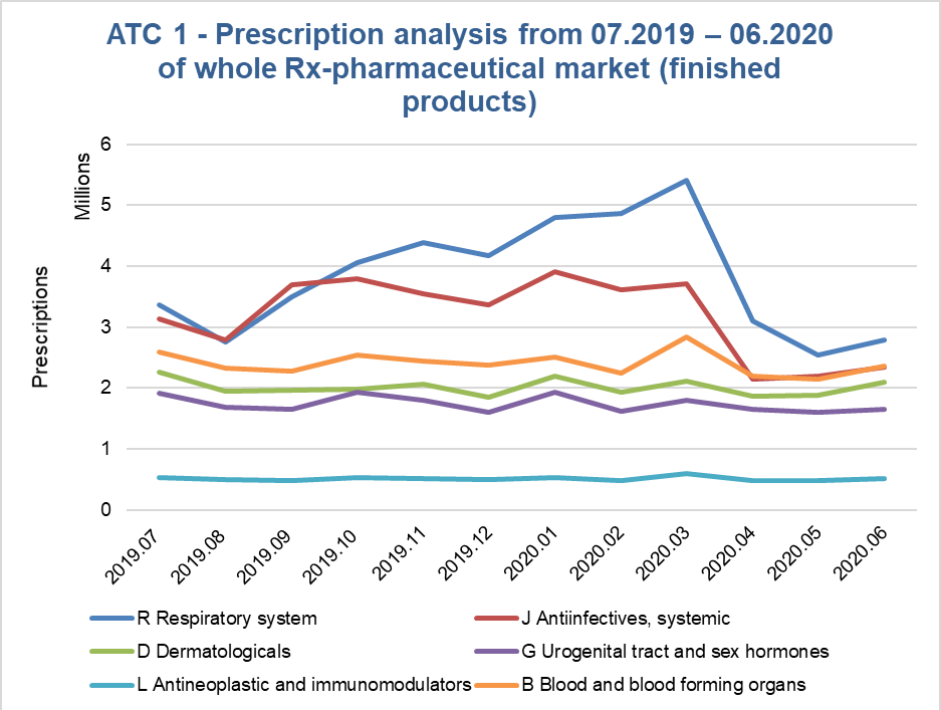


Figure 15: Prescription analysis of whole Rx-pharmaceutical market (finished products) – part 2

A detailed look at the pharmaceuticals with the notified supply bottlenecks with first notification since January 2020 (see figures 16 and 17) shows a slightly different picture of the prescription numbers compared to the prescriptions of the whole Rx-pharmaceutical market including pharmaceuticals with and without supply bottlenecks. Five ATC 1 groups had their highest prescription numbers at the beginning of the period under review in July 2019: A Digestive tract and metabolism, G Urogenital tract and sex hormones, M Muscular and skeletal system, B Blood and blood forming organs, A Digestive tract and metabolism. D Dermatologicals, Nervous system and J Antiinfectives, systemic had their highest prescription numbers in January 2020. In March 2020, C Cardiovascular system, R Respiratory system and H Hormones, system, except sex hormones had their highest prescription numbers. The lowest prescription numbers out of eight pharmaceuticals groups were in May and June. Only A Digestive tract and Metabolism had the lowest number of prescriptions in February and C Cardiovascular system in April (Figure 16 and 17).

Figure 16 shows, that the six ATC 1 groups shown there: N Nervous System, R Respiratory System, J Antiinfectives, systemic, C Cardiovascular system, A Digestive tract and metabolism, H Hormones, system, except sex hormones, recorded relative stable prescription numbers in 2019, whereas it fluctuated in 2020, with a higher

decrease from March to April. Figure 17 shows that L Antineoplastic and immunomodulators and B Blood and blood forming organs had a relatively stable level of prescriptions until January 2020 and then declined. For G Urogenital tract and sex hormones, the number of prescriptions has been decreasing since the beginning of the period under review in July 2020, with a short-term increase from November to December 2020. For ATC 1 groups D Dermatologicals and M Muscular and skeletal system, no substantial changes can be identified in the period under review.

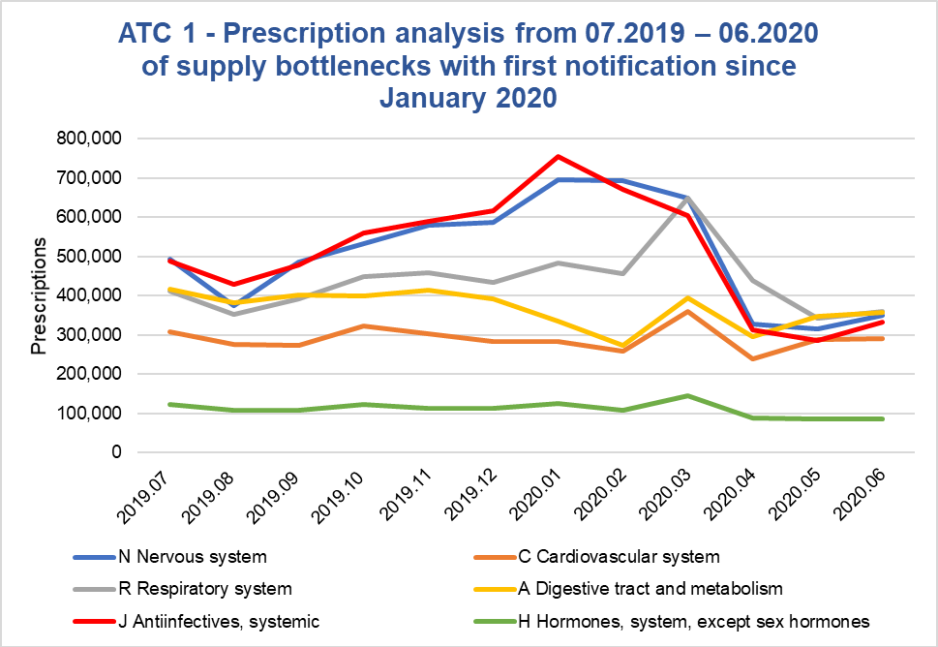


Figure 16: ATC 1 – Prescription analysis of supply bottlenecks with first notification since January 2020 – Part 1

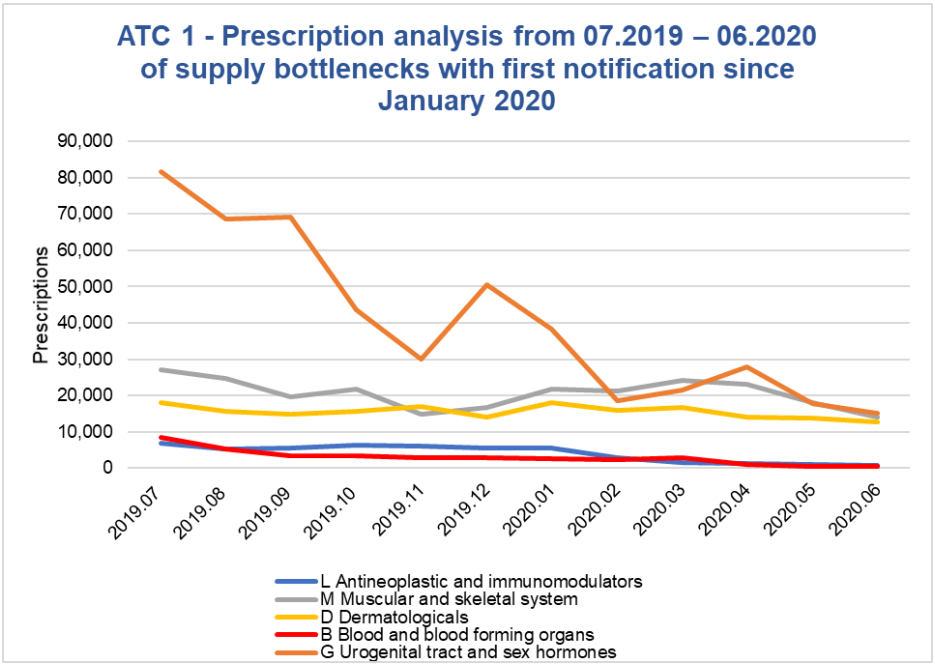


Figure 17: ATC 1 – Prescription analysis of supply bottlenecks with first notification since January 2020 – Part 2

However, it is important to note, as Table 5 shows, that all ATC 1 groups of pharmaceuticals with supply bottlenecks experienced a decline in supply from March to April, except G Urogenital tract and sex hormones which had a decline of -51.68% from January to February, showing a plus in April compared to March, but decreasing in May and June. B Blood and blood forming organs recorded the largest drop in prescriptions from March to April (-65.27%), which continued from April to May with a further decrease (-49,75%). In eight of the ATC 1 groups, prescriptions of pharmaceuticals with supply bottlenecks fell again in May compared to April. This was again undercut in 5 of the ATC 1 groups in May.

Table 5 (in brackets) shows the changes in the whole Rx-pharmaceutical market. On closer inspection, the changes in the number of prescriptions deviate from those for pharmaceuticals with supply bottlenecks. For nine ATC 1 groups, the percentage decrease from March to April was lower than the percentage decrease of the whole market. Only for R Respiratory system and M Muscular and skeletal system was the percentage decrease of the whole pharmaceutical market from March to April bigger than the decrease of the supply bottlenecks.

Table 5: ATC 1 - %-change from 06.2019 – 06.2020 of supply bottlenecks with first notification since January 2020 (whole Rx-pharmaceutical market)

| ATC 1 | 2020.01 - 2020.02 | 2020.02 - 2020.03 | 2020.03 - 2020.04 | 2020.04 - 2020.05 | 2020.05 - 2020.06 |
|---|---|---|---|---|---|
| N Nervous system | -0.33% (-9.38%) | -6.40% (18.16%) | -49.42% (-22.06%) | -4.18% (-0.94%) | 10.99% (6.87%) |
| J Antiinfectives, systemic | -11.28% (-7.48%) | -9.70% (2.52%) | -48.16% (-42.22%) | -8.92% (2.31%) | 16.17% (7.25%) |
| C Cardiovascular system | -9.00% (-11.97%) | 39.38% (34.43%) | -33.78% (-24.69%) | 21.04% (-2.67%) | 0.69% (8.28%) |
| L Antineoplastic and immunomodulators | -47.55% (-8.01%) | -43.71% (25.28%) | -22.46% (-20.36%) | -12.85% (1.47%) | -36.37% (4.54%) |
| G Urogenital tract and sex hormones | -51.68% (-16.73%) | 16.50% (11.75%) | 30.15% (-8.73%) | -36.31% (-2.82%) | -14.42% (2.70% |
| A Digestive tract and metabolism | -18.55% (-11.53%) | 44.57% (23.80%) | -25.25% (-22.26%) | 17.60% (-0.44%) | 2.88% (7.79%) |
| H Hormones, system, except sex hormones | -12.92% (-10.09%) | 33.64% (31.85%) | -38.35% (-28.50%) | -3.81% (-3.56%) | -0.63% (10.38%) |
| R Respiratory system | -5.79% (1.41%) | 42.60% (11.0%) | -32.19% (-42.63%) | -22.11% (-18.24%) | 5.36% (9.67) |
| M Muscular and skeletal system | -2.33% (-10.45%) | 13.46% (12.71%) | -4.44% (-23.08%) | -21.95% (2.79%) | -21.82% (8.87%) |
| D Dermatologicals | -12.67% (-12.10%) | 6.14% (9.31%) | -15.87% (-11.25%) | -3.24% (0.46%) | -6.59% (11.47%) |
| B Blood and blood forming organs | -11.04% (-10.12%) | 22.77% (26.3%) | -65.27% (-22.87%) | -49.75% (-1.83%) | -21.61% (9.74%) |

### 6.2.2 ATC 2 group

In this chapter the supply bottlenecks regarding the ATC 2 groups are analysed in more detail. Table 6 shows the percentage changes from December 2019 to June 2020 of 11 most affected ATC 2 groups by supply bottlenecks. Figure 18 shows a trend analysis of the percentage changes of the four most affected ATC 2 groups from July 2019 to June 2020. The most frequent start month of J01 Antibiotics systemic (57 out of 105), N03 Antiepileptic pharmaceuticals (29 out of 72 PZN), N02 Analgesics (24 out of 44 PZN), was March 2020. For N01 Anaesthetics and narcotics the most frequent start of a supply bottleneck was April 2020 (36 out of 44 PZN).

In Figure 18 in 2019 fluctuations in the five ATC 1 groups can be seen. Particularly noticeable here is the 82.01% change from November to December 2019 in the antiepileptic pharmaceuticals group.

The number of prescriptions of the he ATC 2 group N01 Anaesthetics and narcotics decreased by 57.14%, from March to April by -12.54%, from April to May by -27.3%, from May to June by 13.97%. However, it is important to note that this ATC 2 group mainly concerns supply bottlenecks of Propofol and Midazolam, which are mainly used in hospital surgeries. As already mentioned in chapter 4, the NVI-KT database does not include hospital data.

Regarding to the supply bottlenecks of the groups N02 Analgesics and J01 Antibiotics, systemic, an increase in prescription numbers at the beginning of 2020 cannot be identified. It is noticeable that between March and May the prescription numbers for N02 Analgesics decreased by -55.81% and for J01 Antibiotics, systemic by -53.24%. From May to April the prescription numbers increased again. For N03 Antiepileptic pharmaceuticals, there has been a -30.43% decrease in prescriptions from March to April, but then it increased from April to June (21.83%).

Furthermore, a high increase in the number of prescriptions (243.55%) of C09 Renin-Angiotensin effective preparations from February to March is striking. The R03 Asthma and COPD preparations show an increase of 42.63% from February to March, which then decreased by 54.44% from March to May (see table 6).

Table 6: ATC 2 - %-change from 06.2019 – 06. 2020 of supply bottlenecks with first notification since January 2020 (most 11 affected)

| ATC 2 | 2019.12 - 2020.01 | 2020.01 - 2020.02 | 2020.02 - 2020.03 | 2020.03 - 2020.04 | 2020.04 - 2020.05 | 2020.05 - 2020.06 |
|---|---|---|---|---|---|---|
| J01 Antibiotics, systemic | 21.84% | -12.70% | -10.51% | -48.52% | -9.15% | 17.66% |
| N03 Antiepileptic pharmaceuticals | -16.62% | -3.54% | -2.11% | -30.43% | 3.76% | 17.42% |
| N01 Anaesthetics and narcotics | 14.36% | -25.98% | 57.14% | -12.54% | -27.30% | 13.97% |
| N02 Analgesics | 20.64% | 3.59% | -10.30% | -55.30% | -1.13% | 12.71% |
| L01 Antineoplastic agents | 1.14% | -9.89% | 28.84% | 34.31% | -1.09% | -28.21% |
| C09 Renin-Angiotensin effective preparations | -18.03% | -8.84% | 243.55% | -22.55% | 26.07% | -33.88% |
| H03 Thyroid hormone therapy | 10.48% | -12.92% | 33.64% | -38.35% | -3.81% | -0.63% |
| J05 Virustatics, systemic | 78.13% | 47.64% | 7.77% | -43.57% | -5.53% | -6.63% |
| N06 Psychoanaleptics except antiadiposita | 4.15% | -23.76% | 38.88% | -24.84% | -7.08% | -6.18% |
| C07 Beta-receptor blockers | 4.38% | -5.82% | 20.89% | -42.65% | 33.88% | 8.96% |
| R03 Asthma and COPD preparations | 11.54% | -5.74% | 42.63% | -32.22% | -22.22% | 5.44% |

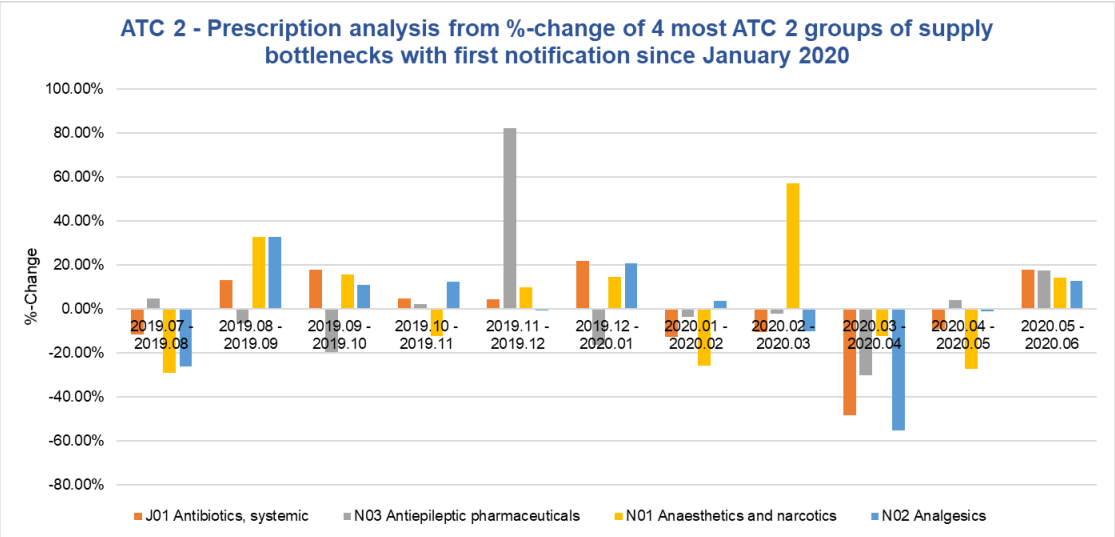


Figure 18: ATC 2 - Prescription analysis from %-change of 5 most ATC 2 groups of supply bottlenecks with first notification since January 2020

### 6.2.3 Supply relevant pharmaceuticals

In this chapter, the supply bottlenecks of supply relevant API are analysed. In August 2019, the number of prescriptions was 1,773,885. By March, they had risen steadily to 2,611,637 except for minor decreases. From March to April, in the phase of the first lockdown, where also many supply bottlenecks started, there was a high decrease in prescriptions of -39.91% (1,569,307) which fell by a further 4.15% from April to May on a low level (1,504,192). From May to June, a slight increase of 6.73% compared to the previous month (1,605,397) can be observed.

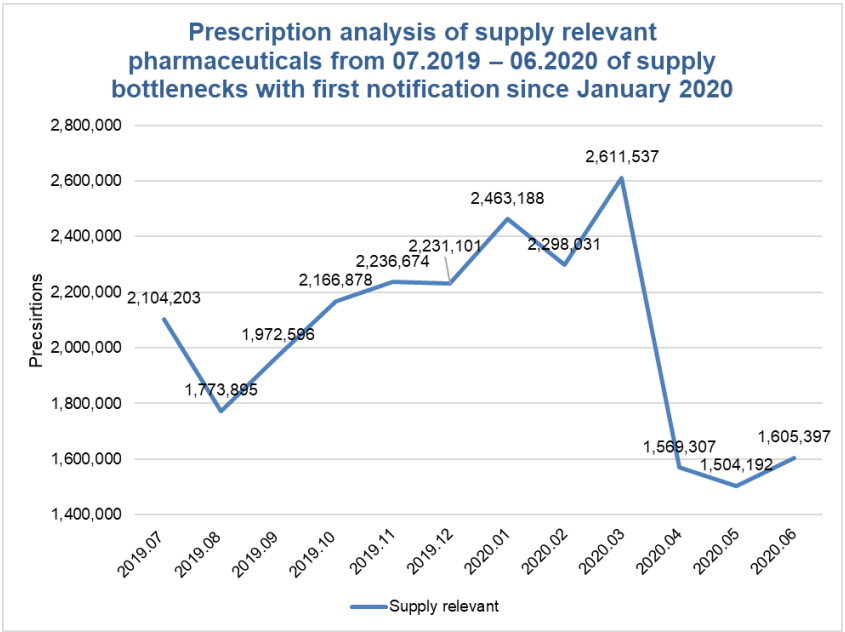


Figure 19: Prescription analysis of essential pharmaceuticals of supply bottlenecks with first notification since January 2020

### 6.2.4 Most concerned API – ATC 1 group

In this chapter, the supply relevant API most affected by the supply bottlenecks are sorted into the respective ATC 1 group in a trend analysis in Figures 21 to 26. Pregabalin, Lamotrigine and Topiramate were not analysed as the prescriptions were always below 5000 prescriptions.

Salbutamol (Figure 20) shows an increase of 42.86% from February to March, but then a decrease of -54.95% from March to May. For all 7 PZN (3 Products), the detailed reason given was an increased demand/sale in the market in March (starting month of supply bottlenecks: 3 PZN in March, 4 PZN in April).

Amoxicillin (starting months of supply bottlenecks: 12 PZN in March, 6 PZN in April) and Azithromycin (starting months of supply bottlenecks: 3 PZN in March, 1 PZN in April) were at a relatively high level of prescriptions from January to March 2020, and then from March to May, prescriptions fell to a low level (Amoxicillin: -57.32%, Azithromycin: -79.63%) (Figure 21). Aciclovir increased by 52.17% between February and March and then remained at a relatively high level. For these API, increased demand/sales in the market were also reported for 35 out of 48 pharmaceuticals sold.

In the ATC 1 group N Nervous system (Figures 22 and 23), the prescriptions of the API Paracetamol (9 PZN, 5 Products) increased by 36.81% from February to March (starting months of supply bottlenecks: 7 PZN in March, 2 PZN in April). From March to May, however, the prescriptions fell by -69.53%. For 7 PZN an increased demand/sales in the market in March was given as a detailed reason. From January to April, Morphine (starting months of supply bottlenecks: 1 PZN in March, 2 PZN in April, 4 PZN in May) prescriptions fell by -48.68% overall, but then rose by 40.02% from April to May. Midazolam and Propofol (most starting month: April 32 out of 38 PZN), as already mentioned in Chapter 6.2.2. together, had a high increase from February to March, but then decreased until May. Here, 37 out of 38 PZN (8 products) were also given as the cause of a supply bottleneck ‘increased demand/sales in the market’. For Ibuprofen (starting month April, 4 PZN, 3 products), a steady increase in prescription numbers can be identified from August 2019 to February 2020. From February to March there was then a decrease in prescriptions of -25.88%. From March to April, the decrease in prescriptions became even more pronounced, with a decrease of -79.85%. Increased

demand/sales in the market were also cited as the reason for the supply bottleneck for all PZN.

In the case of Metoprolol (starting month of supply bottleneck: February 8 PZN, 4 products), no clear pattern of change in 2020 towards 2019 can be identified (Figure 24). The prescription numbers in February rose by 34.45% compared to January, fell by -41.36% in April compared to February and then rose again in May by 111.92%. However, no clear pattern can be identified.

For Metronidazole (starting months of supply bottlenecks: 5 PZN in March, 2 PZN in May, 1 PZN in June), the number of regulations was at a low level until February. From February to March, the prescription numbers then increased by 212.60%, then remained at the same level in April and then fell by 70.84% to May (Figure 25). Additionally, 'increased/demand sales in the market' as also cited as the detailed reason for the supply bottlenecks (for four out of six PZN).

For Levothyroxine (21 PZN, 3 products), the prescription figures were at a relatively stable level with small fluctuations until February 2020. From February to March, prescriptions increased by 38.22% and then decreased by -44.1% from March to April (Figure 26). For 13 of the 22 PZN, the reason was also increased demand/sales in the market (starting months of supply bottlenecks: 2 PZN in January, 4 PZN in February, 13 PZN in March, 2 in April).

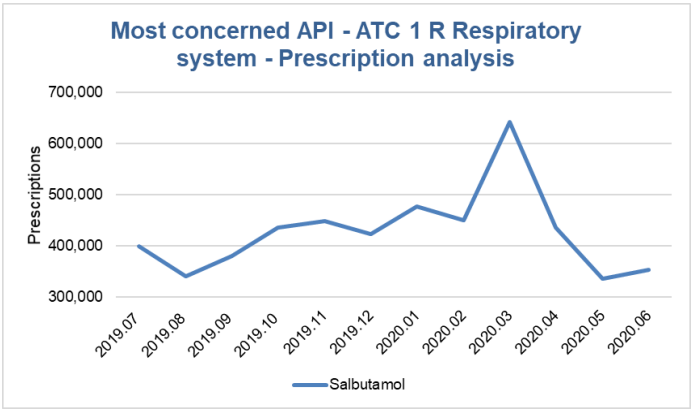


Figure 20: Most concerned API – ATC 1 R Respiratory system – Prescription analysis of supply bottlenecks with first notification since January 2020

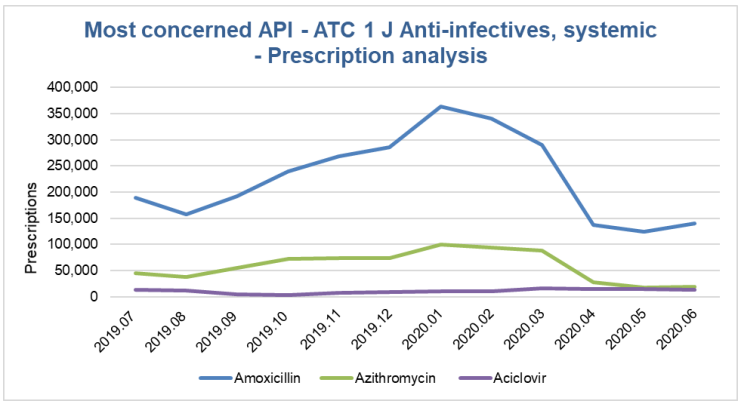


Figure 21: Most concerned API – ATC 1 J Antiinfectives, systemic – Prescription analysis of supply bottlenecks with first notification since January 2020

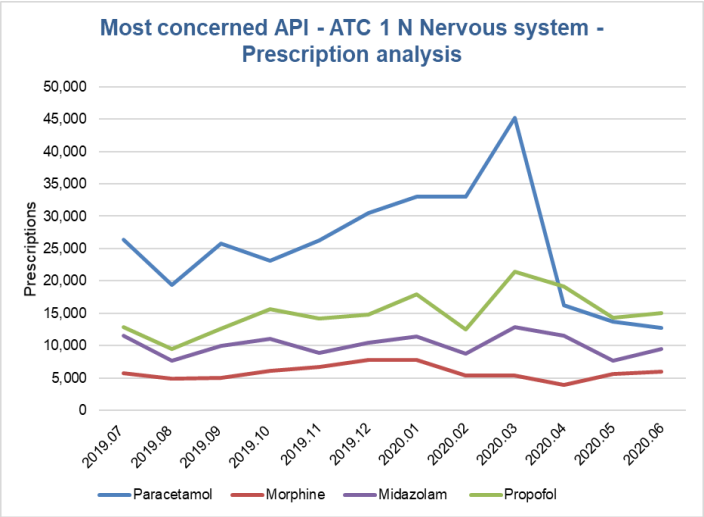


Figure 22: Most concerned API – ATC 1 N Nervous system – Prescription analysis of supply bottlenecks with first notification since January 2020

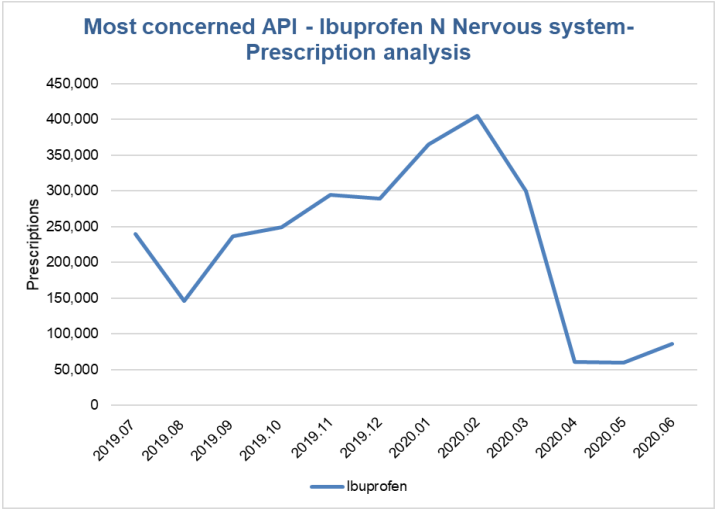


Figure 23: Most concerned API – ATC 1 Ibuprofen N Nervous system – Prescription analysis of supply bottlenecks with first notification since January 2020

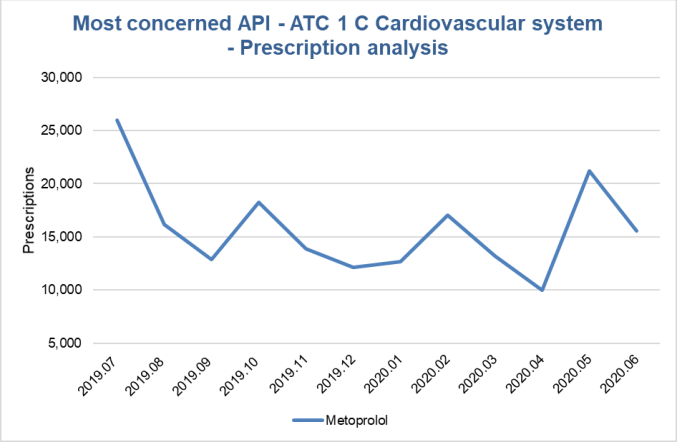


Figure 24: Most concerned API – ATC 1 C Cardiovascular system – Prescription analysis of supply bottlenecks with first notification since January 2020

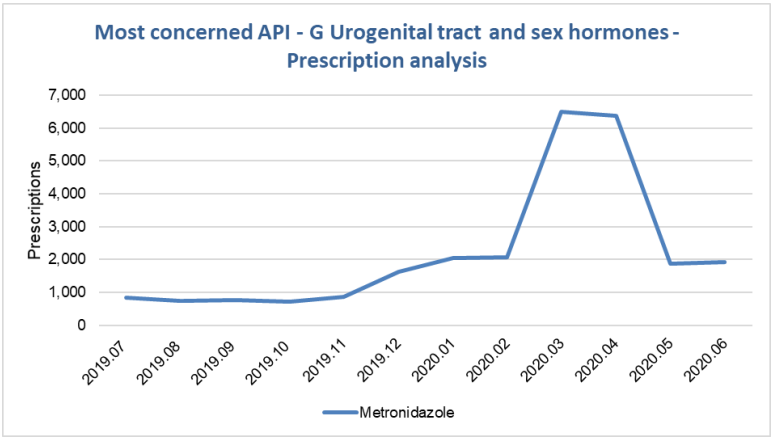


Figure 25: Most concerned API – ATC 1 G Urogenital tract and sex hormones – Prescription analysis of supply bottlenecks with first notification since January 2020

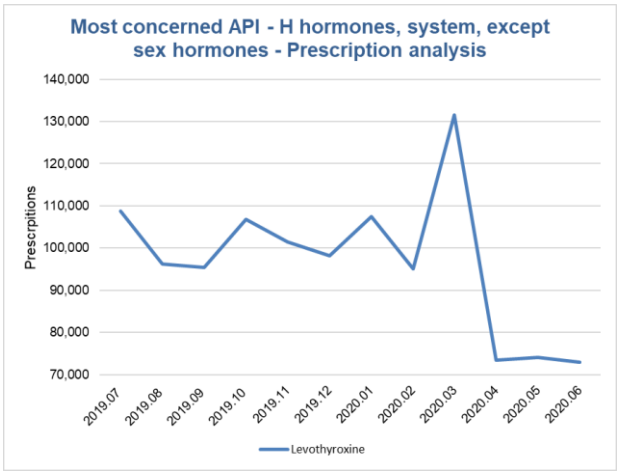


Figure 26: Most concerned API – ATC 1 H hormones, except sex hormones – Prescription analysis of supply bottlenecks with first notification since January 2020

#### 6.2.4.1 ATC 1 group - CEP

Table 7 shows the country of the production facilities for the API that a CEP owned in the period from January to June 2020. Production sites in China and India have a CEP for almost every API. In the European Union, however, manufacturers also have CEPs for every selected API. The low number of production sites for the API Ibuprofen (n=6), Midazolam (n=5), Propofol (n=5) and Salbutamol (n=7) is striking.

Table 7: Most concerned API and their location of CEP holders

| API | China | India | European Union | Other |
|---|---|---|---|---|
| Salbutamol | 0 | 5 | 2 | 0 |
| Amoxicillin | 5 | 4 | 11 | 2 |
| Azithromycin | 5 | 4 | 3 | 0 |
| Aciclovir | 1 | 2 | 5 | 1 |
| Metronidazole | 2 | 1 | 2 | 0 |
| Ibuprofen | 1 | 3 | 1 | 1 |
| Paracetamol | 4 | 3 | 1 | 2 |
| Morphine | 0 | 0 | 11 | 0 |
| Propofol | 0 | 1 | 2 | 2 |
| Metoprolol | 4 | 9 | 4 | 4 |
| Levothyroxine | 0 | 3 | 4 | 0 |
| Midazolam | 0 | 3 | 2 | 0 |

# 7 Results of the interviews

The results of the expert interviews have been arranged in eight categories. As described in chapter 5.2.3 the most important statements of the experts were translated from the transcripts (APPENDIX G) into English and assigned to the eight main categories. These most important statements can be seen in Table 9 in APPENDIX F. In this chapter the most important points of the experts in the respective categories are mentioned.

The eight main categories are:

1 Overall changes in the German pharmaceutical market in the Corona pandemic
2 Cause of supply bottlenecks
3 Changes in prescription of pharmaceuticals from March to May 2020
4 Supply bottlenecks: ATC 1 / ATC 2
5 Supply bottlenecks: API
6 From supply bottleneck to supply shortage of the population?
7 Other Complications
8 Future proposals for change / Lessons learned

1 Overall changes in the German pharmaceutical market in the Corona pandemic

A general, consistent picture of the changes in the pharmaceutical market showed that there was an increased demand in the Rx-pharmaceutical and OTC market due to the corona pandemic. The supply bottlenecks that have existed for some time before have also become even more noticeable due to the Corona pandemic. According to the high street pharmacist (HS.P) broadly based supply bottlenecks across many indications and many manufacturers occurred (HS.P; A1).

Wholesaler 2 (W2) stated that, in times of the pandemic, logistical processes also had to be adapted in the wholesale sector to continue to be able to guarantee a comprehensive, nationwide, and quick supply, as older employees and employees with families were also partially absent (W2; A1). In addition, Wholesaler 1 explicitly mentioned that there was an increased shift from high street pharmacies to the mail order business. More Rx-pharmaceuticals were transacted via the mail order business

or online pharmacy than before the pandemic. In case of OTC-pharmaceuticals, this was already common before the pandemic that pharmaceuticals being purchased via mail order business or online pharmacies. For Rx-pharmaceuticals, this was not a common method before the Corona pandemic (W1; A1).

Also, many more N3 packages (larger packages that last three months or longer) were prescribed than N1 packages (that last for about a month), which also has economic consequences. It leads to a margin drop. Smaller packages have a bigger margin, this is related to the pharmaceutical price regulation, which is dictated to the wholesale trade (W1; A1; HS.P; A5). The high street pharmacist also mentioned that substitution of Rx-pharmaceuticals in the pharmacy at the time of the first peak of the Corona pandemic were made easier by laws and regulations because of the protection against refunds (HS.P; A1). Additionally the high street pharmacist stated after the phase of increased demand, sales in the OTC market also fell in pharmacies (HS.P; A17).

2 Cause of supply bottlenecks

With regard to the causes of the supply bottlenecks that occurred in the period from January to June 2020, the experts mentioned two main causes. One is the ‘interrupted or restricted production of API and their interrupted supply chain’ and the other main reason is the ‘increased demand’ on the part of pharmacies and patients (HO.P; A1, HS.P; A3, W1; A2, W2; A2).

Raw materials are produced in the Far East, especially in countries such as India and China. Many manufacturers of raw materials and API are located in Wuhan. If production in these regions is reduced to a low level or even stopped, this means global consequences for the availability and production of pharmaceuticals. In consequence, the pandemic has weakened the global supply chain and therefore supply capacity has been limited (HO.P; A1, HS.P; A3, W1; A2, W2; A2). The high street pharmacist also mentioned he believes in information by media that China banned exports of certain API (HS.P; A3). Already in December/January it was announced that supply bottlenecks would occur due to restriction of the production of important API (HS.P; A7, W1; A2).

On the other hand, there was an increased demand by pharmacies and patients.

Additionally, there was so-called panic buying. In case of prescription of pharmaceuticals, more larger packages were probably prescribed and thus stockpiled (HS.P.; A3; A5, W1; A1; A3, W2; A1).

W2 gave an example:
*"At the end of the day there are of course chronically ill people or people or families who say: Ok, I don't know what to expect, I just want a bit of security to be able to take my important pharmaceutical, which I need for my heart, for example, I just want to make sure that I am taken care of, because I don't know how it will develop in the coming months"* (W2; A1).

However, by the experts the 'increased demand' was not clearly confirmed as the main cause of the occurred supply bottlenecks. Wholesalers 1 and 2 stated that it took place, but the impact and magnitude are not clearly identifiable (W1; A3, W2; A1). The high street pharmacist also doubts that the most common reason for the supply bottleneck is the 'increased demand/sales in the market'. The pharmacies are not in a position to stock up for a long period (HS.P; A3). There are for example dangers of changing prices and changing rebate contracts (HS.P; A3). Therefore, the high street pharmacist sees the 'interrupted supply chain' as the main reason of the supply bottlenecks.

He stated:
*"Once the supply bottleneck is there, it will not disappear the next day, as the supply chains were interrupted"* (HS.P; A3).

In addition, the rebate contracts of the health insurance funds may have played a role in the cause of the supply bottlenecks that occurred. In some cases, as a result of the rebate contracts, all of the pharmaceuticals are based on one or a few manufacturers. Many manufacturers are limiting their production of certain pharmaceuticals because, for example, they are not receiving important rebate contracts and have therefore even moved to withdraw completely from the production of pharmaceuticals with certain API (HS.P; A21). W2 described a 'domino effect' of supply bottlenecks. If a package of one size or other potency is not available, then later the others are not available either (W2; A2).

However, it was also mentioned that supply bottlenecks had already existed in the past

and have been a problem until today (HO.P; A1).

3 Changes in prescription of pharmaceuticals from March to May 2020

The high street pharmacist mentioned an extremely good sales performance in the pharmacies in March in contrast to April when the pharmacies were empty and fewer pharmaceuticals were prescribed (HS.P; A3).

4 Supply bottlenecks: ATC 1 / ATC 2

The experts were also asked which of the ATC 1 or ATC 2 groups were most affected by supply bottlenecks from their point of view. HS.P stated that pharmaceuticals of the cardiovascular system, antibiotics, thyroid hormones, inhaled corticoids, antidiabetics, anaesthetics and analgesics were particularly affected in the first peak of the Corona pandemic (HS.P; A9; A10). HO.P mentioned that anaesthetics were particularly concerned by the supply bottlenecks in hospitals (HO.P; A4). W1 had noticed supply bottlenecks, especially of the ATC groups analgesics and cardiovascular System (blood thinners) (W1; A4). Wholesaler 2 noted that renin-angiotensin effective preparations (angiotensin II receptor blockers) and anaesthetics and narcotics were particularly affected by supply bottlenecks. (W2; A3).

5 Supply bottlenecks: API

The experts were also asked which specific API were in their view particularly affected by supply bottlenecks. The high street pharmacist indicated that Paracetamol and Ibuprofen, Amoxicillin, Clavulanic acid, for example Cefuroxime, Cefixime, were particularly affected, the anaesthetics Propofol, Naloxone and Atropine as well. Propofol was declared to be deficiently available. Subsequently, anaesthetists were worried that they would not be able to perform any more operations (HS.P; A9; A11; A12; A13). In hospital supply bottlenecks occurred in the field of anaesthetics and narcotics, especially the API Propofol, Midazolam, Noradrenalin were particularly affected. Analgesics were also reported, but with the explanatory note that there were always problems there, as the raw material comes from Asia and was not accordingly developed during the Corona pandemic (HO.P; A6; A7; A9). W1 listed Ibuprofen as a known API, which was particularly affected by a supply bottleneck in the Corona

pandemic (W1; A4). W2 also mentioned that the anaesthetic propofol was particularly affected by supply shortages during the first peak of the Corona pandemic. (W2; A3).

6 From supply bottleneck to supply shortage of the population?

Overall, it can be said that the experts naturally cannot say exactly whether the supply bottlenecks caused by the Corona pandemic also led to supply shortages, i.e., whether important pharmaceuticals could not be substituted and posed a health threat to certain population groups.

The hospital pharmacist stated that in the first peak of the Corona pandemic an advantage for hospitals was that empty beds were kept free and planned operations were postponed. The hospitals were relatively empty. He also said that of course fewer people admitted to hospital because of the pandemic, but the serious cases were always treated, and no shortage of care arose in their hospital. Even then, it was not the case that standard pharmaceuticals (e.g.: antibiotics, pharmaceuticals for the cardiovascular system, etc.) became short, which would have put the patients at risk. However, problems arose in the field of anaesthetics and narcotics, where demand was much higher than usual. Noticeably more ventilated patients were treated in the intensive care units. Severe COVID-19 cases in the intensive care unit, even if they are put into a so-called artificial coma, require a lot of anaesthetics. These anaesthetics often became scarce and not enough were available. After consulting the doctors, the hospital pharmacist often had to find alternative solutions with the senior and chief physicians (HO.P; A2; A4; A5; A11). Sometimes the physicians needed to use inferior API that probably did not have a licence for a certain case. To find alternative API was not always easy, but in the end solutions were found without endangering patients (HO.P; A5).

The HS.P stated that overall a shortage of care for some patients probably arose. Of course, this also depends on how pharmacies stocked up on their own. In his pharmacy all patients were served because it had enough supplies. But patients also came to his pharmacy who had previously been to other pharmacies where pharmaceuticals had not been available. In general, however, the high street pharmacist stated that there was an overall shortage of medical care, because people did not risk to go to doctors, hospitals, and pharmacies (HS.P; A6; A17).

W1 said he could not observe a real supply shortage of pharmaceuticals and never believed that the health system would reach its limits. It was noticeable that not all pharmacies could get enough reorders for certain pharmaceuticals, but overall, there were still enough pharmaceuticals available (W1; A6; A7).

W2 explained that it is difficult to say whether the supply bottlenecks led to a supply shortage. Overall, he thinks that we in Germany were not able to treat all patients safely or in sufficient quantities. According W2, in Germany we are equipped well with pharmaceuticals, but he can fully understand if there are patients who do not share his opinion at all. For example, in individual cases patients do not receive their preferred preparation, but a substitutional preparation, which they may not tolerate well (W2; A5).

W2 also mentioned the supply bottlenecks in connection with health insurance funds and rebate contracts. According to regulations, the pharmacies were able to substitute more freely and were therefore more flexible. W2 questioned this and argued that the statutory health insurance funds would not open up the rebate contracts on their own initiative, as there were also costs and economic interests behind them (W2; A3).

7 Other Complications

This category presents other complications mentioned by the experts which occurred during the Corona pandemic.

The pneumococcal vaccine is mentioned as an example, that in terms of supply bottlenecks, Germany should not be seen separately. It is a global phenomenon. Pneumovax was scarce in Germany in the first peak of the Corona pandemic.

In the case of pneumococcus, *“we had the vaccine from Japan here, in Japanese writing, which nobody could read, or the fact that they launched a pneumococcal vaccine on the market here, which was actually intended for Iran. This is, of course, difficult. I do not know what the company’s motives were for withholding the vaccine from the market for which it was intended. I cannot understand this. Here the postponements took place”* (HS.P; A8).

Also, according to HS.P., the state also outsourced its responsibility. *“If the state had been aware of its responsibility, as many thousands of pharmacies have done, we*

*would have dealt with the situation quite differently and most pharmacies were not as awkward as the state"* (HS.P; A20). As an example, the procurement of masks is mentioned, which was transferred to private people. In consequence, the responsibility was transferred from the state to others (HS.P; A20).

W2 also mentioned a problem that existed with masks, far from prescription pharmaceuticals.

*"There were existing supply bottlenecks of face masks. The Federal Ministry of Health bought counterfeit goods in China. You could see what a dangerous market it was and many producers in China copied a mask that did not have these technical requirements or were perhaps even made of material that was harmful to health, and if you wear them all day, then I do not know"* (W2; A6).

8 Future proposals for change / Lessons learned

In this category, the recommendations for action and the lessons learned due to the Corona pandemic which are important from the experts' point of view are presented. All experts agree that the production of important pharmaceuticals should be relocated back to Europe, to simply have security , but they also see difficulties or do not believe it will be carried out (HS.P; A19, HO.P; A15, W1; A12, W2; A8 ).

W1 said that he personally does not believe in the relocation of the production of essential pharmaceuticals to Europe, because a manufacturer cannot be forced to produce at a special location (W1; A11). However, to promote the production of important pharmaceuticals in Europa, incentives would have to be created to convince the manufacturers of production in Europe. Pharmaceuticals need reasonable prices, but on the other hand this also puts a burden on the health system.

*"The state could say, I will be a bit more careful with taxes and use them to finance the health system, but I do not think so"* (W1; A12).

W2 suggests that pharmaceutical entrepreneurs should be subsidised by the state or even Europe-wide to produce essential API/pharmaceuticals in Europe (W2; A8). HO.P mentions the problem *"money rules"* and said that the "*health care system will not be able to pay for this either, if pharmaceuticals are produced in the high sector in Europe"*

(HO.P; A15).

Manufacturers and pharmacies should be obliged to hold a stocking up of certain API. Additionally, pharmaceutical companies should not only produce to order or ‘just in time’ but should also have important pharmaceuticals in stock to be able to react (HS.P; A19, HO.P; A14; A16, W2; A7; A8). The HO.P also said that the stocks of certain API must be increased in hospital pharmacies. There was a regulation that certain anaesthetics had to be kept in stock in the hospital in sufficient quantity, which corresponds to an average demand of three weeks. Before the new regulation, a stockpile of only two weeks was valid. The hospital pharmacist said that even before the new regulation, they had a stock of anaesthetics for three weeks in the hospital pharmacy. However, this stock was not sufficient, and he had to increase it for an ‘average need’ corresponding to four to five weeks (HO.P, A14).

Furthermore, the experts mentioned that the rebate contracts with the health insurance funds should be reconsidered. The rebate contracts partly shift the responsibility of certain API to only a few or one manufacturer for a respective health insurance fund. Likewise, rebate contracts exclude manufacturers and, as a result, production for certain API and pharmaceuticals is sometimes concentrated on only a few manufacturers (HS.P; A21, W1; A10; W2; A8). Additionally, W2 calls for more flexibility of dispensation of pharmaceuticals. If patients can only tolerate certain preparations, they should receive them as soon as possible. It often takes a long time before the patients receive the preparations that are well tolerated by them (W2; A8).

W1 emphasises that the high street pharmacies were of great importance in the first phase of the Corona pandemic. The advisory activities, possibilities to produce disinfectants and rapid supply with pharmaceuticals within a few hours were of great importance. The pandemic thus showed the importance of high street pharmacies and they therefore should continue to be strengthened (W1; A13).

# 8 Development of vaccines

This chapter briefly presents the four different types of vaccines which are pursued in COVID-19 vaccine development. The status of the development (status: 05 March 2021) of vaccines at international and national level is also examined.

## 8.1 Types of vaccines

“Different types of vaccines have different characteristics in terms of the immune response they trigger. The pathogens also have different characteristics, so not all vaccine types are suitable for all pathogens” (85). It is therefore necessary to find out which vaccines are best suited to a particular disease (85). Currently there are four different main types of COVID-19 vaccines under development which have their advantages and disadvantages. Which one will be most successful, is not known yet. The four main underlying principles are: Virus-based vaccines, Viral-vector vaccines, Nucleic-acid vaccines, and Protein-based vaccines (86,87).

Virus-based vaccines

The virus-based vaccine is a commonly used method in licensed vaccines (87). There are inactivated (87) (e.g. Hepatitis A (88)) or attenuated vaccines (87) (e.g. measles (89).

In case of COVID-19 vaccines, these virus-based vaccines involve isolating SARS-CoV-2 pathogens from Corona patients, propagating them in cell cultures and then inactivating or greatly attenuating them by various methods (87,90,91). The virus based COVID-19 vaccines are primarily developed in the inactivated form. In these inactivated virus-based vaccines, “the virus is rendered uninfectious using chemicals, such as formaldehyde, or heat” (87). There is also the development with a live attenuated virus. In this form a “virus is conventionally weakened for a vaccine by being passed through animal or human cells until it picks up mutations that make it less able to cause disease” (87).

Viral-vector vaccines

Viral-vector vaccines integrate parts of the genome of SARS-CoV-2 into the genome of viruses that are harmless to humans. These vectors are then introduced into human cells, which then produce SARS-CoV-2 antigens and present them to the autoimmune system. Viral-vector vaccines are divided into replicating vectors (e.g. weakened measles), which can multiply further in the cells, and non-replicating viral vectors (e.g. adenovirus), which cannot replicate. An existing example of a viral-vector vaccine is Ebola (replicating) (87,91,92).

Nucleic-acid vaccines

One hope of the scientific community developing COVID-19 vaccines are the nucleic-acid vaccines, the DNA vaccines and especially the RNA vaccines, because they are safe and easier to develop (87) and there is no risk of infection during vaccination. Moreover, the production of larger quantities is possible (scaling up production), which is an advantage in an emergency situation like the Corona pandemic (92). However, before the licenced RNA vaccines against COVID-19, no RNA or DNA vaccines have yet been approved for licensed vaccination of humans, so the long-term clinical benefit of these vaccines is still not determined (87).

This approach involves inserting nucleic acid containing the genetic information of SARS-CoV-2 directly into the human cell, “which then churn out copies of the virus protein; most of these vaccines encode the virus's spike protein” (87). These vaccines are also called gene-based vaccines because they contain selected genes from the virus (91).

Protein-based vaccines

Protein-based vaccines are divided into two forms. Either protein subunits of the pathogen (not the whole virus) are injected directly into the body or the outer, empty shell (Virus-like particles – VLP) of the coronavirus is injected into the body to elicit an immune response (87). An existing example for the VLP vaccine is human papilloma virus (HPV) (93) and for the protein subunit vaccine against Herpes-Zoster (94).

## 8.2 Steps of development

As seen in Figure 27, vaccine development is a long process and usually takes 15 years or even more. First, the antigens must be identified and isolated. Pre-clinical tests (e.g. animal experiments) and toxicology studies normally take two to four years. The estimated time for each of the three clinical phases is about two years. Phase I will be the first to test to evaluate the overall safety and tolerability of a vaccine and its ability to induce an immune response on healthy people. In Phase II, the safety is tested on patients and the correct dose, tolerability and immune response are tested on a larger number of volunteers. In Phase III, the effectiveness of the vaccine will be tested on several thousand to several tens of thousands of volunteers. The aim is to test whether the vaccine really protects against infection and what side effects occur (74,95).

Following these steps it takes one to two years before the vaccine is approved in Europe. This is different to the COVID-19 vaccine. Due to the corona pandemic, the COVID-19 vaccine is being developed as quickly as possible. The discovery phase is also no longer necessary, as knowledge of the development of SARS-CoV and MERS-CoV vaccines was already available and existing processes were adopted. Likewise, the phases I-III of the clinical trials are not consecutive but overlap. “In the meantime, vaccine producers have started the large-scale production of several vaccine candidates, at risk” (95). The approval process in Europe is also shorter than usual as well. (96). The EMA also starts ‘rolling-reviews’, it is one of the regulatory pathways that EMA uses to speed up the assessment of a promising vaccine during a public emergency like the Corona pandemic. The committee started evaluating first batches of data on vaccines, which come from laboratory studies, before formal application of vaccines is submitted (97,98).

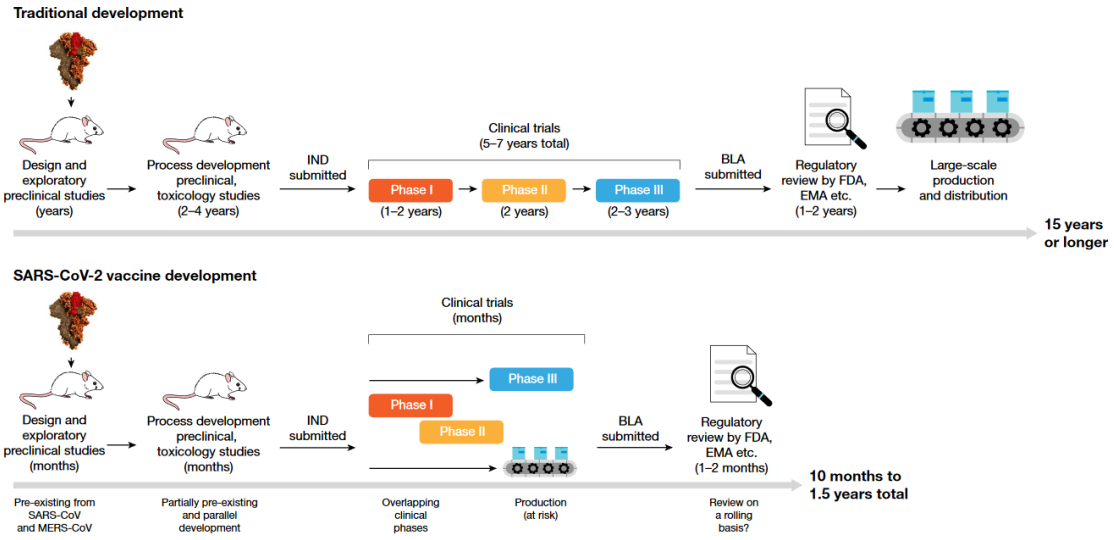


Figure 27: Steps of development of traditional and SARS-CoV-2 vaccines (95)

## 8.3 Status of development

The WHO regularly announces the status of development of vaccine candidates against SARS-CoV-2. WHO currently counts 260 vaccine developments worldwide (status: 05 March 2021). Table 8 shows an overview of the status of development of the various COVID-19 vaccines according to the WHO these, 78 candidate vaccines are in clinical evaluation. 16 candidates are in Phase III, five in Phase II-III, six in Phase II, 24 in Phase I-II, 27 in Phase I. In Phase III of the most advanced clinical development there are six virus-based inactivated vaccines, four non-replicating viral-vector vaccines, two RNA based, one DNA based and two protein subunit vaccines. 182 candidate vaccines are currently in preclinical evaluation (86).

Table 8: Status of development of COVID-19 vaccines according to WHO (86)

| | | Preclinical evaluation | Phase I | Phase I-II | Phase II | Phase II-III | Phase III |
|---|---|---|---|---|---|---|---|
| | | | Clinical stage | | | | |
| **Virus-based** | Inactivated | 11 | 2 | 1 | 1 | | 6 |
| | Attenuated | 2 | 1 | | | | |
| **Viral-vector** | Replicating | 19 | | 3 | 1 | | |
| | Replicating + Antigen Presenting Cell | | 1 | 1 | | | |
| | Non-Replicating | 22 | 8 | | | | 4 |
| | Non-Replicating + Antigen Presenting Cell | | | 1 | | | |
| **Nucleic-acid** | RNA | 23 | 5 | | 1 | | 3 |
| | DNA | 15 | 4 | 4 | | 2 | 1 |
| **Protein-based** | Protein subunit | 68 | 6 | 12 | 3 | 2 | 2 |
| | VLP | 18 | | 2 | | 1 | |
| | **Total** | **178 (+4 others)** | **27** | **24** | **6** | **5** | **16** |

## 8.4 Development and market authorisation of vaccines in Germany

COVID-19 vaccines are also being developed in Germany and as already described in Chapter 3.3.5, three German vaccine projects are subsidised by the state. These vaccines will be presented in this chapter.

BioNTech, in collaboration with Pfizer, has developed an RNA vaccine that is in Phase III (86). The Committee for Medicinal Products for Human Use (CHMP) at the EMA started the second 'rolling review' process for the BioNTech BNT162b2 vaccine against COVID-19 for Europe at the beginning of October (98). Previously, the first rolling review of the non-replicating viral vector vaccine ChAdOx1-S of the British manufacturer AstraZeneca in cooperation with Oxford University was started (97).

BioNTech applied for approval in the European Union on 30 November 2020 at the same time as the American company Moderna which has also developed an RNA vaccine (99,100). On 21 December 2021, the EMA recommended vaccine approval for BioNTech & Pfizer's COVID-19 vaccine (101). Subsequently, the EU granted a conditional marketing authorisation in the 27 EU countries. Conditional, because manufacturers must continue to submit data on long-term efficacy, allergic reactions and side effects to the EMA (102,103). On 6 January 2021, the vaccine of the company Moderna and on 29 January 2021 the non-replicating viral-vector vaccine of AstraZeneca were also approved in the EU and have subsequently received conditional marketing authorisation in Germany (104,105). On 11 March 2021, the European Commission granted a conditional market authorisation for the non-replicating viral-vector vaccine of Johnson & Johnson (106).

The company CureVac, with headquarters in Tübingen is also developing an RNA-based COVID-19 vaccine and is currently in phase III of clinical trials (86,99).

Together with the DZIF - German Centre for Infection Research, IDT Biologika GmbH is developing the non-replicating viral-vector vaccine MVA-SARS-2-S for the immunisation of adults and older risk groups. MVA is an attenuated smallpox virus. This vaccine candidate has been in Phase I clinical trials since the beginning of October, and on 9 October a first female volunteer was injected with the vaccine. MVA-SARS-2-S has already been produced and filled in large quantities by IDT Biologika

(74,86,99,107).

With these three COVID-19 vaccine projects funded by the state, it was agreed with the vaccine developers that larger quantities of a potential vaccine would be made available to the population in Germany and Europe (74).

## 8.5 Race of effective vaccines worldwide

The large number of vaccines being developed worldwide (n=260) illustrates the international race of vaccine developers (86). On 11 August 2020 Russia also licensed a vaccine early on, which was not fully tested, the phase III clinical trials had not started at the time of approval. The Gamaleya Institute in Russa developed the non-replicating Viral-vector vaccine on Adenovirus basis named ‘Gam-COVID-Vac’ / ‘Sputnik V’ (108–110). Thereupon, the PEI issued a warning regarding the approval of Sputnik V. “Low transparency and, according to the information, missing safety, and efficacy data from clinical trials on several thousand test persons were to be criticised. […] A vaccine should only be authorised if the demonstrated benefits clearly outweigh the potential risks” (111). The EMA has now initiated a rolling review of the Sputnik V vaccine on 4 March 2020 (112).

Also, a vaccine of the Chinese company CanSino Biologicals the non-replicating Viral-vector vaccine candidate on Adenovirus basis, named ‘Ad5-nCoV’, was licenced for military use in China before the clinical trial phase III started (110,113).

## 8.6 European Union Corona vaccine strategy and German national COVID-19 vaccination strategy

“On 17 June 2020, the European Commission presented a European vaccine strategy to accelerate the development, manufacturing and deployment of vaccines against COVID-19.” (114). “The aim of the Corona vaccines strategy is to ensure “the quality, safety and efficacy of vaccines, securing timely access to vaccines for Member States and their population while leading the global solidarity effort, ensuring equitable and affordable access for all in the EU to an affordable vaccine as early as possible” (115).

To secure the vaccines for the EU, advance purchase agreements were signed with manufacturers of promising COVID-19 vaccines that would allow sales in the EU once the vaccine has been tested and approved. The European Commission signed contracts with the manufacturers Moderna (up to 460 million doses), BioNTech & Pfizer (up to 600 million doses), AstraZeneca (up to 400 million doses), Johnson & Johnson (up to 400 million doses), Sanofi & GSK (up to 300 million doses), and CureVac (up to 405 million doses) to allow them to purchase vaccine doses on behalf of all EU member states once the manufacturer's vaccine candidate has been tested for efficacy and approved in the EU. Further exploratory talks with the intention for further advance purchase agreements are conducted with Novavax (up to 200 million doses) and Valneva (up to 60 million doses).

The German National COVID-19 vaccination strategy is based on the one of the European Union. The Federal Government procures vaccines via a centralised EU procurement mechanism, which has agreed the Advance Purchase Agreements with the manufacturers (116). Germany will receive 64.1 million doses of BioNTech & Pfizer's licensed vaccine through the EU, 50.5 million doses of Moderna's vaccine, 56.3 million doses of AstraZeneca's vaccine and 36,7 million doses of Johnson & Johnson's vaccine. In addition, there is another option for a further 30 million vaccine doses from BioNTech & Pfizer. Additional doses of Moderna's vaccine are still being negotiated nationally. If more vaccines are licenced, Germany will receive even more vaccine doses. By 10 March 2021, 12.5 million vaccine doses had been delivered to the federal states. The vaccine from Johnson & Johnson has not yet been delivered (117).

Germany's vaccination strategy is divided into 2 phases. In phase I A, a targeted centralised vaccination is planned, as there is still little vaccine available at this time. In phase I B, when more vaccine doses are available, an expanded centralised vaccination is intended. When the vaccine will be widely available, a broad decentralised routine vaccination is proposed (116). A kind of tier system has also been introduced, which determines which population groups are vaccinated first. First and foremost, over 80 years old, people in nursing homes, medical staff in intensive care units and in emergency rooms and rescue services will be vaccinated. Then 70-80-year-olds and certain risk groups and their contacts are vaccinated. This will be further phased in until broad decentralised vaccination can take place (74). Additionally, the Ständige

Impfkommission (STIKO) divided the vaccine schedule into six levels in even more detail (118). Moreover, by 15 January 2021, over 1 million people have been vaccinated in Germany (cumulated first and second vaccination). By 12 March 2021, 8,863,270 people in Germany had already been vaccinated (cumulated first and second vaccination) (119). An important addition is that two vaccine doses per person must be given at least 3 weeks apart, depending on the vaccine (74). However, the vaccine from Johnson & Johnson only needs to be vaccinated once (106).

## 8.7 Equitable access of COVID-19 vaccines worldwide

The equitable access of COVID-19 worldwide is of high relevance to overcome the Corona Pandemic worldwide. COVAX (COVID-19 Vaccines Global Access) was initiated by the WHO, Gavi and the Coalition for Epidemic Preparedness Innovations (CEPI). It is a pillar of The Access to COVID-19 Tools Accelerator to purchase and fairly distribute 2 billion COVID-19 vaccine doses worldwide by the end of 2021 (120,121). COVAX is supported by 186 countries worldwide, including Germany. Of these, 92 are countries with low and middle income. Wealthier nations contribute more than poorer countries to the cost of the vaccines that COVAX negotiates with the vaccine manufacturers. If countries have no financial resources, they are entitled to free supplies to ensure equitable access to vaccines worldwide (121–124).

To what extent this worldwide support will work and whether a fair distribution will take place is not yet clear, because parallel to COVAX, the countries themselves also secure vaccines from the manufacturers.

The EU's participation in the COVAX initiative (contribution of €500 million) also runs in parallel with the Advanced Purchase Agreements (122).

Furthermore, the Head of WHO Tedros Adhanom Ghebreyesus warned at the World Health Summit on 25 October 2020 against 'vaccine nationalism': "Let me be clear: vaccine nationalism will prolong the pandemic, not shorten it" (125). He also stressed: "It is natural that countries want to protect their own citizens first but if and when we have an effective vaccine, we must also use it effectively. And the best way to do that is to vaccinate some people in all countries rather than all people in some countries" (125). At the UN special summit on 3 December 2020, he warned once again that the

gap between rich and poor countries is widening. The global crisis has to be treated as a public good worldwide and a worldwide solution has to be found (126).

# 9 Discussion

This analysis showed that the Corona pandemic has led to dynamic changes in the German pharmaceutical market.

In the description of the background in the subchapters 2.1 to 2.3 the worldwide and national dynamic development of COVID-19 was presented. It has led to contact restrictions and ‘lockdowns’ worldwide. The international economy also suffered, the worldwide production of industrial goods and raw materials was shut down and international supply chains were interrupted.

In Chapter 3.3 the changes and regulations in the German pharmaceutical market, which were a reaction due to COVID-19, became clear. The regulatory changes, such as the COVID-19 agreement on the framework agreement according to § 129 (2) SGB V, the subsequent SARS-CoV-2 Pharmaceutical Supply Regulation and the Medical needs Health Care Insurance Regulation-MedBVSV were introduced as reactions to the dynamic developments in the Corona pandemic, to be able to continue to guarantee high-quality health care with pharmaceuticals. Rebate contracts were restricted nationwide, and pharmacies were no longer limited in the dispensation of pharmacies as before, i.e., substitution of pharmaceuticals was made much easier and pharmacies were no longer bound to certain package sizes.

The results of this research show two different facets of the dynamic changes in the German pharmaceutical market. In Chapter 6 Results of the exploratory data analysis and in 7 Chapter Results of the interviews, the supply bottlenecks were analysed, and it was investigated in more detail whether the supply bottlenecks also led to supply shortages in the population. Thus, the changes in the supply bottlenecks of pharmaceuticals were examined more closely. In Chapter 8 on the other hand, the development of new vaccines, to stop the Corona pandemic, was examined worldwide and nationally.

The results of the exploratory data analysis showed that in March and April of 2020, an increased number of supply bottlenecks were reported. Supply bottlenecks have been a problem in the European and German pharmaceutical market since 2012 and have now been exacerbated by the Corona pandemic.

A postponement of the voluntarily given causes for a supply bottleneck could also be identified. The most common cause of the supply bottlenecks with a ‘change notification’ was ‘quality issues/product contamination’. The situation was different for supply bottlenecks with a ‘change notification’ from January to June 2020. Many manufacturers stated as a reason ‘increased demand/sales in the market’. The interrupted supply chain was another reason for the supply bottleneck. Some manufacturers even explicitly stated the Corona pandemic as the cause of the occurred supply bottlenecks.

The determined supply bottlenecks in the quantitative analysis corresponded mostly with the supplementary data of the experts of the expert interviews. Cardiovascular pharmaceuticals, pharmaceuticals of the N Nervous system especially the N01 Anaesthetics and narcotics and the N02 Analgesics, J Antiinfectives, especially the J01 Antibiotics were found as most affected by a supply bottleneck in the quantitative analysis and were also identified as such by the experts.

Three experts mentioned that Propofol was particularly affected by supply bottlenecks as well as Midazolam which the hospital pharmacist also mentioned as an API particularly affected by supply bottlenecks. According to Bundesverband Deutscher Krankenhausapotheker e.V. (ADKA), which represents around 2400 hospital pharmacists in Germany, the supply situation of Midazolam was classified as particularly critical, so that in “a BMG/ADKA Midazolam relief campaign, 12 hospital pharmacies produce 100,000 Midazolam units ready for distribution on behalf of the federal government to ensure the intensive medical care of patients for the time of the existing pandemic situation” (127).

Furthermore, Naloxone, Atropine, Noradrenaline, Cefuroxime and Cefixime were named by the experts as API that have also become scarce. No supply bottleneck could be identified for Naloxone and Atropine in the quantitative analysis. Some few supply bottlenecks could be however identified, for the API Cefuroxime, Cefixime and Noradrenalin, but were not particularly affected according to the quantitative analysis.

The trend analysis of prescriptions from July 2019 to June 2020 showed a relatively homogeneous picture from February to May 2020 (first peak phase of the corona pandemic). The prescriptions in the whole pharmaceutical market as well as the prescriptions of the supply bottlenecks that occurred show that more pharmaceuticals were prescribed in March compared to the previous month. These prescriptions then recorded a large decrease until May 2020, and a slight increase is generally seen in June 2020. This is also consistent with the statement of the high street pharmacist. The analysis also showed that in March a lot more N3 packages were prescribed than in the previous month and the number of N1 packages decreased. This shift is also in line with the experts' statements. More and more larger packs were dispensed, and shifts have taken place there.

The reasons for the shifts in the number of prescriptions can only be assumed. The manufacturers mentioned as a main cause for the indicated supply bottlenecks 'increased demand/sales in the market', which was also given as the main cause for the supply bottlenecks of the supply-relevant API most concerned. According to the experts an increased demand on the part of the patients and pharmacies is confirmed, who increasingly stocked up with prescription pharmaceuticals, which could result in the so-called 'panic buying'. Nevertheless, the experts somewhat weakened this cause for supply bottlenecks, naming an equally important reason for the supply bottlenecks that occurred as the interrupted supply chain and the discontinued or restricted production of raw materials in the Far East, especially India and China, which produce many supply relevant API which are not much produced in Europe. This also coincides with media reports for this period (5,64,128). In addition, it is important to note that the supply chains of API and finished products are very sensitive and prone to disruption (129).

Moreover, it is important to mention the Pro Generika e.V. and Mundicare study on API found, that Asia, especially China and India, holds almost twice as many CEP as Europe. Furthermore, this study documented dependencies that relate to the production of API. Europe and Germany are dependent on non-European manufacturers, still concentrated on a few regions of the world. In India and China, many production sites are also concentrated in a few provinces. Also, for many API only a few manufacturers produce this API. For more than half of the API, there are only a few manufacturers worldwide who hold one to five CEP. In fact, one sixth of the existing API are no longer

produced in Europe at all (130). Here, the dependence on Asia especially, China and India in the production of API becomes clear once again, which the Corona pandemic exacerbated and brought into focus.

Thus, a possible explanation for the increase in prescriptions in the overall market and the supply bottlenecks, based on the quantitative and qualitative results, could be that pharmacies and patients wanted to stock up on pharmaceuticals when it became clear that a lockdown was coming. Then, in April and May, fewer pharmaceuticals were prescribed, and combined with the increased demand in March and the limited production of API in the Far East and in addition the resulting disruption of supply chains led to increased supply bottlenecks. This is a possible explanation but is by no means a confirmatory statement.

Rebate contracts were also mentioned as a possible cause for the supply bottlenecks that occurred, although rebate contracts have always been considered problematic, as the responsibility for important API is often reduced to only one or a few pharmaceutical companies. According to a study by the IGES Institute, the more contract partners involved in a discounted API, the less often pharmacies must dispense alternative preparations. This is three times more often the case when exclusive instead of open-house contracts with several partners exist between statutory health insurance funds and pharmaceutical manufacturers (131).

An important aspect of this investigation was also to find out if the supply bottlenecks which occurred also led to supply shortages. This could not be deduced from the exploratory trend analysis. All in all, the experts interviewed could not say exactly, if the arisen supply bottlenecks of pharmaceuticals also led to a supply shortage in certain population groups. According to the experts, in general, no real supply shortage with pharmaceuticals occurred in the population due to the supply bottlenecks. Furthermore, the German health care system did not reach its limit. In individual cases, a supply shortage probably occurred because, for example, according to the high street pharmacist, customers came to the pharmacy who had not received a pharmaceutical from several pharmacies. It was also mentioned that individual patients are not comfortable with not receiving their usual medication.

The experts also said that in general, doctors’ surgeries and hospitals were not fully

occupied. Media reports have brought to light cases where patients did not dare to go to the hospitals or to a doctor and therefore could not be treated (132–134) . The Scientific Institute of the AOK (WIdO) examined the decline in the number of cases of hospital treatments due to the coronavirus lockdown in spring using a valid nationwide database of 27 million AOK-insured persons. During the first lockdown in March and April 2020, the number of hospital patients fell by around 39 percent compared to the same period the previous year. There was also a decrease in the treatment of life-threatening emergencies such as heart attacks (-28%) and strokes with cerebral infarction or cerebral hemorrhage (-15%) (135). In contrast, according to the statements of the hospital pharmacist interviewed in this study, the severe cases during the first peak of the Corona pandemic were still treated in hospital.

According to the hospital pharmacist, an increased need for anaesthetics in hospitals was identified because noticeably more ventilated patients were treated in intensive care units and these severe COVID-19 cases, even if they were put into a so-called artificial coma, require a lot of anaesthetics. Here, according to the expert, a supply bottleneck occurred in hospitals, but solutions for substitutions could be found to treat the patients.

Due to the acute nature of the topic, comparisons to already existing publications are difficult to make, but one conducted publication in the past showed what kind of observations pharmacists made regarding supply bottlenecks and possible supply shortages. In 2017 the Drug commission of pharmacists in Germany (AMK) conducted a survey about implications of supply bottlenecks and shortages in terms of outpatient and inpatient safety. In total, 482 high street (community) and 36 hospital pharmacies participated (136). As you can see in Figure 28, one question was: '*Which observations have you made in your pharmacy in the last three months concerning delivery and supply shortages which have occurred (multiple answers are possible)?'.* 60.4% of the high street (community) pharmacists answered that the patient's therapy adherence was impaired or interrupted while the substitute pharmaceutical was being used. 72.7% of the hospital pharmacists and 54.9% of the high street pharmacists stated that 'a less suitable pharmaceutical agent was prescribed ("2nd Choice")'. Additionally, 56.1% of the high street pharmacists and 63.6% of the hospital pharmacists answered that 'a less suitable delivery / dosage form was applied'. Even 25.8% of the high street pharmacists and 6.1% of the hospital pharmacists observed that a treatment was discounted, and

patient risks were involved. It was also observed that a vital therapy was not possible or was delayed by the delivery bottleneck. The pharmacists were also asked: '*How often, in the last three months, have you experienced supply bottlenecks at your pharmacy that, in your opinion, led, or could have led to health issues for the patients involved?'* It is to be likewise seen that pharmacists observed in the past in individual cases that supply bottlenecks and/or supply shortages occurred, which could have led to health consequences (see Figure 29). This could have been occurred in the Corona pandemic likewise according to the interviewed experts in individual patients (137).

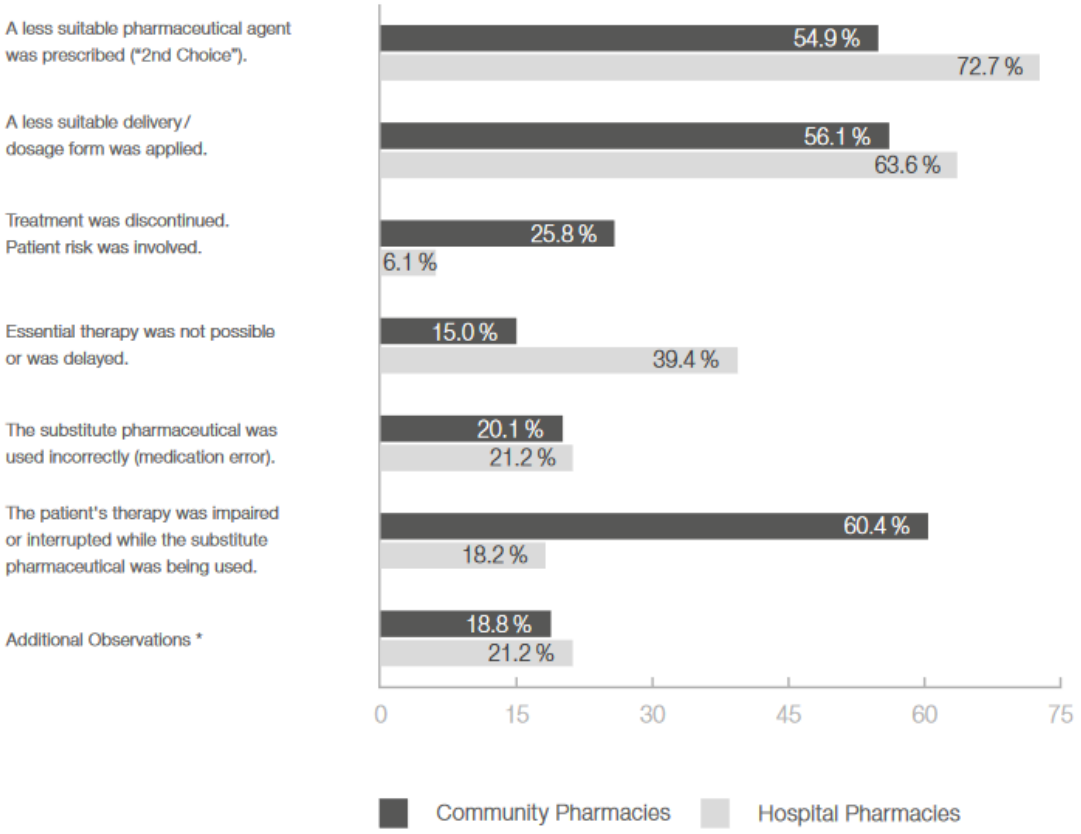


Figure 28: AMK Survey 2017, which observations have you made in your pharmacy in the last three months concerning delivery and supply shortages which have occurred (multiple answers are possible)?

| | Community Pharmacies | Hospital Pharmacies |
|---|---|---|
| never | 11.4 % | 19.4 % |
| < 5 times | 27.6 % | 25.0 % |
| 5 – 10 times | 28.2 % | 33.4 % |
| 11 – 15 times | 10.4 % | 2.8 % |
| > 15 times | 22.4 % | 19.4 % |
| | 100 % | 100 % |

Figure 29: AMK Survey 2017, how often, in the last three months, have you experienced supply bottlenecks at your pharmacy that, in your opinion, led, or could have led to health issues for the patients involved?

Supply bottlenecks have already been discussed in politics in the past, due to the Corona pandemic, the limits of globalisation were pointed out. Then, the problems were discussed more intensively again, and possible changes were discussed to combat the supply bottlenecks and possible arising supply shortages in the European Union and nationally in Germany. Especially with the GKV-FKG, already presented in chapter 3.1.6, Germany took an important step towards being able to better manage supply bottlenecks that may occur in the future. On request of the BfArM, pharmaceutical manufacturers and wholesalers are obliged to provide data on available stocks, production, and sales volume as well as information on impending supply bottlenecks of the respective pharmaceutical to reduce or counteract the supply bottlenecks. Likewise, certain specifications on stockholding can be made to pharmaceutical companies or wholesalers. The Advisory Board (see chapter 3.1.3) was also introduced in July 2020 to permanently monitor the current situation regarding to supply bottlenecks. Pharmacists are also allowed to substitute rebate pharmaceuticals more quickly if they are not available. In this case, the patient also does not bear any additional costs.

However, these steps were not sufficient to deal with the supply bottlenecks in the first peak of the Corona pandemic. First the COVID-19 agreement on the framework agreement according to § 129 (2) SGB V (chapter 3.3.1), then the SARS-CoV-2 Pharmaceutical Supply Regulation (chapter 3.3.2) and then the Medical needs Health Care Insurance Regulation-MedBVSV (chapter 3.3.3) had to be introduced for a certain

period during the pandemic to secure the supply of medicines to the population in Germany. The rebate contracts had to be made even more flexible, pharmacies were even freer in their choice of packaging, could dispense partial packages and were even allowed to change the strength of API if they had no concerns. Pharmacies were also protected from retaxation.

Discussion of Development of vaccines

The results in Chapter 8 Development of vaccines have shown the global race for an effective vaccine. According to the WHO, 260 vaccines are being developed worldwide, of which 16 candidates are in phase III clinical trials (status: 05 March 2021). China and Russia had even approved vaccines that had not been fully tested.

Overall, it can be said that the Corona pandemic and vaccine development is triggering a geopolitical power struggle worldwide to win the ‘race’ of vaccine development. COVID-19 vaccine development is shedding new light on pharmaceutical manufacturers, which often had a rather negative image.
Only pharmaceutical companies have competence and know-how to develop vaccines (138) to stop the Corona pandemic.

Likewise, vaccine development is subsidised internationally and nationally. Germany has also subsidised the development of potentially successful vaccine candidates and agreed with the manufacturers to receive vaccines for Europe and Germany from these manufacturers. Equitable distribution of vaccines will be a challenge throughout 2021. With COVAX, an important tool has been introduced to enable a worldwide equitable COVID-19 vaccine distribution and thus contain the pandemic. However, countries and the European Union are negotiating independently with manufacturers because, of course, wealthier nations are concerned about securing enough vaccines for themselves. Especially, vaccine manufacturers have a special moral responsibility to sell vaccines for an adequate price, to ensure equitable global distribution to stop the pandemic and to avoid a consolidation of the global inequality (138). How the worldwide COVID-19 vaccine distribution will develop cannot be foreseen, and there is still a risk that unequitable vaccine development will not occur. However, national vaccine strategies must also consider vulnerable groups to distribute the vaccine equitably within a country.

## 9.1 Limitations

In this chapter, the limitations regarding the data, the methodology and the presentation of the results are presented and explained.

Data (origin, volume, quality)

Regarding the quality and origin of the processed data, it should be noted that the database ‘supply bottlenecks of pharmaceuticals for human use in Germany (excluding vaccines)’ of the BfArM is based on data voluntarily provided by the manufacturers. Although manufacturers have declared a voluntary commitment to report supply bottlenecks for supply relevant pharmaceuticals, there is still no legal regulation. The information about the reasons for supply bottlenecks is also qualitative information on a voluntary basis, which is not given for every supply bottleneck, and should therefore be treated with caution.

However, this database is so far the only official source in Germany where supply bottlenecks for finished pharmaceuticals products are reported. The Gelbe Liste website, which was also used as an additional data source, is a commercial site and is also not a compulsory report by the manufacturers.

The ‘NVI-KT’ database, which was used for the further exploratory trend analysis, does not include online-pharmacy or mail-order business included in this database, which, however, only accounts for 1.2% of the Rx-pharmaceutical market in 2019 (125). Furthermore, data from hospital pharmacies are not included in the NVI-KT database. This is a disadvantage especially for the analysis of N01 Anaesthetics and Narcotics, as these are particularly needed in intensive medical care and operations in hospitals, and thus the exploratory data analysis is limited to the outpatient pharmaceutical market. However, the outpatient SHI market is extensively covered due to the database.

Regarding the status of COVID-19 vaccine development, it is important to mention that it is an ongoing development and are subject to constant change. Therefore, data may quickly become outdated and the presentation of vaccine development should be seen as an inventory. Data from the WHO, which lists possible vaccine candidates, had to be relied on as far as possible. In addition, media reports had to be used for topics such as the distribution of vaccines and applications for marketing authorisations, as this is

a current topic that is not necessarily based on scientific data.

Methods and results

The methodology of the quantitative data analysis also has limitations. The analysis includes all reported supply bottlenecks with ‘first notification’ in the period from 01 January 2020 to 30 June 2020. This analysis therefore only covers the beginning of the Corona pandemic and, in Germany, only the first peak in spring 2020. Thus, no conclusions can be drawn about the changes in the pharmaceutical market and the supply bottlenecks that occurred during the entire period of the Corona pandemic. The analysis also includes supply bottlenecks that had not yet ended at the time of data collection and partly includes the estimated end of the supply bottlenecks indicated by the manufacturers.

The analysis of the development of prescriptions is purely exploratory trend analysis of the prescription numbers. Factors why a pharmacy could not dispense the prescribed pharmaceutical were not evaluated. The selection of the most affected ATC 2 groups and the most affected supply-relevant API could be biased. The API were selected based on the greatest number of affected PZN and products by supply bottlenecks. This leaves out the fact that some supply relevant API are only produced by a few manufacturers and may only have a few dosage forms, pack sizes or potencies. Thus, potentially strongly affected API may have been disregarded. Furthermore, only the data of the supply bottlenecks were analysed for the API and the ATC 2 groups and no comparison was made with the whole pharmaceutical market, as this would exceed the scope of this research. All in all, however, the exploratory trend analyses provide a good overview of the development of prescription numbers of the whole pharmaceutical market and the occurred supply bottlenecks in the period of the first peak of the Corona pandemic. To add, another limitation of this work is that pharmaceuticals used specifically to treat COVID-19 were not additionally included in the prescription trend analysis.

The expert interviews also have limitations. In order to find experts who voluntarily participated in the interviews, the convenience method of snowball sampling was used. Experts were interviewed who were recommended by others and were willing to participate voluntarily in the interview. Due to the snowball sampling, all interviewers were from Northern Germany, which leaves out possible regional differences.

An interview bias could also have arisen in the conduction of the interviews. The interviewer could have given certain directions through questions and follow-up questions and thus steered the interviewer's answers in a certain direction.

Likewise, 'recall bias' on the part of the interviewees could limit the results, as the interviews were only conducted in September and October 2020.

The two wholesalers interviewed are both working in the sales department. To complete the supply chain, an expert from the purchasing department would have been important to be able to identify the reasons for the supply bottlenecks in more detail.

## 9.2 Recommendations for action

In this subchapter, recommendations for action are given and previous planned measures on the part of the European Union are commented on to be able to cope better with future pandemics and to avoid supply bottlenecks in the inpatient and outpatient sector which could otherwise lead to a supply shortage in the population.

On 25 November 2020 the European Union adopted a 'Pharmaceutical Strategy for Europe', which is being developed to avoid the existing weaknesses in the pharmaceutical sector highlighted by the Corona pandemic. The main objectives are to guarantee access to innovative and supply relevant pharmaceuticals for the population and to meet unmet medical needs, such as the treatment of rare diseases. It also aims to combat supply bottlenecks, support the sustainability of the pharmaceutical industry, strengthen the development of innovations of effective environmentally friendly pharmaceuticals, and promote competitiveness to play a leading role in the pharmaceutical sector. It also aims to promote crisis management and security of supply (139–141).

It also aims to create international health data for interoperable action and being accessible to each country in the EU (140).

In order to counteract the supply bottlenecks, which have been a problem for a long time and thus increase the security of supply for the population, the EU announced to "revise the basic pharmaceutical legislation" (140). Preventive and mitigation measures

are also to be taken to minimize the impact of supply bottlenecks on security of supply. Also, on 11 November 2020, the ‘European Health Union Package’ was announced to monitor and mitigate supply bottleneck during an epidemic or pandemic and to strengthen the capacity of the EMA. In future, a ‘structured dialogue’ with all actors in the pharmaceutical production chain and the competent authorities is to be established. They will have to assume greater supervision of the supply chain and the quality of pharmaceuticals and raw materials to identify weaknesses in the pharmaceuticals sector and take further measures. They will also identify the EU’s dependencies in the pharmaceutical sector, evaluate weaknesses in the global supply chain and take measures to address these weaknesses (139–141).
The German government also wants to advocate in the EU that pharmaceutical companies must publish information on the origin of the manufacturers of the API used (142).

In the following, recommendations for action are made for an EU pharmaceutical strategy to avoid supply bottlenecks, ensure security of supply and better manage future crises. Recommendations for action are also given specifically for Germany. Also, some recommendations of the interviewees were taken up.

One option to counterfeit supply bottlenecks would be to support production in Europe. The Corona pandemic has shown the dependence on Asia of certain API. If production facilities in Asia fail or the supply chain is interrupted, Europe and Germany suffer. In order to be able to continue to guarantee the secure supply of pharmaceuticals in a pandemic, incentives must be created so that important supply relevant API and the production of critical pharmaceuticals, such as antibiotics, are increasingly produced in Europe again, though this is more expensive than in Asia. Consequently, in future it will be important that not only the cheapest price of a pharmaceutical counts, but also sustainability and quality (129). There could be nationwide or EU-wide subsidies to promote EU-wide production of important API. In order to promote European production of API and pharmaceuticals, however, close cooperation of all important actors at the European level is needed.

Furthermore, Germany and the European Union should increasingly monitor the production and quality of API and pharmaceuticals in the producing countries to be able to counteract possible supply bottlenecks at an early stage.

Stockpiling of pharmaceuticals with supply relevant API would also be a possibility to be able to act more flexibly during a pandemic. Pharmaceutical manufacturers should be legally obliged not only to produce important supply relevant API and pharmaceuticals on order, but to keep always certain predefined quantities at stock to be able to react quickly in an emergency and to ensure that pharmaceuticals are permanently available. A certain stockpiling of designated important supply relevant API should also apply to wholesalers throughout the EU to have sufficient reserve stocks.

Likewise, German hospitals, since there was a shortage of intensive care pharmaceuticals in hospitals during the pandemic, should be permanently obliged to stockpile at least four to five weeks' supply (of average need) of important intensive care pharmaceuticals to have sufficient stocks of all necessary API in an emergency situation so that no supply shortage of pharmaceuticals occurs. This compulsory stockpiling should not only apply during a pandemic.

Pharmaceutical companies should be required by law to disclose information on which manufacturer and from which country the API for the pharmaceuticals they produce come from (142). A separate database could be set up for this purpose.

Likewise, a legal obligation to report potential supply bottlenecks of pharmaceuticals with supply relevant API should be introduced EU-wide to obtain a controlled early warning system. Unforeseeable supply bottlenecks should have to be reported immediately. For this purpose, an international Eu-wide database on supply bottlenecks should be created. For example, this coordination could be taken over by the EMA and the 'structured dialogue'. Each country should also have its own database on supply bottlenecks to manage them individually. To this end, it is important that communication between manufacturers and the competent authorities in the countries (Germany: BfArM, Europe: EMA) is strengthened to improve the analysis of trends in supply bottlenecks. In this way, participants could react accordingly quickly to implement a functioning EU-wide early warning system and have a permanent overview of the availability of medicines, not only during a pandemic. Manufacturers must also be obliged to provide continuously data on available stocks of API and finished pharmaceuticals and data on their sales volumes. Production capacities should also be identified and communicated. This collaborative approach could ensure that the availability of medicines is continuously monitored and impending supply bottlenecks

are identified at an early stage.

Especially in Germany, the already existing database on supply bottlenecks of the BfArM should be revised. The causes for the supply bottlenecks are only partly given and not in detail. Likewise, PZN are sometimes mixed up or entered incorrectly. Consideration should also be given to clustering the database according to ATC groups and API to have a permanent overview of which groups of pharmaceuticals are currently most affected by supply bottlenecks and to take steps to halt them as quickly as possible.

Furthermore, communication between the BfArM, the GKV-Spitzenverband and the DAV should be improved. During the pandemic, the GKV-Spitzenverband and the DAV reached the COVID-19 agreement on the framework agreement according to § 129 (2) SGB V to make it easier for pharmacies to dispense pharmaceuticals so that a safe supply of pharmaceuticals could be provided. The BfArM reacted only with a delay of three weeks with issuing the legal SARS-CoV-2 Pharmaceutical Supply Regulation. Continuous communication should take place between all important actors and the necessary regulations should be worked on quickly. Consideration should also be given allowing pharmacies to react flexibly in emergencies, not only in the pandemic, and to be flexible in the choice of packages without having to pay penalties. This could avoid an interruption of therapy or even discontinuation in individual cases.
In addition, doctors should be encouraged (e.g., via the competent associations of panel doctors) to continue prescribing pharmaceuticals as usual in the event of a pandemic to avoid stockpiling of patients. Here, the advancing digitalisation could be used and supported to issue e-prescriptions more quickly and to redeem them in pharmacies or by mail order. To avoid large crowds of customers in pharmacies, the courier service could be expanded.

The current rebate contracts in Germany should be reconsidered. Exclusive contracts with only one partner for an API should no longer be possible. Only multi-partner contracts with at least three to four manufacturers should be allowed to widen the responsibility among several manufacturers. After all, if one manufacturer in the exclusive contract faces any supply problems, it is difficult to find a substitute. Likewise, multi-partner contracts do not exclude a number of manufacturers who might stop production for that API because of the exclusive contracts. For the patients, it is also

ensured that hopefully they will always get a preparation in the pharmacy or due to the mail order business. Furthermore, it is important that in future not only the lowest price will count when rebate contracts are concluded. The price for generics has been pushed down in recent years by the rebate contracts, although generics account for about 80% of the supply of pharmaceuticals. According to Pro Generika e.V., pharmaceutical manufacturers who have demonstrably invested in strengthening their supply chains and, for example, have two API suppliers and one of which even has its production site in Europe, should rather get an advantage in tenders (129).

To ensure equitable access to COVID-19 vaccines worldwide, all nations around the world must work intensively together and support the COVAX initiative to combat the pandemic.

# 10 Conclusion

This Master thesis shows that dynamic changes took place in the whole German Rx-pharmaceutical market during the first peak phase of the Corona pandemic. A peak in sales in March with a sharp drop through May and a slight rebound in June became visible for the whole pharmaceutical market and for many of the reported supply bottlenecks.

All in all, supply bottlenecks have been a problem for some time, but the Corona pandemic has exacerbated them and highlighted the problems that do exist. The dependence on Asia for API production and weaknesses in supply chains became apparent. The supply bottlenecks were probably reinforced by so-called ‘panic buying’. This became evident through the expert interviews. In some cases, supply bottlenecks probably resulted in supply shortages, which could have led to an interruption of the therapy. Due to an increased need for necessary API in intensive medical care, obviously more action is needed in Germany and across the EU to strengthen supply chains, to strengthen the production of supply relevant API and pharmaceuticals in the EU and to better monitor supply bottlenecks in future to be able to react quickly in a pandemic. In conclusion, it can also be said that the supply of pharmaceuticals in Germany was still ensured throughout the country, even in the first peak phase of the pandemic. How this developed in the second peak phase at the end of 2020 could be

determined in a further analysis and by interviews of experts.

Vaccine development, on the other hand, shows a dynamic picture of the pharmaceutical industry. The pharmaceutical industry is helping to combat the pandemic more quickly with its rapid vaccine development. Germany is funding potential successful COVID-19 vaccines with up to 750 million euros. Every country would like to have a vaccine as soon as possible and wants to win the dynamic race for an effective vaccine. We will have to wait and see how the worldwide distribution of the vaccine develops in 2021 to combat the Corona pandemic.

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# APPENDIX A – Overview of most affected supply-relevant API

Table 9: Overview of most affected supply-relevant API

| **ATC 1** | ATC 2 | API | Manufacturer | Products |
|---|---|---|---|---|
| R Respiratory system | R03 Asthma and COPD preparations | Salbutamol | Hexal | Salbuhexal N |
| R Respiratory system | R03 Asthma and COPD preparations | Salbutamol | ratiopharm | Salbutamol Ratiopharm N |
| R Respiratory system | R03 Asthma and COPD preparations | Salbutamol | ratiopharm | Salbutamol Ratiopharm |
| J Antiinfectives, systemic | J01 Antibiotics, systemic | Amoxicillin | 1 A Pharma | Amoxi 1A Pharma |
| J Antiinfectives, systemic | J01 Antibiotics, systemic | Amoxicillin | ratiopharm | Amoxicillin Ratiopharm |
| J Antiinfectives, systemic | J01 Antibiotics, systemic | Amoxicillin | Hexal | Amoxihexal |
| J Antiinfectives, systemic | J01 Antibiotics, systemic | Azithromycin | 1 A Pharma | Azithromycin 1A Pharma |
| J Antiinfectives, systemic | J01 Antibiotics, systemic | Azithromycin | ratiopharm | Azithromycin Ratiopharm |
| J Antiinfectives, systemic | J01 Antibiotics, systemic | Azithromycin | Aliud | Azithromycin AL |
| J Antiinfectives, systemic | J05 Virustatics, systemic | Aciclovir | 1 A Pharma | Aciclovir 1A Pharma (J05B3) |
| J Antiinfectives, systemic | J05 Virustatics, systemic | Aciclovir | Hexal | Acic (J05B3) |
| N Nervous system | N02 Analgesics | Ibuprofen | Zentiva Pharma | Ibuflam WTP (N02B2) |
| N Nervous system | N02 Analgesics | Ibuprofen | Aliud | Ibuprofen AL (N02B2) |
| N Nervous system | N02 Analgesics | Paracetamol | 1 A Pharma | Paracetamol 1A Pharma |
| N Nervous system | N02 Analgesics | Paracetamol | Aliud | Paracetamol AL |
| N Nervous system | N02 Analgesics | Paracetamol | Hexal | Paracetamol Hexal (N02B2) |
| N Nervous system | N02 Analgesics | Paracetamol | Zentiva Pharma | Paraceta |
| N Nervous system | N02 Analgesics | Paracetamol | Dexcel | Paracetamol Dexcel |
| N Nervous system | N02 Analgesics | Morphine | Merck Serono | Morphin Merck |
| N Nervous system | N02 Analgesics | Morphine | Teva | Morphinsulfat Gry |
| N Nervous system | N02 Analgesics | Morphine | Mundipharma | MSI Mundipharma |
| N Nervous system | N01 Anaesthetics and narcotics | Propofol | Braun Mels. | Propofol Lipuro |
| N Nervous system | N01 Anaesthetics and narcotics | Propofol | Aspen Germany | Disoprivan AE: |
| N Nervous system | N01 Anaesthetics and narcotics | Propofol | Baxter Deutschl | Propofol Baxter |
| N Nervous system | N01 Anaesthetics and narcotics | Midazolam | ratiopharm | Midazolam Ratiopharm |
| N Nervous system | N01 Anaesthetics and narcotics | Midazolam | Braun Mels. | Midazolam B Braun |
| N Nervous system | N01 Anaesthetics and narcotics | Midazolam | Cheplapharm | Dormicum CH/ |
| N Nervous system | N01 Anaesthetics and narcotics | Midazolam | hameln pharma | Midazolam Hameln |
| N Nervous system | N01 Anaesthetics and narcotics | Midazolam | PUREN Pharma | Midazolam Puren |
| N Nervous system | N03 Antiepileptics | Lamotrigine | Dexcel | Lamotrigin Atid |
| N Nervous system | N03 Antiepileptics | Lamotrigine | Acis | Lamotrigin Acis |
| N Nervous system | N03 Antiepileptics | Lamotrigine | Stadapharm | Lamotrigin Stada |

| | | | | |
|---|---|---|---|---|
| H Hormones, system, except sex hormones | H03 Thyroid hormone therapy | Levothyroxine | Hexal | L Thyrox Hexal |
| H Hormones, system, except sex hormones | H03 Thyroid hormone therapy | Levothyroxine | 1 A Pharma | L Thyroxin 1A Pharma |
| H Hormones, system, except sex hormones | H03 Thyroid hormone therapy | Levothyroxine | Merck Serono | Euthyrox |
| C Cardiovascular system | C09 Renin-Angiotensin effective preparations | Candesartan | ratiopharm | Candesartan Ratiopharm |
| C Cardiovascular system | C09 Renin-Angiotensin effective preparations | Candesartan | ABZ Pharma | Candesartan ABZ |
| C Cardiovascular system | C09 Renin-Angiotensin effective preparations | Candesartan | Hennig | Candesartan cilexetil Hennig |
| C Cardiovascular system | C09 Renin-Angiotensin effective preparations | Candesartan | Stadapharm | Candesartan Stada |
| C Cardiovascular system | C07 Beta-receptor blockers | Metoprolol | Hexal | Metohexal succinat |
| C Cardiovascular system | C07 Beta-receptor blockers | Metoprolol | 1 A Pharma | Metoprololsuccinat 1A Pharma |
| D Dermatologicals | D10 Acne remedies | Metronidazole | Galderma | Metrogel |
| D Dermatologicals | D06 Antibacterial/antiviral agents | Aciclovir | 1 A Pharma | Aciclovir 1A Pharma (D06D1) |
| G Urogenital tract and sex hormones | G01 Urogenital tract and sex hormones | Metronidazole | ratiopharm | Metronidazol Ratiopharm |
| G Urogenital tract and sex hormones | G01 Urogenital tract and sex hormones | Metronidazole | 1 A Pharma | Metronidazol 1A Pharma |
| G Urogenital tract and sex hormones | G01 Urogenital tract and sex hormones | Metronidazole | Hexal | Metronidazol Hexal |
| M Muscular and skeletal system | M01 Antiphlogistics/Antirheumatic pharmaceuticals, systemic | Ibuprofen | Aliud | Ibuprofen AL (M01A1) |

# APPENDIX B – Participant information

## Informationen über den Umgang mit dem Interviewmaterial für Interview-Teilnehmer

Meine Masterarbeit schreibe ich zum Thema:

„Changes in the Dynamics of the German pharmaceutical market due to the Corona pandemic: Supply bottlenecks, increased demand, and the development of vaccines“.

Für diese Masterarbeit würde ich Sie gerne interviewen und möchte über mein Vorgehen berichten. Der Datenschutz verlangt Ihre ausdrückliche und informierte Einwilligung, dass ich das Interview speichern und auswerten darf.

Die Verantwortung obliegt dem Studenten Leon Stephan, Masterand an der HAW Hamburg im Studiengang M.Sc. Health Sciences. Der Interviewer unterliegt der Schweigepflicht und ist auf das Datengeheimnis verpflichtet. Die wissenschaftliche Arbeit dient allein dem Zweck, eine Analyse im Rahmen der Masterthesis durchzuführen, um die quantitativen Daten rund um die Lieferengpässe und verordneten Arzneimitteln im Rahmen der Corona-Pandemie um qualitatives Experten-Fachwissen zu ergänzen, damit die Masterthesis durch Feld nahe Berichte ergänzt und erforscht wird, ob es auch zu Versorgungsengpässen in der Bevölkerung gekommen ist. Abschließend soll, mit den gewonnen qualitativen Daten, Handlungsempfehlungen und Konsequenzen für zukünftige Pandemien herausgearbeitet werden. Hierzu werden Experten befragt, die aus unterschiedlichen Bereichen des Gesundheitssektors kommen und mit dem Arzneimittelmarkt und in der gesundheitlichen Versorgung der Bevölkerung eine Rolle spielen. Ich versichere Ihnen folgendes Verfahren zu, damit Ihre Angaben nicht mit Ihrer Person in Verbindung gebracht werden können:

- Ich gehe sorgfältig mit dem Erzählten um: Ich nehme das Gespräch auf Band auf. Das wichtigste wird transkribiert und anschließend gelöscht. Auch das stichpunktartige Transkript können Sie erhalten.

- Ich werde das gekürzte Transkript anonymisieren, d.h. ich anonymisiere die personenbezogenen Daten.

- Ihr Name und Ihre E-Mail-Adresse werden am Ende des Projektes in meinen Unterlagen gelöscht, so dass lediglich das anonymisierte stichpunktartige Transkript existiert. Die von Ihnen unterschriebene Erklärung zur Einwilligung in die Auswertung wird in einem gesonderten Ordner an einer gesicherten Stelle aufbewahrt. Sie dient lediglich dazu, bei einer Überprüfung durch den Datenschutzbeauftragten nachweisen zu können, dass Sie mit der Auswertung einverstanden sind. Sie kann mit Ihrem Interview nicht mehr in Verbindung gebracht werden.

Die Datenschutzbestimmungen verlangen auch, dass ich Sie noch einmal ausdrücklich darauf hinweise, dass aus einer Nichtteilnahme keine Nachteile entstehen. Sie können Antworten bei einzelnen Fragen verweigern. Auch die Einwilligung ist freiwillig und kann jederzeit von Ihnen widerrufen werden. Ebenfalls kann die Löschung des Interviews von Ihnen verlangt werden.

## APPENDIX C – Written informed consent

### Einwilligungserklärung zur Erhebung, Verarbeitung und Weitergabe personenbezogener Interviewdaten

Zwischen

Leon Rick Stephan (Masterstudent HAW Hamburg), Geburtsdatum, Adresse

und

Interview-Teilnehmer

Ich bin über das Vorgehen bei der Verschriftlichung, Datenspeicherung und Auswertung des von mir gegeben Interviews persönlich mittels eines schriftlichen Handzettels informiert worden.

Ich bin damit einverstanden, dass die erhobenen Informationen, als Material für wissenschaftliche Zwecke und für die Erarbeitung der Masterarbeit zum Thema: „Changes in the Dynamics of the German pharmaceutical market due to the Corona pandemic: Supply bottlenecks, increased demand, and the development of vaccines“.

Die Teilnahme an diesem Interview ist freiwillig und ich habe die Möglichkeit zu jeder Zeit das Interview abzubrechen. Mein Einverständnis in eine Aufzeichnung und in ein gekürztes Transkript mit den wichtigsten Stichpunkten des Interviews kann ich jederzeit zurückziehen, ohne dass mir dadurch Nachteile entstehen.

Die Tonaufnahme wird nach Beendigung der Masterarbeit selbstverständlich gelöscht.

Unter diesen Voraussetzungen erkläre ich mich bereit, an dem Experten-Interview teilzunehmen und bin damit einverstanden, dass es aufgenommen, stichpunktartig transkribiert (ins Englische übersetzt) und anonymisiert ausgewertet wird.

Ich bin damit einverstanden, dass das anonymisierte stichpunktartige Transkript meines Interviews zur weiteren wissenschaftlichen Nutzung innerhalb der Masterarbeit verwendet werden darf.

Vorname/Nachname (in Druckschrift) _____

Ort, Datum: _____ Unterschrift_____

## APPENDIX D – Confidentiality declaration

# Verschwiegenheitserklärung / Geheimhaltungsvereinbarung

Zwischen dem
Leon Rick Stephan (Masterstudent HAW Hamburg), Geburtsdatum, Adresse

und

Interview-Teilnehmer

wird folgende Vereinbarung getroffen:

Der Studierende erhält von den Interviewpartnern Informationen. Der Studierende verpflichtet sich, sämtliche Informationen, welche ihm für die Durchführung der Transkription von Interviews zur Verfügung gestellt werden, vertraulich zu behandeln.

Der Studierende verpflichtet sich, die Transkription eigenständig durchzuführen, und somit nicht die Informationen frei weiterzugeben und nur im Rahmen der Masterarbeit zu verwenden.

Nach Beendigung der Masterarbeit verpflichtet sich der Studierende die Informationen, die er erhalten hat, zu löschen (z.B. Audiodateien, elektronische und nicht elektronische schriftliche Dokumente), um ein Ausbreiten der Informationen zu verhindern.

Vorname/Nachname (in Druckschrift): Leon Rick Stephan

Ort, Datum: _____ Unterschrift_____

# APPENDIX E – Interview topic guides

## Interview topic guide – high street pharmacist

- Vorstellung des Interviewers, der Informationen für Interview-Teilnehmer und Inhalt der Masterarbeit

| | |
|---|---|
| **Strukturelle Veränderungen im Arzneimittelmarkt** | |
| **1.** | Die Corona Pandemie hat einige strukturelle Veränderungen in der ganzen Welt mit sich gebracht. Der Lockdown in den meisten Ländern und die Schließungen der Grenzen hat auch zu Veränderungen im Gesundheitswesen geführt.<br><br>*Welche strukturellen Veränderungen bzw. Schwierigkeiten oder sogar Erleichterungen ergaben sich im Arzneimittelmarkt?* |
| **Liefer- bzw. Versorgungsengpässe** | |
| **2.** | Als Grund für die Lieferengpässe wurde am häufigsten eine erhöhte Nachfrage im Markt angegeben.<br><br>*Konnten Sie ebenfalls eine erhöhte Nachfrage von verordneten Medikamenten verzeichnen?*<br><br>*Wenn ja, für welche Arzneimittelgruppen?* |
| **3.** | *Kam es zu spürbaren Lieferengpässen in der Hochzeit der Corona-Pandemie und haben diese auch zu Versorgungsengpässen geführt oder konnten die Lieferengpässe meistens durch ähnlich wirksame Medikamente ausgeglichen werden?* |
| **4.** | *Durch die Pandemie kam es zu Verzögerungen in der Lieferkette von Medikamenten z.B. aus China und Indien. War dies aus Ihrer Sicht spürbar bzw. von Bedeutung für die Versorgung in Deutschland?* |
| **5.** | Anhand der quantitativen Daten war im April im Gesamtmarkt und in den Medikamenten mit den gemeldeten Lieferengpässen ein Rückgang der Verordnungen im April um ca. 20 teilweise 40-50% zum Vormonat zu verzeichnen.<br><br>*Können Sie dies aus Ihren Praxiserfahrungen ungefähr bestätigen und Gründe nennen, woran genau dies lag?* |
| **6.** | *Welche Wirkstoffe für welche Indikationsgruppen waren aus Ihrer Sicht am meisten von Lieferengpässen betroffen?* |
| **7.** | Die Analyse ergab, dass am meisten die ATC-1 Gruppen Nervensystem, Antiinfektiva und das Kardiovaskuläre System betroffen waren. Bei den ATC-2 Gruppen waren die Antibiotika, Antiepileptika und Anästhetika und Narkosemittel und Analgetika am meisten betroffen.<br><br>*Können Sie dies aus Ihrer Sicht bestätigen bzw. kam es dort bei einigen Wirkstoffen zu Liefer- bzw. Versorgungsengpässen, sodass bestimmte Gruppen der Bevölkerung nicht mehr ausreichend versorgt werden konnten?* |
| **8.** | *Würden Sie allgemein sagen, dass durch die Corona-Pandemie einige Patienten-Gruppen nicht mehr genügend versorgt werden konnten und dies sogar eine Gesundheitsgefahr mit sich gebracht hat?* |
| **Zukünftige Veränderungen** | |
| **9.** | *Welche Lehren im Bereich des Arzneimittelmarktes würden Sie aus der Corona-Krise für zukünftige Krisen ziehen?* |
| **10.** | *Was halten Sie davon die Produktion von essenziellen Arzneimitteln bzw. die Produktion von Antibiotika zurück nach Europa bzw. Deutschland zu holen?* |
| **11.** | *Welche weiteren wichtigen Punkte sollten noch erwähnt werden, die den Arzneimittelmarkt bzw. die gesundheitliche Versorgung der Bevölkerung mit Arzneimitteln in der Corona-Krise verändert haben?* |

**Interview topic guide – hospital pharmacist**

- Vorstellung des Interviewers, der Informationen für Interview-Teilnehmer und Inhalt der Masterarbeit

| | |
|---|---|
| **Strukturelle Veränderungen im Arzneimittelmarkt** | |
| **1.** | Die Corona Pandemie hat einige strukturelle Veränderungen in der ganzen Welt mit sich gebracht. Der Lockdown in den meisten Ländern und die Schließungen der Grenzen hat auch zu Veränderungen im Gesundheitswesen geführt.<br><br>*Welche Veränderungen bzw. Schwierigkeiten oder sogar Erleichterungen ergaben sich im Bereich der Versorgung mit Arzneimitteln in der stationären Versorgung?* |
| **Liefer- bzw. Versorgungsengpässe** | |
| **2.** | *Kam es zu spürbaren Liefer- bzw. sogar Versorgungsengpässen in der stationären Versorgung mit Arzneimitteln?*<br><br>*Welche versorgungsrelevanten Medikamente waren nicht verfügbar?*<br><br>*Konnten sie diese Fehlenden Medikamente durch gleichwertige andere Medikamente ausgleichen?* |
| **3.** | *Welche Wirkstoffe für welche Indikationsgruppen waren aus Ihrer Sicht am meisten von Lieferengpässen betroffen?* |
| **4.** | Als Grund für die Lieferengpässe wurde am häufigsten eine erhöhte Nachfrage im Markt angegeben und am zweithäufigsten eine unterbrochene Lieferkette.<br><br>*Können Sie dies bestätigen?* |
| **5.** | *Welche stationären Bereiche waren besonders von hoher Arzneimittel Nachfrage seitens der Patienten betroffen bzw. aufgrund von Nicht-Verfügbarkeit betroffen?* |
| **6.** | Anhand der quantitativen Daten war im April im Gesamtmarkt und bei den Medikamenten mit gemeldeten Lieferengpässen ein Rückgang der Verordnungen um ca. 20 teilweise 40-50% zum Vormonat zu verzeichnen.<br><br>*Können Sie dies für die Versorgung in Ihrem Krankenhaus bestätigen?*<br><br>*Wenn ja, bitte nennen Sie die Gründe dafür?* |
| **7.** | *Würden Sie sagen, dass durch die Corona-Pandemie einige Patienten-Gruppen im Krankenhaus nicht mehr genügend versorgt werden konnten und dies sogar eine Gesundheitsgefahr mit sich gebracht hat?*<br><br>*Oder konnte n Sie alle Engpässe durch Substitutionen ausgleichen?* |
| **Zukünftige Optionen für Engpass-Situationen** | |
| **8.** | *Welche Lehren im Bereich des Arzneimittelmarktes würden Sie aus der Corona-Krise für zukünftige Krisen ziehen?* |
| **9.** | *Was halten Sie davon die Produktion von essenziellen Arzneimitteln bzw. die Produktion von Antibiotika zurück nach Europa bzw. Deutschland zu holen?* |
| **10.** | *Welche weiteren wichtigen Punkte sollten noch erwähnt werden, die den Arzneimittelmarkt und die Auswirkungen für die medikamentöse Versorgung in der Corona-Krise verändert haben?* |

**Interview topic guide – Wholesaler**

- Vorstellung des Interviewers, der Informationen für Interview-Teilnehmer und Inhalt der Masterarbeit

| | |
|---|---|
| **Strukturelle Veränderungen im Arzneimittelmarkt** | |
| **1.** | Die Corona Pandemie hat einige strukturelle Veränderungen in der ganzen Welt mit sich gebracht. Der Lockdown in den meisten Ländern und die Schließungen der Grenzen hat auch zu Veränderungen im Gesundheitswesen geführt.<br><br>*Welche strukturellen Veränderungen bzw. Schwierigkeiten durch die Corona-Pandemie beobachten Sie im Arzneimittelmarkt?* |
| **Liefer- bzw. Versorgungsengpässe** | |
| **2.** | In der Phase des ‚Lockdowns' gab es von März bis Mai eine Vielzahl von Lieferengpässen.<br><br>Als Grund für die Lieferengpässe wurde am häufigsten eine erhöhte Nachfrage im Markt angegeben und als 2. Häufigster Grund eine unterbrochene Lieferkette.<br><br>*Können Sie dies bestätigen bzw. inwiefern wurde dies im Großhandel beim Einkauf/Verkauf bemerkbar?*<br><br>*Konnten Sie ebenfalls in dem genannten Zeitraum eine erhöhte Nachfrage nach Medikamenten verzeichnen?*<br><br>*Wenn ja, für welche Arzneimittelgruppen trifft das zu?* |
| **3.** | *Kam es zu spürbaren Lieferengpässen in der Phase des 1. Lock Downs der Corona-Pandemie und haben diese auch zu Versorgungsengpässen geführt oder waren meistens Medikamente verfügbar, die die fehlenden, substituieren konnten?* |
| **4.** | *Durch die Pandemie kam es zu Verzögerungen in der Lieferkette von Medikamenten z.B. aus China und Indien. War dies aus Ihrer Sicht spürbar bzw. von Bedeutung für die Versorgung in Deutschland?*<br><br>*Welche Medikamentengruppen waren besonders betroffen?* |
| **5.** | Anhand der quantitativen Daten war im April im Gesamtmarkt und in den Medikamenten mit den gemeldeten Lieferengpässen ein Rückgang der Verordnungen im April um ca. 20 teilweise 40-50% zum Vormonat zu verzeichnen.<br><br>*Können Sie dies aus Ihren Praxiserfahrungen ungefähr bestätigen und Gründe nennen, woran genau dies lag?* |
| **6.** | *Welche Wirkstoffe für welche Indikationsgruppen waren aus Ihrer Sicht am meisten von Lieferengpässen betroffen?* |
| **7.** | Die Analyse ergab, dass am meisten die ATC-1 Gruppen Nervensystem, Antiinfektiva und das Kardiovaskuläre System betroffen waren. Bei den ATC-2 Gruppen waren die Antibiotika, Antiepileptika und Anästhetika und Narkosemittel und Analgetika am meisten betroffen.<br><br>*Können Sie dies aus Ihrer Sicht bestätigen bzw. kam es dort bei einigen Wirkstoffen zu Liefer- bzw. Versorgungsengpässen, sodass bestimmte Gruppen der Bevölkerung nicht mehr ausreichend versorgt werden konnten?* |
| **8.** | *Würden Sie allgemein sagen, dass durch die Corona-Pandemie einige Patienten-Gruppen nicht mehr genügend versorgt werden konnten, weil wichtige Medikamente nicht lieferbar waren?*<br><br>*Traf das besonders alte Menschen mit Bedarf an vielen Medikamenten oder andere Bevölkerungsgruppen?* |

| Zukünftige Veränderungen | |
|---|---|
| **9.** | *Welche Lehren im Bereich des Arzneimittelmarktes würden Sie aus der Corona-Krise für zukünftige Krisen ziehen?* |
| **10.** | *Was halten Sie davon die Produktion von essenziellen Arzneimitteln bzw. die Produktion von Antibiotika zurück nach Europa bzw. Deutschland zu holen?* |
| **11.** | *Halten Sie den Arzneimittelrechtlichen Rahmen und die neuen Infektionsschutzgesetze für ausreichend, um zukünftige Pandemien besser zu bewältigen?*<br><br>*Wenn nein, was sollte gesetzgeberisch und/oder ordnungspolitisch angepasst werden?* |

## APPENDIX F – Expert interviews - Comparison table

Table 10: Expert interviews – Comparison table

| Topic | High street pharmacist (HS.P) | Hospital pharmacist (HO.P) | Wholesaler 1 – Sales Department (W1) | Wholesaler 2 - Sales Department (W2) |
|---|---|---|---|---|
| **1 Overall changes in the German pharmaceutical market in the Corona pandemic** | • Broadly based supply bottlenecks across many indications and many manufacturers<br>• June back to normal<br>• Probably an additional contribution was made by the panic buying by pharmacies and patients | • Increased need of pharmaceuticals due to the pandemic<br>• The arisen supply bottlenecks in the field of anaesthetics | • Shift to online business in the pharmaceutical sector has changed<br>• Due to Corona and the lockdown, many people were afraid, especially chronic and multimorbid people, who are known to go mainly to the pharmacy<br>• Rare done by mail order was Rx-pharmaceuticals, and that has certainly increased to some extent, who knows, if that can be reversed<br>• Also changed from N1 to bigger N3 packages (last 3 months or more) | • Increased demand<br>• A new challenge for us as wholesalers, primarily with our special responsibility, which we also bear in the health sector, to ensure the best possible supply of pharmacies and thus also of patients throughout the Corona pandemic<br>• Adapt logistical processes to really guarantee a nationwide supply, as older employees or employees with families have also dropped out |
| **2 Cause of supply bottlenecks** | • Not believe the manufacturers' reasoning: supply bottlenecks are based on increased demand; they were more likely to pay penalties or face restrictions because of the rebate contracts if they could not deliver<br>• I have stocked up a bit, but I doubt that is the main reason with increased demand<br>• Once the supply bottleneck is there, it will not disappear tomorrow, because the supply chains were interrupted<br>• China has banned exports of certain substances | • Has to differentiate, whether there is a great demand for pharmaceuticals due to the corona pandemic, i.e., an increased need for certain API (main cause), or, the fact that supply chains have been broken off due to lockdowns in other countries, mainly China<br>• Many raw materials are often only produced in two countries, India, and China, and if one factory breaks down, this has global consequences<br>• We are not only noticing this through Corona, but it was also the same in the years before<br>• If there was a supply bottleneck, a manufacturer would try to justify it with | • I believe that a lot is produced in the Far East because production costs are lower there<br>• Especially in China and in Wuhan, there are many manufacturing companies that also produce raw materials for certain further steps<br>• It was already predicted in January or December that there would be supply bottlenecks, which will be tight for some pharmaceuticals, simply because raw material production in the Far East came to a standstill<br>• In the case of Rx-pharmaceuticals, some pharmacies have also made panic buying, that is true, but it is difficult to assess the real impact | • Could see how the population reacted in the retail trade, keyword: panic buying<br>• It has been transferred to the pharmaceutical market. Perhaps in a weakened form or perhaps in a stronger form, it is difficult to judge exactly. Increased purchasing also in pharmacies, i.e., pharmacies naturally also wanted to position themselves in the best possible way<br>• In fact, a large part of the raw materials or pharmaceuticals are produced in Far East, Asia, China, India, and we have a very strong dependence<br>• In China there were sometimes no containers moved because there was a lockdown there as well |

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| | • The rebate contracts probably also played a major role in causing these enormous supply bottlenecks | Corona, but I do not think so, because that is what also happened before | | • This has led to major delays, and at the same time to an increased demand for preparations that were not available on the market in large quantities anyway<br>• Domino effect: A pack of one size or other potency is not available, then the others are not available as well |
| **3 Changes in prescription of pharmaceuticals from March to May 2020** | • March was extremely good in pharmacies, April correspondingly bad | • We did not have any problems with the standard pharmaceuticals (antibiotics, pharmaceuticals for the cardiovascular system, etc.) | | |
| **4 Supply bottlenecks ATC 1 / ATC 2** | • cardiovascular pharmaceuticals, thyroid hormones, inhaled corticoids, antidiabetics, anaesthetics<br>• Analgesics, i.e., Paracetamol und Ibuprofen | • Anaesthetics and Narcotics | • Analgesics<br>• Cardiovascular-System (blood thinners) | • Sartane (Renin-Angiotensin effective preparations)<br>• Anaesthetics and Narcotics |
| **5 Supply Bottlenecks API** | • Propofol<br>• Paracetamol und Ibuprofen<br>• Amoxicillin, Clavulanic acid: for example, this was: Cefuroxime, Cefixime<br>• not only the Propofol, but also the Naloxone, Atropine, or such things<br>• Pneumovax | • especially Propofol, Midazolam, Arterenol (Noradrenalin)<br>• Analgesics, i.e., Ibuprofen, there are always these difficulties because the raw material comes from Asia<br>• But that was already the case before, so it was not extreme in the Corona periods<br>• no problems with other pharmaceuticals/API | • Ibuprofen | • Pneumovax, Shingrix<br>• Propofol |
| **6 From supply bottleneck to supply shortage of the population?** | • This has something to do with the way you have hoarded yourself<br>• We have never had to send anybody away at any time without a pharmaceutical, but we may have had to change the company<br>• For this reason, we had the opportunity to gain more customers, | • Advantage for hospitals was, as beds were kept free and planned operations were postponed<br>• The hospitals were empty, so to that extent we had no problems with the other standard preparations<br>• Of course, fewer patients have been to the clinic, but the serious cases to be | • A real supply shortage, no<br>• Well, I was not for one minute afraid that the German health care system would be marginalised<br>• It was already noticeable that not enough reorders for pharmaceuticals were possible, but it was still sufficient | • Yes, it is difficult to say. I do not think we were able to treat every patient safely or in sufficient quantities<br>• For example: Shingrix, the patient has to be vaccinated twice. I have also heard that one patient received an injection and the second one was not yet on the way. I do not |

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| | we already had customers who said: "yes, we have already been to 4 pharmacies, great that you have that"<br>• Probably overall there was a supply shortage<br>• The fact is, it is well known that people have not dared to go to hospital, they have not dared to see a doctor<br>• We also asked ourselves why no customers come to the pharmacy here<br>• You can also see this in the OTC area. People no longer have headaches, do not need aspirin, no ibuprofen, no nasal spray | treated have always been treated and no shortage of care has arisen<br>• And even then, it was not the case that pharmaceuticals failed, which would have put the patient at risk<br>• Problems with Anaesthetics (increased demand), i.e., the preparations with which the severe COVID-19 cases were treated in the intensive care unit or when they were put into a so-called artificial coma<br>• Noticeably more ventilated patients in the intensive care units<br>• Then we did not have enough Anaesthetics, colleagues did not have enough, and the industry did not have enough<br>• Discussions with the chief and senior physicians because they were in panic at first<br>• We discussed alternatives and then they found alternatives, without putting patient at risk<br>• Sometimes API that probably did not have a licence for this case, but they managed it | | assume that really every patient could be treated properly, but overall, yes<br>• Also connected with health insurance<br>• The health insurance company would never open the rebate contracts if there had not been acute supply bottlenecks/shortages during the pandemic. There was also a relaxation. The pharmacies were able to substitute more freely and were therefore more flexible. Why is the statutory health insurance fund doing that? They would never do that, that is are costs<br>• Here, economic interests are in the foreground and you can already see how acute the supply bottleneck of pharmaceuticals was or still is during the Corona Pandemic<br>• Also, we are in a good position, but I can fully understand if there are patients who do not share this opinion at all, because in their individual case they are given their preferred preparation, but a substituted preparation, which they may not tolerate well or tolerate worse |
| **7 Other Complications** | • The pandemic is ultimately a global crisis. But much more attention is paid to the domestic market and not to where it is least<br>• State has outsourced the responsibility. If the state had been aware of this responsibility, as many thousands of pharmacies have done, we would have dealt with the situation quite differently and most | | | • Even far away from prescription pharmaceuticals with the face masks in March there was a big bottleneck, some of the Federal Ministry of Health bought counterfeit goods in China<br>• You could see what a dangerous market it was and many producers in China turned around and copied a mask that did not have these technical requirements or were perhaps even made of material that was |

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| | pharmacies were not as clumsy as the state | | | harmful to health, and if you have them on all day, then I don't know. |
| **8 Future proposals for change / Lessons learned** | • Certain stocks. Of course, they could require companies to keep stocks of API or packages<br>• Relocating production facilities to Europe (e.g. Antibiotics) would be nice, but I doubt that will happen<br>• Support pharmacies, do not rely all on mail-order business and low prices<br>• Rethinking Rebate contracts | • Broken down to our hospital or every single pharmacy, we must increase our stocks. Here was also a regulation that you have to stock up a 3-week supply of aesthetics in stock at the hospital pharmacy. This was two weeks before. But we had that before (was not enough) and we have now increased that to four to five weeks<br>• Support to relocate the production back to Europe, would be great, but I think the health system is not able to pay it<br>• The pharmaceutical companies should also increase their stock level | • I would consider to relocate the production of essential pharmaceuticals to Europe to be very sensible, but I personally do not believe in it, because they cannot force a manufacturer to produce somewhere, at least I cannot think of how the politicians want to achieve this, but an incentive must be created (reasonable prices, but then the health system will also become more expensive)<br>• Rethinking the Rebate contracts<br>• The pandemic has also shown that high street pharmacies are extremely important<br>• High street pharmacies are essential, because of the fast supply and the consultation of patients<br>• Do not push mail order business (Rx-pharmaceutical ban for mail order companies) | • Relocate the production of essential basic materials or pharmaceuticals to Europe<br>• Be able to act a little more flexible, agile, or even independent<br>• Stockpiling of pharmaceuticals<br>• Manufacturers should also have an incentive, that they are subsidised by the state or even Europe-wide<br>• There should also be a rethink about health insurance companies and rebate contracts, which also offers more flexibility and better healing or care of patients by the patients themselves, that it is said that we have this API and the patient really only tolerates this preparation<br>• Rethinking incentives, margins for pharmacists and wholesalers |

# APPENDIX G – Expert interviews - Transcripts

**Interview on 29 September 2020 from 11:05 am to 11:39 am**
**(Duration: 34 minutes)**

| **Stephan** | **High street pharmacist (HS.P)** |
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| **Q1:**<br>Die Corona Pandemie hat einige strukturelle Veränderungen in der ganzen Welt mit sich gebracht. Der Lockdown in den meisten Ländern und die Schließungen der Grenzen hat auch zu Veränderungen im Gesundheitswesen geführt. Welche strukturellen Veränderungen bzw. Schwierigkeiten oder sogar Erleichterungen ergaben sich im Arzneimittelmarkt? | **A1:**<br>• Breit aufgestellte Lieferengpässe über viele Indikationen und viele Hersteller.<br>• Haben sich ab Juni wieder normalisiert.<br>• Mittlerweile sind es wieder die normalen Lieferengpässe wie sie vorher existent waren<br>• Vermutlich auch dazu einen zusätzlichen Beitrag geleistet hat der Hamsterkauf der Apotheken und Patienten<br>• Das Substituieren in der Apotheke ist leichter geworden (oder war), war gefeit vor Retaxationen. |
| **Q2:**<br>Bis wann galt diese Bestimmung? | **A2:**<br>• Nicht sicher, aber darüber hinaus gab es bei vielen Kassen sowas wie still halte Abkommen, dass man weiter substituieren darf. |
| **Q3**:<br>Ich habe die Lieferengpässe analysiert, anhand der BfArM Seite für Lieferengpässe für Humanarzneimittel, in der die Arzneimittelfirmen ihre Lieferengpässe melden. Als Grund für die Lieferengpässe wurde am häufigsten eine erhöhte Nachfrage im Markt angegeben. Konnten Sie ebenfalls eine erhöhte Nachfrage von verordneten Medikamenten verzeichnen und haben die Ärzte auch mehr verschreiben? | **A3:**<br>• Die Patienten haben sich schon bevorratet nur nicht allzu lange, die meisten haben nicht damit gerechnet, dass es so lange anhält.<br>• März war in Apotheken extrem gut, April entsprechend schlecht.<br>• Manches vermutlich auch über Versandhandel abgehandelt.<br>• Glaube die Begründung der Hersteller nicht, diese hatten eher aufgrund der Rabattverträge Strafen zu bezahlen oder Restriktionen zu befürchten, wenn sie nicht liefern konnten.<br>• Leicht zu sagen, die Apotheken haben es vertan.<br>• So viel können sie gar nicht hamstern, Warenlager einer durchschnittlichen Apotheke (an jeder Ecke) ist geschätzt 80.000€, die größeren 200.000-400.000€.<br>• Hat man am AvP-Skandal gesehen, Insolvenz des Rechenzentrums, was da an Rezepten eingelöst wird, die sprechen glaub ich von 100.000 pro Monat eingereicht.<br>• Wenn sie jetzt hamstern und einen Monat in Vorlauf gehen möchten, dann müssen sie 100.000€ investieren und ob sie einen Monat weiterkommen ist die Frage<br>• Wenn der Lieferengpass erstmal da ist er nicht morgen aufgehoben, die Lieferketten waren ja unterbrochen, deswegen glaube ich das nicht.<br>• Glaube gelesen zu haben, dass China für bestimmte Stoffe Exportstopp verhängt hat. |

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| | • Am Hafen war gähnende Leere, bis die großen Pötte wieder ankamen, das hat gedauert. |
| **Q4:**<br>Die unterbrochene Lieferkette war auch der zweitmeiste angegebene Grund, aber Hersteller können es ja freiwillig eingeben. | **A4:**<br>• Wird wohl so eingetragen, wie es am besten passt.<br>• Bei manchen Arzneimitteln können die Firmen immer noch nicht liefern.<br>• Und das wäre ein Indiz für die unterbrochene Lieferkette<br>• Glaube nicht, dass jemand bis zum Jahres Ende vorgekauft hat, da müssen sie sehen wie viel Geld sie da mitbringen und die ganzen Gefahren, dass sich die Preise und Rabattverträge ändern, im Generika-Markt gehen sie ja eher nach unten.<br>• Natürlich habe ich mich auch ein bisschen bevorratet, aber das als Hauptgrund mit erhöhter Nachfrage bezweifle ich. |
| **Q5:**<br>Die Kunden haben auch etwas gehamstert. Hatten Sie das Gefühl, dass diese Angst hatten in die Apotheke zukommen und nach draußen zu gehen und den Ärzten gesagt haben: „Verschreiben Sie mir bitte mehr?“. Geht so was? | **A5:**<br>• Es gibt die Möglichkeit einer Dauerverordnung, für einen bestimmten Zeitraum aber inwiefern die Ärzte davon Gebrauch machen weiß ich nicht, glaube eher weniger.<br>• Aber das mit den Lieferengpässen war ja in der Presse also wäre man doof gewesen und sagt gib mir mal 2 Packungen oder mehr.<br>• Ich habe vorher aber selten gesehen, dass jemand plötzlich 3 Packungen Insulin aufgeschrieben bekommen hat auf einem Rezept.<br>• Die sind da sag ich mal am Monatsende und am Monatsanfang nochmal gekommen.<br>• Oh, der war doch erst letzten Monat da. |
| **Q6:**<br>Haben die Lieferengpässe aus ihrer Sicht sogar zu Versorgungsengpässen geführt, dass manche Patienten ihre wichtigen Medikamente nicht bekommen haben oder konnten Sie das substituieren? | **A6:**<br>• Das hat natürlich was damit zu tun, wie man selbst gehamstert hat.<br>• Wir jetzt mussten im Prinzip zu keiner Zeit jemanden wegschicken ohne ein Medikament, wir haben aber vielleicht die Firma ändern müssen.<br>• Wir haben uns schon im Januar, am 15. Januar glaube ich, haben wir uns schon bevorratet mit Masken und Schilddrüsenhormonen, Herz-Kreislauf-Medikamenten.<br>• Aus diesem Grund hatten wir die Möglichkeit eher Kunden zu gewinnen, man hatte schon Kunden, die meinten: „ja wir waren jetzt schon in 4 Apotheken, klasse dass sie das haben“.<br>• Deshalb haben wir zu jederzeit auch Desinfektionsmittel, Sterillium und alles Mögliche gehabt. Was wir dann auch begrenzt haben in der Abgabe, das wurde nicht einfach so weggekippt. |

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| **Q7:**<br>Und die Schilddrüsenhormone und Herz-Kreislauf-Medikamente haben Sie das vorgekauft, weil es schonmal Lieferengpässe gab? | **A7:**<br>• Ja gab es schon, aber nicht so oft.<br>• Aber dann gab es natürlich in der Fachpresse Hinweise auf Arzneimittel, wenn man sich überlegt wo die Wirkstoffe hergestellt werden. Wo Mögliche Engpässe entstehen könnten. Dann haben wir uns nach dem was wir hier hauptsächlich abgeben, bevorratet.<br>• Gilt nicht nur für Schilddrüsenhormone und Herz-Kreislauf-Medikamente, sondern auch dafür welche potenziellen Arzneimittel kommen zum Einsatz, wenn man so eine Krankheit bekommt.<br>• Wir haben dann auch Antibiotika bevorratet, die dann auch gezielt zur Therapie eingesetzt werden können, so wie die ganzen Inhalativen Geschichten, oder die Arzneimittel, die schleimlösend wirksam oder husten beruhigend sind.<br>• Von den Sachen, von denen ich jetzt spreche, die gehen im 100 Packungen Maßstab, das wäre ein Drama, wenn ein Arzneimittel, dass wir 100-mal an einen oder mehre Patienten abgeben, dass wir das im nächsten Monat nicht mehr haben. Aus dem Grunde haben wir natürlich ein paar Monate vorgezogen. |
| **Q8:**<br>Die Analyse des Gesamtmarktes und die der Lieferengpässe ergab, dass die Verordnungen im März hochgestiegen sind und ein Rückgang der Verordnungen im April um ca. 20 teilweise 40-50% zum Vormonat zu verzeichnen war. Haben Sie das in Ihrer Apotheke auch gemerkt, dass dann im April weniger abgegeben wurde? | **A8:**<br>• Ja klar, da war natürlich weniger Absatz. Wie gesagt, ich kann mir nicht vorstellen, dass sich jede Apotheke bevorratet hat. Wie gesagt ich kenne Apotheken, die sich bevorratet haben, aber ich glaube nicht, dass jede Apotheke sich bevorratet hat.<br>• Sie können davon ausgehen, dass die Infektionszahlen steigen. Nun könnte man sich überlegen entstehen wieder Lieferengpässe, ja oder nein.<br>• Normal sollten die Firmen ausreichend bevorratet sein, wobei es jetzt so ist, dass man nicht nur Deutschland singulär sehen muss, sondern das Weltweite geschehen.<br>• Zum Beispiel so was wie bei dem Pneumokokken-Impfstoff, den wir hier überhaupt nicht mehr zur Verfügung hatten, dass Chargen aus dem Ausland für den Vertrieb in Deutschland freigegeben worden sind.<br>• Bei den Pneumokokken hatten wir hier den Impfstoff aus Japan, in japanischer Schrift, was keiner lesen konnte, drauf, oder aber auch, dass sie hier einen Pneumokokken-Impfstoff auf den Markt gebracht haben, der eigentlich für den Iran bestimmt war. Das ist natürlich schwierig. Ich weiß nicht welche Beweggründe die Firma hatte, dem Markt, für den der Impfstoff bestimmt war, diesen vorzuenthalten. Das kann ich nicht nachvollziehen. Da haben dann die Verschiebungen stattgefunden. |
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| **Q9:**<br>Welche Wirkstoffe für welche Indikationsgruppen waren aus Ihrer Sicht am meisten von den Lieferengpässen betroffen? | **A9:**<br>• Also Herz-Kreislauf-Medikamente, dann die Schilddrüsenhormone, dann bestimmte Inhalative-Kortikoide.<br>• Schmerzmittel, also Paracetamol und Ibuprofen.<br>• Lag vielleicht daran, dass die Firma, die am meisten in Deutschland vertrieben wird, kommt ja aus Frankreich, dass die da die Ausfuhr da reglementiert haben, da sie es für sich selbst brauchten.<br>• Antidiabetika waren auch nicht mitbekommen. |
| **Q10:**<br>Die Analyse ergab, dass am meisten die ATC-1 Gruppen Nervensystem, Antiinfektiva und das Kardiovaskuläre System betroffen waren. Bei den ATC-2 Gruppen waren die Antibiotika, Antiepileptika und Anästhetika und Narkosemittel und Analgetika am meisten betroffen. Können Sie dies bestätigen? | **A10:**<br>• Ja genau klar auf jeden Fall, ganz großes Drama.<br>• Und die Narkosemittel hatte ich noch vergessen. |
| **Q11:**<br>Welche Medikamente waren das? | **A11:**<br>• Propofol beispielsweise. Das habe ich auch hier in größeren Mengen, sonst wird's schwierig. |
| **Q12:**<br>Und welche Wirkstoffe bei den Antibiotika? | **A12:**<br>• Amoxicillin, Clavulansäure: beispielsweise war das: Cefuroxim, Cefixim. Das ging selbst so weit, wenn sie die Antibiotika nehmen, dass die entsprechenden Infusionslösungen, dass es zum Beispiel.: bei Jonosteril, Lieferengpässe gab. |
| **Q13:**<br>Und glaube Sie die Lieferengpässe wurden zum Problem oder konnten Sie das subsituieren? | **A13:**<br>• Bei Propofol ist das schwierig, da gibt es natürlich paar Firmen, die das so machen, das Propofol entscheidet sich so ein bisschen, es gibt 2 Varianten sag ich mal. Das war über alle Firmen hochgradig kontengiert, bei einer Firma war es ein Ausfall einer Produktionsfirma.<br>• Ich weiß nicht, ob es jetzt Braun oder Fresenius war, ein Werk ist ausgefallen und dann hat sich das auf die andere Firma verschoben. Und dann gab es wirklich einen absoluten Mangel, dass da wirklich die Firmen so rangegangen sind, dass man das nur noch pro Monat reduziert beziehen kann. Und die Anästhesisten hatten schon Angst gekriegt, weil ohne Narkosemittel keine Operationen. |
| **Q14:**<br>Ist da nur Propofol was da sinnvoll ist als Narkosemittel? | **A14:**<br>• Ne natürlich, je nachdem welche Operationen sie machen. |
| **Q15:**<br>Aber es ist nicht unbedingt ersetzbar? | **A15:**<br>• Ja doch irgendwie schon, aber es hängt davon ab, welche Operation und wie sie die Narkose machen. Wie |

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| | tief sie sein soll. Dann in Folge hatten sie nicht nur das Propofol, sondern auch das Naloxon oder solche Geschichten, womit sie die Narkose beenden. Das haben Sie dann natürlich auch nicht mehr gekriegt, Atropin oder solche Sachen.<br>• Gut wir waren davon jetzt nicht so betroffen, weil wir Mittel und Wege gefunden haben und Mittel, die Mengen zu bekommen, die wir wollten.<br>• Ist aber immer ein hohes Risiko, wir verdienen wenig an diesen Medikamenten und gehen damit sehr in Vorleistung |
| **Q16:**<br>Das ist ja auch wirtschaftlich dann schwierig, oder? | **A16:**<br>• Ja, ich weiß nicht, ob sie das kennen mit dem Influenza-Impfstoff, jetzt aber kristallisiert sich heraus, dass die Influenza gar nicht stattfinden wird. Denn die Influenza entwickelt sich immer wieder gleich, weil wir den Ursprung der saisonalen Grippen im Ursprung im asiatischen Bereich in China haben. Und jetzt ist es viel weiterverbreitet, dass die da mit Mundschutz rumlaufen und ihre Hände öfter desinfizieren und Abstandregelung einhalten und solche Sachen.<br>• Das hat wohl dazu geführt, dass sich bei der saisonalen Grippe nur wenige Menschen infiziert haben<br>• Und das geht wirklich über den asiatischen Bereich verteilt sich das nach einem bestimmten Muster, bis das Virus dann in Amerika oder hier in Europa ankommt. Jedes Jahr das Gleiche. Jetzt haben sich aber so wenig Leute infiziert. Das heißt jetzt kann man spekulieren, dass auch ganz wenige Leute sich in Deutschland infizieren.<br>• Es gab eher wenig Todesfälle im asiatischen Bereich mit der saisonalen Grippe. Und jetzt haben wir tonnenweise an Impfstoffen und es könnte sein, dass keiner es haben will oder auf der Straße merken oh jetzt ist es nicht mehr so gefährlich, ich brauche das gar nicht.<br>• Wenn Sie dann an einer Packung 6 Euro oder verdienen, und die Packung irgendwie 150 Euro oder so kostet, frage ich mich, ob ich das kaufe oder nicht. Ist ein Risiko. Bei Schilddrüsenhormonen ist es relativ egal, die kosten 12€. |
| **Q17:**<br>In Ihrer Apotheke lief es gut, dass sie keine Patienten nach Hause schicken mussten, würden Sie sagen, dass durch Pandemie einige Bevölkerungsgruppen nicht mehr ausreichen versorgt werden konnten oder es sogar eine Gesundheitsgefahr mit sich gebracht hat? | **A17:**<br>• Ja auf jeden Fall, es ist ja so, es sind ja die Fälle bekannt, dass die Leute sich nicht in die Krankenhäuser getraut haben, die haben sich auch nicht zum Arzt getraut<br>• Wir haben uns auch gefragt, wieso kommen hier keine Kunden in die Apotheke. Dann sind wir mal hier in der Umgebung zu den Ärzten gegangen, da war auch keiner<br>• Sie können das auch im OTC Bereich sehen. Entweder die Leute haben alles im Versandhandel gekauft, was ich |

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| | mir auch nicht so vorstellen kann, viele wohl aber längst nicht alle<br>• Über weite Indikationen, die Leute haben keine Kopfschmerzen mehr, Nasenspray geht das ganze Jahr über, bisschen mehr im Winter, aber 70% des normalen Verkaufs hat gar nicht stattgefunden. Kein Aspirin, Ibuprofen, kein Nasenspray. Drama |
| **Q18:**<br>Bei Ibuprofen hatte die WHO ja deklariert, dass man es besser nicht nehmen sollte. Hatte dies dann etwas mit dem Paracetamol Engpass zu tun? | **A18:**<br>• Bei Paracetamol gibt es ja nur noch wirklich 2 Werke, die das noch herstellen. Ich glaube das letzte Werk hier in Norddeutschland und das in Frankreich ist vor vielen Jahren geschlossen wurden. Ich glaube, als die Meldung kam war der Lieferengpass aber schon Wochen vorher da. Da hatte die Apotheken sich schon eingedeckt, aber da müssen sie wissen, es sind Jahresbevorratungen. Das ist aber üblicherweise im Vorjahr schon<br>• Im Dezember Januar werden die Jahresbevorratungen für das kommende Jahr ausgeliefert, also da haben sie meistens dann genug gehabt.<br>• Da sind die Firmen dazu übergangen erst die Bestellungen einzuholen, weit im Voraus. Jetzt geht das los, dass ich für den Sommer nächsten Jahres Allergie Medikamente bestelle, das heißt, dass produzieren die und noch 10% mehr, falls noch irgendwer was haben will. Das heißt die allgemeine Bevorratungshaltungen bei denen ist gar nicht mehr so groß wie früher. Früher hatten Sie vielleicht ihre Millionen Packungen und haben das Stück für Stück abverkauft. Jetzt haben die das weit vorgezogen mit Vorbestellungen. Deshalb glaube ich, dass es weniger die Sache von Hamstern war, als dass sie gar nicht diese Wirkstoffe so vorhalten können, dass sie planmäßig nachproduzieren können. |
| **Q19:**<br>Welche Lehren aus dem Arzneimittelmarkt würden Sie aus der Corona-Krise für künftige Krisen ziehen? Dass Sie irgendwelche Veränderungen vorschlagen, dass z.B.: wieder die Produktion mit essenziellen Arzneimitteln, wie Antibiotika wieder nach Europa kommen? | **A19:**<br>• Ja genau zum Beispiel oder aber auch bestimmte Vorratshaltungen, das haben sie auch im Apotheken Bereich bei bestimmten Sachen da sind sie verpflichtet bestimmte Sachen vorrätig zu halten. Da könnten sie natürlich verpflichten, dass Firmen Wirkstoffe oder Packungen vorrätig haben.<br>• Die Verlagerung von Produktionsstätten nach Europa, wenn man sich dazu entschließen sollte, das würde ja auch bestimmt ein Jahrzehnt dauern. Aber ich glaube nicht, dass es dazu kommen wird, aber es wäre ja schön. Ich habe das ja nie verstanden, denn so viele Leute arbeiten in den Firmen ja nicht, also warum das da so preisgünstiger sein soll, keine Ahnung |
| **Q20:**<br>Welche weiteren wichtigen Punkte sollten noch erwähnt werden, die den Arzneimittelmarkt bzw. die gesundheitliche | **A20:**<br>• Ja wichtig ist natürlich zum einen das Austauschen von Arzneimitteln, das ist das Eine |

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| Versorgung der Bevölkerung mit Arzneimitteln in der Corona-Krise verändert haben oder die wichtig wären? | • Zum anderen ist am Ende auch die Pandemie eine globale Krise, das haben die meisten ja noch gar nicht realisiert<br>• Da wird noch viel mehr auf den heimischen Markt geschaut und nicht geguckt, wo es tatsächlich am wenigsten ist<br>• Ich sehe das natürlich als Apotheker und in Bezug auf den Versandhandel. Natürlich ist der Versandhandel günstiger. Der zahlt hier keine Gewerbesteuer und nimmt hier auch nicht die kompletten Aufgaben wahr, die eine Apotheke vor Ort wahrnimmt, das muss man wissen, möchte man nur auf den Preis gehen oder möchte man nie wieder in so eine Situation kommen.<br>• Und in dieser Situation, in der wir da waren, haben nur die Apotheken ohne große Probleme, ohne dass sie sich eine Krone aufgesetzt haben, sehr viel geleistet<br>• Und das werden Sie, Sie sind ja jung, ihre Generation wird das bezahlen. Da gibt es Hochrechnungen, dass sie im Durchschnitt zehn Prozent ihres jährlichen Gehalts verlieren werden. Das ist ja noch nicht richtig ausdiskutiert wer das alles richtig bezahlen soll.<br>• Wenn der Staat diese Verantwortung nicht ausgelagert hätte, oder wenn er sich dieser Verantwortung bewusst gewesen wäre, so wie es viele 1000 Apotheken getan haben, dann wären wir ganz anders mit der Situation umgegangen und die meisten Apotheken waren nicht so dämlich wie der Staat.<br>• Der Staat hat ja, wenn sie nur an die Masken denken, Anfang April hat er das vom Beschaffungsamt der Bundeswehr umgelagert auf irgendwelche privaten Leute.<br>• Da hat mein Großhändler schon längst Masken aus Südafrika besorgt und die 1000 Apotheken haben die schon an die Patienten weitergegeben. Ich habe ja nicht den Informationsfluss wie der Staat und ich habe mich schon im Januar mit Masken und Desinfektionsmittel beschäftigt, dann muss ich mich fragen was die Bundesregierung gemacht hat, was Krankenhäuser gemacht haben oder andere Einrichtungen gemacht haben. Das ist was ich schwer nachvollziehen kann. Da macht es schon Sinn, dass man die Kompetenz der Leute nutzt. |
| **Q21:**<br>Würden Sie sagen, dass die Rabattverträge verändert werden müssen? Weil das ja schon ein Problem war in der Pandemie. Es gab auch Erleichterungen diesbezüglich, aber es gab auch Schwierigkeiten. | **A21:**<br>• Es gibt Schwierigkeiten mit den Rabattverträgen<br>• Man grenzt ja andere Firmen aus<br>• Das war eigentlich schon mit Einführung der Rabattverträge abzusehen, dass Produktionskapazitäten abgebaut werden, das Firmen auch große Generika Firmen überlegen, wenn ich den Rabattvertrag da nicht kriege, dann stelle ich den Kram Ganz ein oder auf niedrigem Niveau. |

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| | • Wenn es dann zu einer Pandemie oder irgendwelchen Ereignissen kommt, dann haben Sie natürlich das Problem, dass sie nur noch eine handvoll Firmen haben, die wirklich über Möglichkeiten verfügen Arzneimittel herzustellen.<br>• Ich halte von Rabattverträgen nichts, also eine nachträgliche Rabattierung das ist ein System vollkommen undurchsichtig bis nicht zielführend.<br>• Wahrscheinlich haben die Rabattverträge auch wesentlich dazu beigetragen, dass wir diese enormen Lieferengpässe hatten<br>• Wie bei Ibuprofen alles stürzt, sich auf einen Hersteller, Zentiva oder Ibuflam. Hat dieser Hersteller einen Lieferengpass oder machen die Franzosen die Grenzen zu, dann stehen sie doof da und zack ist aus. Das ist das Problem. Ob wir daraus lernen weiß ich nicht. |

**Online-Interview on 19 October 2020 from 14:10 am to 14:30 am (Duration: 20 minutes)**

| Stephan | Hospital pharmacist (HO.P) |
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| **Q1:**<br>Die Corona Pandemie hat einige strukturelle Veränderungen in der ganzen Welt mit sich gebracht. Der Lockdown in den meisten Ländern und die Schließungen der Grenzen hat auch zu Veränderungen im Gesundheitswesen geführt. Welche Veränderungen bzw. Schwierigkeiten oder sogar Erleichterungen ergaben sich im Bereich der Versorgung mit Arzneimitteln in der stationären Versorgung? | **A1:**<br>• Man muss da zum einen unterscheiden, ob das ein großer Bedarf durch die Corona-Pandemie an Medikamenten ist, also ein erhöhter Bedarf und zum anderen, dass Lieferketten abgerissen sind, durch Lockdown in anderen Ländern, Hauptsächlich China.<br>• Viele Rohstoffe werden ja oftmals nur in 2 Ländern hergestellt, Indien und China und wenn dann mal eine Fabrik ausfällt, dann hat das weltweite Konsequenzen.<br>• Das merken wir jetzt nicht nur durch Corona, das war in den Jahren davor auch so. |
| **Q2:**<br>In der heiklen Corona-Phase März bis April sind mehr Lieferengpässe entstanden. Laut der BfArM Datenbank also es waren mehr Medikamente von einem Lieferengpass betroffen. Haben Sie das auch gemerkt? | **A2:**<br>• Mit den Standardmedikamenten hatten wir jetzt ehrlich gesagt keine Probleme, wenn da jetzt mal ein Lieferengpass gab, hat dann ein Hersteller versucht das mit Corona zu begründen, das glaub ich aber nicht, denn das gab es vorher auch schon. |
| **Q3**:<br>Als Grund für die Lieferengpässe wurde am häufigsten eine erhöhte Nachfrage im Markt angegeben und am 2. Häufigsten eine unterbrochene Lieferkette. Können Sie dies aus Ihrer Sicht bestätigen? | **A3:**<br>• Eher die erhöhte Nachfrage |
| **Q4:**<br>Kam es in der stationären Versorgung denn zu spürbaren Lieferengpässen oder konnten Medikamente z.B. die Standardmedikamente substituiert werden, gab es da spürbare Veränderungen? | **A4:**<br>• Also mit Standardmedikamente meine ich Antibiotika und Herz-Kreislauf-Medikamente etc.<br>• Wo wir spürbare Engpässe gehabt haben, das waren die Anästhetika, das heißt die Präparate, mit denen auf der Intensivstation die schweren COVID Fälle behandelt wurden bzw. wenn sie in das so genannte künstliche Koma versetzt wurden.<br>• Das heißt man hat spürbar mehr beatmete Patienten gehabt auf den Intensivstationen.<br>• Die haben auch im Vergleich zu anderen Patienten sehr viel mehr Anästhetika verbraucht. Dann sind wir leergelaufen, dann sind Kollegen leergelaufen und die Industrie ist leergelaufen. |
| **Q5:**<br>Konnte man das mit anderen Anästhetika ausgleichen? | **A5:**<br>• Ja das gab Diskussionen mit den Chef- und Oberärzten, denn die sind natürlich erstmal in Panik gewesen.<br>• Wir haben aber dann Alternativen diskutiert und dann haben die aber auch Alternativen gefunden. |

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| | • Manchmal Sachen die zwar nicht unbedingt, immer lege artis waren, das heißt die wohl möglich auch keine Zulassung hatten für diesen Fall, aber man hat sich damit beholfen. |
| **Q6:**<br>Die Analyse ergab, dass das Propofol stark von Lieferengpässen betroffen war. Ist das eins der Medikamente? | **A6:**<br>• Bei Propofol ist es der Sonderfall, dass es bereits vor COVID schwer verfügbar war und es war auch kontingentiert.<br>• Das heißt man hat von den Firmen, es gab nur 2 Firmen am Markt, seine Monatsmengen zugeteilt bekommen, damit ist man auch knapp ausgekommen, aber in dem Fall wo die erhöhte Nachfrage war, ist es dann zusammengebrochen. |
| **Q7:**<br>Können Sie mir noch andere Medikamente in dem Bereich nennen, die knapp waren? | **A7:**<br>• Midazolam, das war auch ganz extrem und Arterenol das war auch so eine Sache.<br>• Arterenol das nimmt man auch für die Patienten, die halt künstlich beatmet werden, wenn der Kreislauf dann absackt. Das sind so die Hauptmedikamente, wo es Stress gab. |
| **Q8:**<br>Gibt es noch andere Arzneimittelgruppen außer den Anästhetika, wo es Engpässe gab oder eher nicht? | **A8:**<br>• Wir hatten da bisschen Angst bei den Antibiotika, die aus China kamen, aber das hat sich nicht bestätigt. |
| **Q9:**<br>Die Analyse ergab auch, dass die Antiinfektiva, Herz-Kreislauf-Medikamente, Antiepileptika, Anästhetika und Schmerzmittel von Lieferengpässen betroffen waren. War da etwas spürbar? | **A9:**<br>• Schmerzmittel: Ibuprofen, da gibt's immer wieder diese Schwierigkeiten, weil eben der Rohstoff aus Asien kommt. Aber das war vorher auch schon so, also nicht extrem in der Corona-Zeit. |
| **Q10:**<br>Anhand der Daten war im April im Gesamtmarkt und bei den Medikamenten mit gemeldeten Lieferengpässen ein Rückgang der Verordnungen um ca. 20 teilweise 40-50% zum Vormonat zu verzeichnen.<br><br>Können Sie dies für die Versorgung in Ihrem Krankenhaus bestätigen bzw. mussten weniger Patienten im Krankenhaus versorgt werden? | **A10:**<br>• Das kam uns natürlich zugute, denn Betten wurden freigehalten und geplante Operationen wurden verschoben.<br>• Die Krankenhäuser waren leer, also insofern, haben wir bei den anderen Präparaten keine Probleme gehabt. |
| **Q11:**<br>Durch die Corona Pandemie haben es ja auch vielleicht vermieden ins Krankenhaus gehen. Kam es da aus ihrer Sicht zu einem Versorgungsengpass oder einer Gesundheitsgefahr für die Bevölkerung? | **A11:**<br>• Ich denke nicht. Also die schwerwiegenden zu behandelnden Fälle wurden auch immer behandelt.<br>• Und auch da war es nicht so, dass Medikamente ausgefallen sind, die dann eine Patienten Gefährdung zur Folge gehabt hätten. |

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| **Q12:**<br>Gab es Erleichterungen, die auch im Krankenhaus das Substituieren leichter gemacht haben? | **A12:**<br>• Also Rabattverträge betreffen uns nicht und deshalb sind wir auch ganz frei in unserem Einkaufen. Wir rechnen die Medikamente auch nicht mit den Krankenkassen ab, sondern zahlen das mit unserem Budget. |
| **Q13:**<br>Gab es dann bei den Offizin-Apothekern mehr Probleme? | **A13:**<br>• Da wurde dann ein Präparat verordnet, das war nicht verfügbar, dann durften sie das einfach nicht abgeben, weil sie dafür kein Geld kriegen.<br>• Aber ich glaube, die Krankenkassen waren da relativ kooperativ. |
| **Q14:**<br>Welche Lehren im Bereich des Arzneimittelmarktes würden Sie aus der Corona-Krise für zukünftige Krisen ziehen, wie z.B. bei den Anästhetika? | **A14:**<br>• Jetzt auf unser Krankenhaus oder jede einzelne Apotheke runtergebrochen, müssen wir natürlich unsere Bestände hochfahren, machen wir auch.<br>• Es gab auch eine Verordnung, dass man einen 3 Wochen Bedarf mit Ästhetikern vorrätig halten muss in der Krankenhausapotheke. Das war vorher 2 Wochen. Das hatten wir aber vorher auch schon und das haben wir jetzt aber auch auf 4-5 Wochen hochgesetzt.<br>• Es gibt Initiativen, das gab es aber auch schon vor Corona, dass man die Produktion bestimmter Arzneimittel zurück nach Europa holt, das kriegt jetzt natürlich Aufwind. |
| **Q15:**<br>Glauben Sie denn, dass es sinnvoll wäre die Produktion von bestimmten Stoffen zurück nach Europa zu holen bzw. würde es die Probleme, die entstanden sind, lösen? | **A15:**<br>• Ja also ich unterstütze das schon, aber ich bin auch Realist und ich glaube, dass da „Money rules“ ist und das wird dann auch das Gesundheitswesen nicht mehr bezahlen können, wenn das hier im hohen Sektor hergestellt wird. |
| **Q16:**<br>Die Arzneimittelfirmen hatten ja früher eine größere Bevorratung und inzwischen wird auf Bestellung produziert. Würden Sie sagen, dass Arzneimittelfirmen Medikamente bevorraten sollen? | **A16:**<br>• Auf jeden Fall, man muss da die Pharmafirmen auch in die Pflicht nehmen, dass die nicht mehr „Just in Time“ produzieren, sondern ihre Lagerbestände erhöhen.<br>• das muss auch von der Politik ausgehen. |
| **Q17:**<br>Welche weiteren wichtigen Punkte sollten noch erwähnt werden, die den Arzneimittelmarkt und die Auswirkungen für die medikamentöse Versorgung in der Corona-Krise verändert haben? | **A17:**<br>• Zum Thema Grippeimpfstoff. Es gibt schon jetzt Lieferengpässe für den Grippeimpfstoff. Die Nachfrage ist erhöht, weil sich viel mehr Menschen impfen lassen wollen.<br>• Jetzt als Beispiel haben wir jährlich immer 800 Grippedosen geimpft, die bestellen wir auch immer Anfang des Jahres und die haben wir auch schon bekommen.<br>• Aber die Nachfrage ist fast doppelt so hoch. Jetzt versuchen wir seit Wochen nochmal 650 nachzubekommen, die gibt es nicht. |

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| **Q18:**<br>Hat Deutschland da zu wenig eingekauft oder wurde nicht mit so einer großen Nachfrage gerechnet? | **A18:**<br>• Ja ich glaube, das ist so wie vor 2 Jahren, da war das schonmal ähnlich, es gibt genug der wird aber wohl irgendwie schlecht verteilt. |
| **Q19:**<br>Werden es denn aus ihrer Sicht viele Grippe Fälle geben? | **A19:**<br>• Seit Frühjahr haben Sie bestimmt auch nicht so viele Infekte gehabt wie die Vorjahre. Jeder den ich frage meinte: „Ja dieses Jahr war ich fast gar nicht krank“.<br>• Das hat schon was mit dem Infektionsschutz zu tun. Die Influenza kommt aus Asien und kommt über die Südhalbkugel im Sommer und da waren dieses Jahr kaum Fälle, also ich glaube nicht, dass wir eine große Grippewelle bekommen werden. |

**Interview the 27 October 2020 from 11:00 am to 11:35 am**
**(Duration: 35 minutes) minutes)**

| Stephan | Wholesaler (W1) – Sales Manager |
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| **Q1:**<br>Die Corona Pandemie hat einige strukturelle Veränderungen in der ganzen Welt mit sich gebracht. Der Lockdown in den meisten Ländern und die Schließungen der Grenzen hat auch zu Veränderungen im Gesundheitswesen geführt.<br><br>Welche strukturellen Veränderungen bzw. Schwierigkeiten durch die Corona-Pandemie beobachten Sie im Arzneimittelmarkt? | **A1:**<br>• Aus meiner Sicht zumindest verändert hat sich auch im Arzneimittelsektor die Verlagerung ins Online Geschäft<br>• Das ist würde ich sagen etwas was schon viele Branchen betraf, dass der Online Versandhandel zunimmt in allen Bereichen, der Arzneimittelsektor war dar bislang nur marginal von betroffen. Wenn ich marginal sage geht es da schon um hunderte von Millionen, aber gemessen an der Gesamtsumme war es nicht viel<br>• Was so gut wie gar nicht wirklich lief über den Versandhandel, das waren rezeptpflichtige Arzneimittel und das hat sicherlich ein Stück weit zugenommen, wer weiß, ob sich das zurückkurbeln lässt.<br>• Das ist was die Vor-Ort-Apotheke stark betreffen würde, wenn die Rezepte weggehen in den Versandhandel, dann hat eine Vor-Ort-Apotheke viel größere Probleme finanziell, als sie es jetzt schon haben, das ist also eine klassische Einnahmequelle einer Vor-Ort-Apotheke<br>• Durch Corona und durch den Lockdown hatten viele Menschen Angst, gerade Chroniker und multimorbide Menschen, die bekanntlich hauptsächlich in die Apotheke gehen. Es ist klar, wenn sie Angst haben sich anzustecken und nicht mehr vor die Tür gehen, haben sie auch Angst in die Apotheke zu gehen, da muss man lange anstehen, weil man nur 2-3 Leute Innen bedienen kann. Dann wird es Überlegenswert das mit dem Versandhandel zu machen<br>• Das hat im März/April zu strukturellen Veränderungen geführt. Da hat sich die Warenkorbstruktur bei uns im Großhandel und in der Apotheke verändert, wenn die Apotheke gewisse Dinge nicht mehr verkauft, fehlen die uns auch.<br>• Das hat die Corona Pandemie auf jeden Fall bewirkt. Wir sagen dazu wir haben einen Spannenverlust im Bereich der rezeptpflichtigen Arzneimittel<br>• Das merkt die Apotheke halt auch, weil die Ärzte nicht mehr die klassischen N1 Packungen verschreiben, wo ein Patient in der Regel 1 Monat mit klarkommt, sondern er verschreibt häufig N3, das möchten die Krankenkassen auch, dass das so passiert. Also die halten ca. 3 Monate, es gibt mittlerweile auch Packungen die länger halten.<br>• Dadurch sieht der Arzt den Patienten weniger und das ist natürlich in einer Pandemiephase ja auch wünschenswert, dass der Patient weniger zum Arzt kommt, außer er muss umgestellt werden oder es kommt irgendwas anderes hinzu.<br>• Und das führt schon bei uns zu einem Spannenfall, bei kleineren Packungen haben wir ein größerer Mage, das hängt mit der Arzneimittelpreisverordnung zusammen, die dem Großhandel quasi vom Gesetzes wegen her diktiert wird.<br>• Die Spanne des Großhandels bei rezeptpflichtigen Arzneimitteln. Zum Beispiel, ein Artikel kostet 10 Euro. Wir kaufen den für 10 Euro beim Hersteller ein. Dann können wir nicht irgendeine |

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| | Spanne darauf schlagen, wie im normalen Handel. 85 Prozent, das ist der rezeptpflichtige Umsatz, das ist der Anteil am Gesamtumsatz. An diesen knappen 85 Prozent dürfen wir pro Packung 70 Cent draufschlagen und 3,15%. Das ist bei einem Artikel der Zehn Euro kostet alles noch in Ordnung, da sind die 70 Cent, irgendwie sieben Prozent, das lässt sich noch alles rechnen.<br>• Je teurer der Artikel wird umso kritischer wird das mit den 70 Cent. Die Apotheken, sind was die Spanne angeht etwas besser bestellt, aber das muss auch, weil die Apotheke weniger abgibt, also kleinere Werte. Bei uns ist es über Masse. Aber nochmal diese 70 Cent, wenn man sonst ein Packungsschnitt von 25 Euro hatte und nun ein von 30 Euro, ist also um Fünf Euro gestiegen, das hat schon an Spanne gekostet.<br>• Ich weiß auch nicht, wenn die Pandemie dann irgendwann vorbei ist, ob das zurückgedreht wird, weil die Barriere rezeptpflichtige Arzneimittel online zu bestellen genommen wurde, die sicherlich der eine oder andere hatte, weil er lieber in die Vor-Ort-Apotheke geht<br>• Man muss sehen, ob das wieder zurückgeht. Die Frage ist auch, werden Ärzte weiterhin N1 verschreiben, werden Krankenkassen darauf pochen, dass es hauptsächlich N3 Packungen gibt? |
| **Q2:**<br>In der Phase des ‘Lockdowns‘ gab es von März bis Mai eine Vielzahl von Lieferengpässen. Als Grund für die Lieferengpässe wurde am häufigsten eine erhöhte Nachfrage im Markt angegeben und als 2. Häufigster Grund eine unterbrochene Lieferkette.<br><br>Können Sie dies bestätigen bzw. inwiefern wurde dies im Großhandel beim Einkauf/Verkauf bemerkbar? | **A2:**<br>• Also das sind jetzt nur Vermutungen, ich sitze nicht im Einkauf, ich glaube, dass viel in Fernost produziert wird, weil dort die Produktionskosten geringer sind.<br>• Gerade in China und in Wuhan, gibt es viele Herstellungsbetriebe, die auch Rohstoffe für gewisse weitere Schritte produzieren.<br>• Da wurde uns im Januar oder Dezember schon prognostiziert, das wird Lieferengpässe geben, das wird bei einigen Arzneimitteln auf jeden Fall eng werden, weil einfach die Rohstoffproduktion in den Fernost-Gebieten zum Erliegen kam.<br>• Ich glaube es hat was mit der Rohstoffproduktion zu tun, weil man diese nicht mehr so produzieren konnte, wie man es normalerweise kennt. |
| **Q3**:<br>Gab es auch Hamsterkäufe seitens der Apotheke? | **A3:**<br>• Also bei rezeptpflichtigen Arzneimitteln haben auch einige Apotheken Hamsterkäufe getätigt, das ist richtig, aber was das jetzt tatsächlich für eine Auswirkung hatte, ist schwer einzuschätzen, aber es war bei einigen Apotheken zu sehen, dass sie hamstern. |
| **Q4:**<br>Welche Medikamente oder welche Wirkstoffe waren knapp bzw. schwierig zu bekommen? | **A4:**<br>• Ibuprofen, wobei das ja nur ab 600mg verschreibungspflichtig ist, aber das war jetzt so ein Wirkstoff, da gibts nach wie vor Probleme.<br>• Also wenn sie jetzt Dolormin in der Apotheke kaufen wollen, das ist so der Markenhersteller bei Ibuprofen, dann wird schwierig. Die |

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| | haben nach wie vor Lieferengpässe. Die können den Markt immer noch nicht so bedienen, aber da gibt es jetzt natürlich auch Generika, wie Ibuflam zum Beispiel.<br>• Aber das ist jetzt so das was im März April stark nachgefragt wurde, wo es dann auch tatsächliche Lieferengpässe gab.<br>• Ich kann mich sonst nicht an einen Artikel erinnern. Ein Blutverdünner glaub ich. |
| **Q5:**<br>Gab es Lieferengpässe bei den Anästhetika oder Narkosemitteln, zum Beispiel Midazolam oder Propofol? | **A5:**<br>• Ja Propofol stimmt, auf jeden Fall.<br>• Das ist allerdings nicht so ein Thema was uns hier so sehr beschäftigt hat, weil wir in erster Linie Apotheken beliefern und keine Krankenhausapotheken.<br>• Das Anästhetikum wird in erste Linie an Krankenhäuser verkauft, manche Apotheken haben es auch, aber eher wenig. |
| **Q6:**<br>Glauben Sie, dass es insgesamt zu Liefer- bzw. Versorgungsengpässen gekommen ist, sodass bestimmte Gruppen der Bevölkerung nicht mehr ausreichend versorgt werden konnten? | **A6:**<br>• Ein richtiger Versorgungsengpass, nein.<br>• Also ich habe nicht eine Minute Angst gehabt, dass das deutsche Gesundheitssystem an den Rand kommt. |
| **Q7:**<br>Weil man eben noch genug Medikamente hatte und genug nachbekommen hat? | **A7:**<br>• Ja also es war schon spürbar, dass man nicht genug nachbekommen hat, aber es war noch genug da. Die Frage ist ja auch immer, was ist ein wichtiges Arzneimittel, was man braucht. |
| **Q8:**<br>Wenn es knapp wurde bei entsprechenden Medikamenten, konnte man dann auch substituieren? | **A8:**<br>• Es ist für mich schwierig, ich bin kein Chroniker oder sonst irgendwas, gibt natürlich schon Menschen, die regelmäßige Medikamente nehmen müssen, weil sich sonst ihre allgemeine Situation deutlich verschlechtert.<br>• Aber ich wüsste jetzt tatsächlich gerade kein Medikament, wo es so einen Engpass gab, dass diese Menschen hätten Angst haben müssen, das Medikament nicht mehr zu kriegen.<br>• Es kann aber sein, dass es das gibt, aber fällt mir gerade nicht ein. |
| **Q9:**<br>Eine weitere Frage wäre, betreffen die Rabattverträge auch den Großhandel und hat sich das im März, April bemerkbar gemacht? | **A9:**<br>• Also glaub ich nicht, bei Rabattvertragsartikeln fällt mir gerade nicht ein, dass es so Probleme gab.<br>• Also es gibt allgemein viele Probleme mit Rabattvertragsartikeln, also dieser ständige Wechsel, dann kriegt der Hersteller für den Wirkstoff den Zuschlag, dann der, dann werden die natürlich gedrückt im Preis.<br>• Das führt dazu, dass viele Hersteller keine Lust mehr haben an diesem System in Deutschland, das führt wiederum auch zu Engpässen, weil manche lieber die Ware im Ausland verkaufen, weil sie dort mehr verdienen als in Deutschland.<br>• In dem, mit dem reichsten Land der Welt, sind mittlerweile viele Medikamente billiger als in Ländern wie Spanien, Portugal, Italien, denen es definitiv nicht so gut geht. |

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| | • Das haben die Krankenkassen mit den Rabattverträgen geschafft, die haben den Preis nachhaltig gedrückt und das wiederum führt dazu, dass Hersteller kostenbedingt irgendwo weit weg zu produzieren, weil irgendwo müssen sie es ja reinholen, wenn sie für das Produkt weniger bekommen.<br>• Und das sind natürlich Dinge, die in einer Pandemie, ich sag mal deutlicher wurden. Also die Probleme gab es schon immer, aber ich glaube es ist bei vielen Dingen so, dass die Pandemie dafür gesorgt hat, dass man mit der Lupe auf die Probleme raufguckt. Man fokussiert sich jetzt mehr drauf, denn aus meiner Sicht traten die Probleme, die eh schon da waren, nun zu Tage. |
| **Q10:**<br>Die Lieferengpässe gab es auch schon vorher und wurden immer mehr? | **A10:**<br>• Das ist aus meiner Sicht politisch gewollt, uns wird die Arbeit dadurch wirklich schwer gemacht. Bei Rabattvertragsartikeln bedeutet das auch für den Großhandel, dass wir uns ständig auf neue Ware einstellen müssen und auch Ware von den Apotheken zurückbekommen, weil der Rabattvertrag ausgelaufen ist.<br>• Als wir hier neu hinkamen, hatte eine Kasse zum Beispiel, die hier mehr vertreten ist als in anderen, die wir vorher auch gar nicht richtig kannten, hat zum Beispiel dann spezielle Verträge mit Medikamenten, die hatten wir nicht mal im Lager.<br>• Also das war dann zum Beispiel ein Artikel, den mussten wir von dem Hersteller beziehen, mit dem hatten wir vorher auch keine Geschäftsbeziehungen, den wollten wir eigentlich auch nicht, weil das ein Hersteller ist, der uns keinen Rabatt gewährt.<br>• Da gab es dann plötzlich diese Nachfrage. Aber weil wir uns auf die Fahne schreiben, dass wir alles liefern wollen und keinen Hersteller ausschließen, mussten wir diese Geschäftsbeziehung eingehen.<br>• Wir hätten keinen Dispensationszwang, könnten Hersteller ausschließen, wollen aber unsere Kunden mit allem beliefern.<br>• Dann ändert sich der Rabattvertragsartikel und die Apotheker kann den Artikel nicht mehr abgeben, weil der Vertrag sich ändert und ein anderer Hersteller mit reingenommen wurde. Das ärgert dann die Hersteller, die haben dann kein Interesse mehr, früher hatten wir für den Grippe-Impfstoff 20-30 Hersteller, die das gemacht haben, aber weil auch da der Preis immer gedrückt wurde, gibt es da nur noch 4 Hersteller weltweit, die das herstellen. Wenn dann eine Produktionsstätte ausfällt, haben wir ein Problem. |
| **Q11:**<br>Was halten Sie davon die Produktion von essenziellen Arzneimitteln bzw. die Produktion von Antibiotika zurück nach Europa bzw. Deutschland zu holen? | • Ich würde das für sehr sinnvoll erachten, ich persönlich glaube da aber nicht dran, weil sie können einen Hersteller nicht zwingen irgendwo zu produzieren, mir fällt zumindest nichts ein, wie die Politik das schaffen will.<br>• Da wird sich jeder Hersteller gegen wehren. Die würden natürlich sagen, ja klar wir produzieren wieder in Europa, wenn ihr anfängt faire Preise zu bezahlen.<br>• Jetzt kann man sich über faire Preise streiten, es gibt Arzneimittel ganz normal 20 Tabletten, die kosten 20.000 Euro, 30.000 Euro oder Spritzen, die kosten 1,3 Millionen Euro. |

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| | • Den Menschen, die an dieser Krankheit leiden, hilft es wirklich. Jetzt kann man sagen moralisch gesehen, ist es alles ok. Aber man kann natürlich auch die Frage stellen, ist das ok, dass die so teuer sind. Also haben die Hersteller auch eine moralische Verpflichtung.<br>• Aber so wie sie von den Krankenkassen in den letzten Jahren gedrückt worden sind, muss ein Anreiz geschaffen werden, die Ware wieder in Europa herzustellen. |
| **Q12:**<br>Welche Lehren im Bereich des Arzneimittelmarktes würden Sie aus der Corona-Krise für zukünftige Krisen ziehen? | • Hinsichtlich der Arzneimittelproduktion, wirklich wichtige Arzneimittel sollte man wieder nach Europa zurückholen, dafür muss der Preis angemessen sein, anders wird man es nicht schaffen.<br>• Dann wird aber das Gesundheitssystem teurer. Wir dürfen uns da aber nichts vor machen, jetzt haben Leute zu Recht gesagt, dass Pflegekräfte zu wenig bezahlt und zu wenig angesehen werden, das ist eine Schande.<br>• Jetzt sagen alle, die müssen viel mehr verdienen, finde ich auch, aber wer bezahlt das am Ende des Tages. Das zahlen wir, und wenn man sagt, dass kostet dann 100 Euro mehr im Euro, dann finden wir Leute das nicht mehr ganz so gut. Der Krankenkassenbeitrag muss steigen, wenn wir die Arzneimittelproduktion wieder zurück nach Europa holen, die Pflegekräfte und Ärzte besser bezahlen. Das geht aber meiner Auffassung nach nur über unser Portemonnaie, das muss jedem klar sein. Der Staat könnte sagen, ich gehe etwas sorgfältiger mit Steuern um, und finanziere damit das Gesundheitssystem, aber das glaub ich nicht.<br>• Also ich fände es gut, wenn alles so käme, aber wir müssten dafür mehr bezahlen.<br>• Die Pandemie hat auch gezeigt, dass vor Ort Apotheken enorm wichtig sind. Sie sind eine Stütze der Gesellschaft, die wir brauchen, auch das wird in der Politik nicht immer so gesehen.<br>• Wir sind auch in er Politik aktiv und versuchen auf Politiker darauf hinzuweisen, dass sie mit der Politik tatsächlich das Apotheken sterben vorantreiben und es immer weniger werden.<br>• Und die Bevölkerung nimmt das kaum wahr, weil an jeder Ecke noch immer Apotheken sind. Die Bevölkerung unterliegt dem irrigen Glauben, dass das die Kostentreiber im Gesundheitssystem sind, was aber nicht stimmt, wirklich „non-sense“ hoch 10.<br>• Aber das kann man jemanden der sich nicht täglich damit auseinander setzt auch nicht vorwerfen, der sieht fünf Apotheken in einer Straße und fragt sich warum, reicht doch auch eine. Ich sage: „sei doch froh, dass da fünf sind, man fördert untereinander den Wettbewerb, man wird besser behandelt, der Verbraucher wird mehr wahrgenommen. Wenn hier nur eine wäre, und man müsste 10km weiterfahren zur nächsten, der könnte einen behandeln wie Dreck. Sei doch froh, dass der Wettbewerber so ist wie er ist.“<br>• Kostentreiber sind es nicht, jeder Apotheker muss selbst sehen, wie er klarkommt. Nur weil es weniger Apotheken gibt, wird unser Krankenkassenbeitrag ja nicht sinken, weil die Anzahl an |

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| | Medikamente ja nicht abnimmt, sondern eher zunimmt. Das verteilt sich dann, also die Einheiten werden größer. Es werden viele Apotheken schließen und einige werden größer. Es verteilt sich nur anders, es werden ja nicht weniger Arzneimittel verschrieben. |
| **Q13:**<br>Wieso wurde es gerade in der Pandemie Hochphase bemerkbar, dass Apotheken so wichtig sind? | • 1. Die schnelle Versorgung. Da kann Amazon und Doc Morris machen was sie wollen. Ich gehe in die Apotheke mit meinem Rezept, dann haben sie spätestens nach 2-3 Stunden ihr Medikament, dazu trägt der Großhandel bei. Es sei denn es ist mal ein Medikament schwierig zu kriegen.<br>• Andere Länder, Großbritannien zum Beispiel, da warten sie eine Woche. Da ist es nicht gewährleistet, selbst für ein Antibiotikum nicht, dass sie am selben Tag noch mit der Behandlung starten können.<br>• Dieses Gesundheitssystem in Deutschland ist definitiv eins der besten der Welt. Die Politik ist dabei, zumindest im Bereich der Distribution von Arzneimitteln, also die Apotheken, das zu zerstören, weil sie den Versandhandel protegiert, weil das ja so modern ist und das kann man ja nicht verbieten.<br>• Also ich glaube in 16 oder 18 EU-Ländern ist der Versandhandel mit rezeptpflichtigen Arzneimitteln verboten, nur Deutschland schafft es nicht das zu verbieten. Es gibt kein Rx-Verbot für Versandhändler<br>• Und die werden im Ausland noch nicht mal richtig kontrolliert. Die können ja auch liefern, wie sie wollen, in dem Moment, wenn das Medikament an UPS oder DHL übergeben wird, ist es raus aus der Kette. Da brauche ich keine Temperaturführung mehr, gar nichts.<br>• Wenn wir an unsere Apotheken liefern, brauchen wir spezielle Autos, die wir seit einigen Jahren haben müssen. Wir mussten die ganze Logistik verändern, das hat Millionen gekostet und ein Versandhandel darf machen, was er will. Wie wichtig es ist eine Apotheke zu haben, merkt man dann immer erst im Notfall. Ist wie bei einer Versicherung, da zahlen sie Jahre Geld und sind aber froh, wenn sie sie brauchen. Das ist bei der Apotheke auch bisschen so und es ist wichtig, dass man in der Apotheke Sachen selbst herstellen kann, wie Desinfektionsmittel zum Beispiel. Da sind die Pharmazeuten ursprünglich da und werden oft zu Tablettenmaklern degradiert. Das ist irgendwo nicht fair. |

**Telephone-Interview on 29 October 2020 from 15:00 am to 15:30 am (Duration: 30 minutes)**

| Stephan | Wholesaler 2 (W2) – Sales Manager |
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| **Q1:**<br>Die Corona Pandemie hat einige strukturelle Veränderungen in der ganzen Welt mit sich gebracht. Der Lockdown in den meisten Ländern und die Schließungen der Grenzen hat auch zu Veränderungen im Gesundheitswesen geführt. Welche Veränderungen bzw. Schwierigkeiten oder ergaben sich im Bereich der Versorgung mit Arzneimitteln, was Sie als Großhändler beobachten konnten? | **A1:**<br>• Wir haben denk ich alle mit großer Spannung die Nachrichten verfolgt und dann kam es, das war glaub ich der 15. oder 16. März zum ersten Lockdown.<br>• Eine Situation, die denk ich, für alle Beteiligten, für die ganze Welt, und es gerade hier in Deutschland bisher glücklicherweise noch nicht existent war.<br>• Eine neue Herausforderung auch für uns als Großhändler in erster Linie mit unserer besonderen Verantwortung, die wir auch im Gesundheitswesen tragen, flächendeckend eine Versorgung der Apotheken und somit auch der Patienten während der Corona-Pandemie bestmöglich zu gewährleisten.<br>• Man hat gesehen, wie die Bevölkerung reagierte im Einzelhandel, Stichwort: Hamsterkäufe. Das haben wir im Einzelhandel gesehen, denk ich jeder von uns. Somit hat sich das auch auf die eine Art und Weise auf den pharmazeutischen Markt logischerweise auch übertragen. Sei es vielleicht in einer abgeschwächten Form, sei es vielleicht in einer stärkeren Form, das ist schwierig genau zu beurteilen.<br>• Aber in jedem Fall haben auch Hamsterkäufe in der Apotheke stattgefunden, das sage ich komplett wertfrei, weil am Ende des Tages gibt es natürlich auch Chroniker oder Menschen und Familien, die sagen: „Ok ich weiß nicht, was auf mich zukommt, ich möchte einfach ein Stück weit Sicherheit, um mein wichtiges Medikament, was ich für zum Beispiel für mein Herz benötige, da möchte ich einfach sicherstellen, dass ich versorgt bin, weil ich nicht weiß, wie sich das entwickelt in den nächsten Monaten“.<br>• Die Angst ging rum, somit verstärktes Einkaufen auch in Apotheken, das heißt auch Apotheken wollten sich natürlich bestmöglich aufstellen, dementsprechend war das natürlich auch eine Herausforderung für uns Großhändler, da eine flächendeckende Versorgung zu gewährleisten.<br>• Das haben wir meines Erachtens sehr gut gemacht. Wir mussten natürlich auch logistische Prozesse anpassen, aufgrund der gestiegenen Nachfrage. Zudem ist es natürlich auch so, dass Mitarbeiter mit Familien oder ältere Mitarbeiter dann auch teilweise ausgefallen sind. Da war etwas weniger Personal, wobei wir da immer noch gut aufgestellt waren. Aber in so einer Notsituation zählt jeder Mann und jede Frau. Da mussten wir, wie auch jeder andere Großhändler die logistischen Prozesse anpassen, um wirklich eine flächendeckende Versorgung zu gewährleisten. |
| **Q2:**<br>In der Phase des ‚Lockdowns‘ gab es von März bis Mai eine Vielzahl von Lieferengpässen, die gab es vorher ja auch schon, wurden aber in dieser Zeit mehr. Als Grund für die Lieferengpässe | **A2:**<br>• Wie Sie schon gesagt haben, das Thema ist seit langer Zeit schon ein sehr wichtiges und relevantes Thema und wird sehr kritisch diskutiert.<br>• Es geht darum, dass tatsächlich ein Großteil der Rohstoffe bzw. Arzneimittel in Fernost produziert wird, Asien, China, Indien und |

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| wurde am häufigsten eine erhöhte Nachfrage im Markt angegeben und als 2. häufigster Grund eine unterbrochene Lieferkette. Die erhöhte Nachfrage hatten Sie bereits angesprochen.<br>Können Sie sagen, wie es bei der Lieferkette aussah? | wir eine sehr starke Abhängigkeit haben. Wir sind selbst nicht mehr in der Lage, ich meine mit wir Europa und Deutschland, nicht in der Lage, kurzfristig zu reagieren bzw. da autark zu agieren.<br>• Wenn man der Corona Krise etwas Positives abgewinnen möchte, dann hat die Corona-Krise schonungslos offengelegt, was in diesem Gesundheitssystem nicht optimal bzw. falsch läuft. Das sind dann beispielsweise die Lieferengpässe, die Logistik ging eingeschränkt vonstatten, das heißt in China haben sich teilweise keine Container bewegt, weil auch dort ein Lockdown war.<br>• Das heißt, das hat zu großen Verzögerungen geführt, parallel eine große Anfrage auf Präparate, die ohnehin schon nicht in großen Mengen am Markt zur Verfügung standen. Das ist dann auch eine Kettenreaktion, das heißt ein bisschen dieser Domino Effekt. Also beispielsweise gab es im letzten Jahr Ibuprofen 800 nicht mehr, warum, weil irgendeine Charge aus Fernost verunreinigt wurde, dementsprechend wurden gewisse Planmengen nicht erfüllt und somit waren dann auch schnell die Ibuprofen 600 oder 400 ausverkauft. Also erst immer ein Präparat, dann kommt das andere in geschwächter Form oder in anderer Packungsgröße relativ schnell nicht mehr lieferbar. Das ist ein Punkt, den die Corona-Krise schonungslos offengelegt hat. |
| **Q3**:<br>Könnten Sie mir bei den Arzneimittelgruppen sagen, welche besonders von einem Lieferengpass betroffen waren? | **A3:**<br>• Ja also die Sartane beispielsweise, das ist schon seit geraumer Zeit ein Thema, dass es da einen Engpass beziehungsweise eine Unterabdeckung sich im Markt befindet.<br>• Darüber hinaus ein berühmtes Beispiel ist das Thema Shingrix und Pneumovax. Jetzt beispielsweise auch kürzlich möchten sich beispielsweise viel mehr Leute gegen Grippe impfen lassen, wo jetzt auch teilweise auch BMG Ware zugeteilt wurde. Da gibts jetzt nochmal zusätzliche Ware vom Bundesministerium für Gesundheit, das Thema wird auch politisch, das sage ich auch vollkommen wertfrei, stark beworben, natürlich sagt die Bevölkerung ok Corona, ich möchte mich da sicherer aufstellen und auch keine Grippe haben. Was da momentan los ist an vielen Ecken, um jetzt mal ein paar Beispiele zu nennen.<br>• Beispielsweise aber auch Betäubungsmittel und Narkosemittel, von denen ich gehört habe, beispielsweise Propofol war ein sehr gutes Medikament, auch da gab es zwischenzeitlich Lieferengpässe.<br>• Es hängt natürlich auch mit den Krankenkassen zusammen. Sind natürlich viele Akteure am Rad. Da ist die Frage, warum soll jemand Externes, in dem Fall die Krankenkassen darüber bestimmen, was der Patient für Präparate erhält. Also die Entscheidung wird ja nicht zum Wohle des Patienten gefällt, dass man sagt, du bekommst Präparat X,Y, weil du die Krankheit hast, sondern teilweise unterschiedliche Präparate mit dem gleichen Wirkstoff, aber mit differenzierten Hilfsstoffen, die auch noch mit drin sind. Dahingehend ist auch ein Thema die Verträglichkeit.<br>• Also die Krankenkasse würde niemals die Rabattverträge öffnen, wenn es nicht zu akuten Engpässen gekommen wäre während der Pandemie. Da gab es auch eine Lockerung. Die Apotheken |

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| | konnten freier substituieren, waren dementsprechend etwas flexibler aufstellt. Warum macht das denn die Krankenkasse, die würden das niemals machen, das sind Kosten, das sind nicht die vereinbarten Rabatte. |
| **Q4:**<br>Also die würden es nicht machen, wenn es wirklich zu einem Versorgungsengpass kommen könnte? | **A4:**<br>• Genau das meine ich damit. Da stehen wirtschaftliche Interessen im Vordergrund und da sieht man auch schon wie akut der Arzneimittelengpass während der Corona Pandemie war oder immer noch ist. Ich bin sehr gespannt, wie es sich in den nächsten Monaten verhält. |
| **Q5:**<br>Würden Sie allgemein sagen, dass einige Patienten Gruppen nicht mehr genügend versorgt werden konnten bei einigen Patienten-Gruppen, weil wichtige Medikamente nicht mehr lieferbar waren oder konnte noch ausreichend geleifert werden, sodass in der Hochphase von März bis Mai noch alle Patienten genug versorgt werden konnten? | **A5:**<br>• Ja es ist schwierig zu sagen. Ich denke nicht, dass wir jeden Patienten sicher oder in ausreichenden Mengen versorgen konnten.<br>• Zum Beispiel Shingrix, da muss der Patient zweimal geimpft werden. Ich habe auch schonmal davon gehört, dass einer eine Spritze erhalten hat und die zweite noch nicht auf dem Weg war. Ich gehe nicht davon aus, dass wirklich jeder Patient einwandfrei versorgt werden konnte, im Großen und Ganzen ja.<br>• Natürlich haben wir auch unter Großhändlern Möglichkeiten Ware zu besorgen über den Verbund beispielsweise, aber am Ende des Tages sind wir alle abhängig von der Lieferfähigkeit der Industrie. Wenn die auch nur eingeschränkt produzieren können oder die Ware jetzt gerade beim Zoll oder auf dem Weg nach Europa ist, dann sind einem die Hände gebunden. Wir sind gut aufgestellt, aber ich kann es vollkommen verstehen, wenn es Patienten gibt, die diese Meinung überhaupt nicht teilen, weil sie in ihrem individuellen Fall nicht ihr bevorzugtes Präparat erhalten, sondern ein substituiertes Präparat, welches sie vielleicht auch nicht gut vertragen oder schlechter vertragen. |
| **Q6:**<br>Das ist auch die Umstellung für einen Patienten, die bei einem Lieferengpass entstehen, da sie ein anderes ungewohntes Präparat bekommen? | **A6:**<br>• Am Ende des Tages stehen da die Apotheker in erster Reihe und ist ja auch verständlich, wenn zum Beispiel ein Rentner oder eine Rentnerin in die Apotheke kommt, wenn sie ihr wichtiges Herzmedikament oder Blutdruck senkendes Medikament benötigt, und nicht erhält, was sie schon seit 20 Jahren bekommt. Klar verstehe ich da auch ältere Menschen, dann schürt das erstmal Angst, dann gibt es zum Beispiel welche die weinen oder vielleicht wütend, aggressiv reagieren, unterschiedliche Reaktionen.<br>• Apotheker stehen da natürlich an erster Reihe und geben das dann indirekt an den Großhandel weiter. Aber sie sind natürlich auch im Thema und wissen, dass nicht der Großhandel daran schuld ist. Eine Schuldzuweisung bringt auch nichts. Das ist vielleicht jetzt durch die Pandemie zu erkennen, wo vielleicht die signifikanten Probleme sind im Gesundheitswesen.<br>• Auch fernab von verschreibungspflichtigen Medikamenten, Nitrilhandschuhe da gibt es jetzt einen Engpass, bei den Gesichtsmasken im März gab es einen großen Engpass, da wurde teilweise vom Bundesministerium für Gesundheit gefälschte Ware in China gekauft, da hat man auch gesehen was für ein |

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| | gefährlicher Markt es war und viele Produzenten in China umgeschwenkt haben und eine Maske nachgebaut haben, die nicht diese technische Anforderungen hatten oder vielleicht sogar noch aus gesundheitsschädlichem Material hergestellt wurden, und wenn man die dann den ganzen Tag auf hat, dann weiß ich auch nicht. |
| **Q7:**<br>Welche Lehren im Bereich des Arzneimittelmarktes würden Sie aus der Corona-Krise für zukünftige Krisen und allgemein für das Gesundheitswesen ziehen, oder Vorschläge wie zum Beispiel die Produktion essenzieller Arzneimittel, z.B.: Antibiotika nach Europa zurück zu holen? | **A7:**<br>• Das ist der wichtigste Punkt, den hätte ich jetzt auch als erstes genannt.<br>• Natürlich muss man darüber nachdenken ein wenig flexibler, agiler bzw. auch unabhängiger agieren zu können. Gerade in so einer sensiblen Branche und in so einer von der Infrastruktur her wichtigen Branche, dass man dort gewisse Sicherheiten hat, sei es in der Bevorratung von Arzneimitteln. |
| **Q8:**<br>Bevorratung der Hersteller? | **A8:**<br>• Von den Herstellern natürlich, aber auch das beispielsweise darüber nachgedacht wird wieder Standorte in Europa aufzubauen, die diese Grundstoffe bzw. Arzneimittel herstellen, dass die auch einen Anreiz haben, dass die staatlich oder auch europaweit subventioniert werden, dass nicht nur der Preis zählt, sondern das auch subventioniert wird vom Staat. Sodass wir einfach Sicherheit haben. Es gibt auch Standorte in Europa, sodass man darüber nachdenken kann auch wieder zu produzieren. Das ist aber auch ein Thema, was rein logistisch nicht von heute auf morgen geht, sondern das dauert Jahre, bis man ein fertiges Werk in Europa etabliert hat und dort halt individuell produzieren kann.<br>• Darüber hinaus mit den Krankenkassen, das ist nämlich auch nochmal ein Punkt, den ich wichtig finde. Die Krankenkassen schließen die Rabattverträge mit den Herstellern ab. Dann wird sich für einen großen Hersteller für ein bestimmtes Präparat oder Wirkstoffe entschieden oder der macht das Rennen und der darf produzieren. Die anderen sagen sich: „Ok, das Business wird für mich in Zukunft uninteressant, das heißt ich stell mich anderweitig um“. Somit sind wir, was diesen Wirkstoff angeht, im schlimmsten Fall von einem Hersteller abhängig. Jetzt kann es passieren, dass in Indien oder China eine Aufsichtsbehörde vorbeikommt, überprüft und eine Charge-Verunreinigung feststellt oder sagt Prozesse werden nicht richtig gemacht, das können wir so nicht auf den Markt bringen. Dann ist da das Problem. Auch da sollte es ein Umdenken geben, das auch da mehr Flexibilität gegeben ist bzw. auch eine bessere Heilung oder Versorgung der Patienten durch den Patienten selbst, aber auch durch den Arzt oder den Apotheker, dass da gesagt wird, wir haben diesen Wirkstoff und der Patient verträgt wirklich nur dieses Präparat. Meistens ist es auch so, dass das billigste Präparat verkauft wird, bis der Patient am Ende des Tages die guten Präparate erhält.<br>• Also es sollte ein Umdenken geben hinsichtlich der Anreize, der Margen für Apotheker und den Großhandel. Klar sind Kosten und |

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| | Preise wichtig, aber am Ende ist die Sicherheit wichtig, was so in den letzten Jahren aus den Augen gerückt ist. |

## Statutory declaration student

I hereby confirm that I am the author of the Master Thesis presented. I have written the Master Thesis as applied for previously unassisted by others, using only the sources and references stated in the text.

15.03.2021