securPharm

German Medicines
Verification Organisation

STATUS REPORT 2020

Implementation of the Falsified Medicines Directive
in Germany:
Introduction and operation of the securPharm-system

2

ABDA

BPI Bundesverband der Pharmazeutischen Industrie e.V.

PHAGRO

Bundesverband der Arzneimittel-Hersteller e.V. B.A.H beraten • analysieren • handeln

vfa. Die forschenden Pharma-Unternehmen

About securPharm e.V

securPharm e. V. is the German organisation for the authentication of pharmaceuticals and responsible for operating the authentication system for prescription drugs pursuant to the requirements of the Falsified Medicines Directive 2011/62/EU and the Delegated Regulation (EU) No. 2016/161. The objective is to protect patients from falsified pharmaceuticals in the legal supply chain in Germany. securPharm e. V. is sponsored by the following associations of the pharmaceutical companies, wholesalers and pharmacists: BAH, BPI, vfa, PHAGRO and ABDA. securPharm is the German component in the EU-wide network EMVS against falsified pharmaceuticals.

For more information, please visit: www.securPharm.de.

This status report is available in German and English for downloading at www.securpharm.de.

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Foreword

Overall, the number of falsified pharmaceuticals in the legal supply chain in Germany is small. However, since falsified pharmaceuticals can be associated with considerable risk to patients, any falsified pharmaceutical is one too many. Therefore, it is the foremost objective of all partners in pharmaceutical care to keep the distribution chain secure and to ensure that falsified pharmaceuticals are detected early.

As a result, a protective system was introduced across Europe in February 2019 that expands the existing controls of pharmaceuticals on their way to the patient by additional checks. Before being dispensed to patients, pharmaceuticals are authenticated by means of an individual serial number through the securPharm system. Behind this digital protection are highly developed IT systems and complex processes on each level of the legal supply chain – from pharmaceutical companies over wholesalers to the pharmacy. Thanks to years of good preparation by the partners in pharmaceutical supply, the introduction of this digital protection was successful. However, the work is not yet complete. As with the introduction of other IT systems, continuous integration of experiences and insights from ongoing internationally networked operations is required. This is accomplished through technical evolution of the system for which the pharmaceutical supply partners maintain a dedicated collaboration on a Europe-wide scale. securPharm e. V. as the German organisation for the authentication of pharmaceuticals monitors the stability of the securPharm system but is also concerned with networking all parties involved to ensure that this evolution succeeds.

Trust in a safe pharmaceutical supply is a precious asset. Therefore, the pharmaceutical supply partners are engaging in a constant improvement process in order to ensure that patients can continue to visit their pharmacy with a good feeling that they will receive safe pharmaceuticals there.

1. Introduction

With Directive 2011/62/EU, the so-called Falsified Medicines Directive, the European Union has defined principles for preventing falsified medicinal products from entering the legal supply chain. These principles pertain to the verification of pharmaceuticals at the package level and the ability to ascertain their integrity. The Delegated Regulation (EU) 2016/161, which was published in the Official Journal of the European Union on 9 February 2016 and became effective on 9 February 2019, defined technical, organisational and time requirements for the implementation of this directive. securPharm e. V. is the entity that sets up and manages the national data repository and fulfills the functions stipulated by the legislature. securPharm e. V. has established the German system for authentication and started it on time as of the legal effective date. The users of the securPharm system – pharmaceutical companies, wholesalers, pharmacies and healthcare institutions – have prepared for the introduction of the new protective system from falsified pharmaceuticals and are completely connected to the system in Germany.

Ever since the legal effective date, the securPharm system has been operating with a continuously increasing load. Both the system and the processes have proven to be largely robust and stable. However, experience from the first year of operation has also shown that the set-up work is not yet concluded - neither in Germany nor in the other member states of the European Union and the European Economic Area. In the future, insights and experiences from the internationally networked operation will continue to have to be incorporated in the securPharm system via updates. In Germany, system handling must be further developed in order to minimise handling and coding errors, so that pharmaceuticals can be dispensed smoothly. While the system guarantees patient protection, some functions of the system still require automation. This particularly applies to reports for the authorities. securPharm e. V. and the trade associations that sponsor securPharm continue to drive the evolution of the protective system together with their European partners.

1.1 Legal Principles

1.1.1 Falsified Medicines Directive

The work of securPharm must be viewed in context with a series of measures required by the European Union to protect patients from falsified pharmaceuticals in the legal supply chain. The legal foundation for this is the Falsified Medicines Directive 2011/62/EU. Among others, the Falsified Medicines Directive stipulates the following measures:

- The introduction of safety features (unique identifier and anti-tampering device) on the package of prescription drugs for human use;
- An EU-wide logo based on which patients can verify the legality of an online pharmacy; and
- Stricter rules for importation of active pharmaceutical ingredients.

1.1.2 Delegated Regulation

On 9 February 2016, the Delegated Regulation (EU) 2016/161 amending Directive 2001/83/EC (hereafter referred to abbreviated as "Delegated Regulation") was published in the Official Journal of the European Union with an implementation period of three years.

Since 9 February 2019, only prescription drugs bearing a unique identifier and whose integrity is visibly recognisable have been allowed to be circulated in Germany. Packages that were released for sale or distribution prior to this date (Article 48) are not limited in their marketability until their expiry date, even without the safety features. In each of the member states of the European Union and the European Economic Area, a national medicines verification organisation must be established, which sets up the respective national system for the authentication of pharmaceuticals based on the unique identifier and which connects to the European system via a centralised router (hub). Based on these requirements, securPharm e.V. is the German organisation for the authentication of pharmaceuticals and the securPharm system serves as the national data repository and retrieval system.

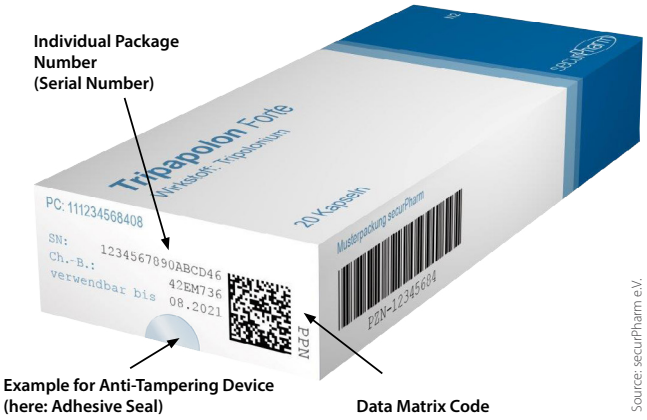
In addition, the Delegated Regulation names requirements for the implementation in pharmaceutical companies, wholesale companies, pharmacies, hospitals and other healthcare institutions.

1.1.3 New safety features for pharmaceutical packages

Prescription drugs circulated in the EU and EEA member states after 9 February 2019 must bear two safety features on their packaging: the unique identifier and an anti-tampering device.

The unique identifier is a randomly generated serial number in connection with the product code in question, which renders each package unique. The serial number clearly stands in the context of the product code. The unique identifier represents the basis for authentication through the securPharm system.

The anti-tampering device facilitates verification as to whether the outer packaging of a pharmaceutical was manipulated. In order to create a joint and reliable basis for the manufacturing industry, experts from industry, associations and government agencies have developed a uniform European standard under the umbrella of the German Institute for Standardisation (Deutsches Institut für Normung - DIN) and the European Committee for Standardisation (CEN) with the DIN EN 16679 in 2015. This standard was subsequently transferred into the ISO 21976 standard in 2018.



Source: securPharm e.V.

1.1.4 Extension of the scope of the safety features

The member states can extend the scope of the two safety features. On 11 April 2017, the German Federal Institute for Drugs and Medical Devices (BfArM) and the Paul Ehrlich Institute (PEI) jointly announced that all products which are not subject to the Falsified Medicines Directive may voluntarily bear an anti-tampering device. As a result, e.g. OTC products may also bear this safety feature.

A mandatory extension of the unique identifier is not yet planned for Germany. Regardless of this fact, all products that are not subject to the Falsified Medicines Directive may also bear a Data Matrix Code, as long as it does not contain a serial number (see Chapter 2.5).

1.1.5 Regulatory information for affixing the safety features

The Falsified Medicines Directive additionally imposes significant regulatory requirements on the pharmaceutical companies. Affixing the safety features to the outer packaging of pharmaceuticals subject to mandatory verification is required in terms of the labelling and regulatory approval provisions of Section 10 para. 1c of the German Medicinal Products Act (AMG). Since the safety features represent a piece of information that is relevant for marketing authorisation, the pharmaceutical company must inform the regulatory agency in charge of this fact. This also applies to pharmaceuticals that have already received marketing authorisation and the marketing authorisation dossier must be updated.

1.1.6 Assignment of pharmaceuticals subject to mandatory verification

The higher federal authorities PEI and BfArM have classified pharmaceuticals that must bear the safety features pursuant to the Delegated Regulation (Article 43) accordingly in the AMIS Database. Pharmaceutical companies had the opportunity to check the classifications by 9 February 2019 and to contact the BfArM in case of discrepancies.

Furthermore, the Delegated Regulation (Article 46) provides the option that a product can be included in the so-called "White List" of Annex 1, if a pharmaceutical has e.g. a low potential for falsification. In these cases, the regulatory agencies in charge must be contacted. They will then go through the Federal Ministry of Health to contact the European Commission for final investigation and inclusion in the "White List".

1.1.7 Legal adjustments

In 2018, the national legislature started to adjust the German pharmaceutical law to the requirements of the Delegated Regulation. With the "Regulation to adjust pharmaceutical law and other provisions to the Delegated Regulation (EU) 2016/161 of the European Commission of 2 October 2015 supplementing Directive 2001/83/EG of the European Parliament and the Council by stipulating exact provisions regarding the safety features on the packaging of medicinal products for human use and to Regulation (EU) 2016/679 of the European Parliament and the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) and the amendment of pharmaceutical and pharmacy provisions" (Federal Law Gazette 2018, No. 24, p. 1080), the Pharmaceutical Trading Regulation and the Regulation of Pharmacy Operations were adjusted, among others. For the implementation of the Delegated Regulation, the "Greater Safety in Pharmaceutical Care Act" (Federal Law Gazette I 2019, No. 30, p. 1202) was published in 2019 and primarily amended the German Medicinal Products Act (AMG).

The two laws adjusted the obligations of the participants in the pharmaceutical supply chain within the domestic legislation and take into account the verification and reporting obligations of the parties involved as well as the powers of the supervising authorities arising from the requirements of the Delegated Regulation. The membership associations of securPharm e.V. accompanied the legislative process.

2. Coding agreement

2.1 General

Pursuant to Article 4 of the Delegated Regulation, the unique identifier includes the following data elements::

- Product code;
- Serial number;
- Batch number; and
- Expiry date.

The national reimbursement number is mentioned as an additional element in Article 4. For pharmaceuticals meant for the German market, this number is already included in the product code in the form of the PZN and therefore need not be listed additionally. As a result, there is no so-called fifth element as far as Germany is concerned.

Coding is done in the Data Matrix Code in accordance with ISO/IEC 16022. This ensures that these data elements are machine-readable and form the technical prerequisite for implementing the EU Falsified Medicines Directive and additional expected legal requirements for the verification of pharmaceutical packages. At the same time, the requirements from Article 5 "Carrier of the unique identifier" of the Delegated Regulation are met.

2.2 Coding rules

In terms of Article 4 (d) of the Delegated Regulation, an unambiguous product code on a Europe-wide scale is needed. To meet this requirement, the Pharmacy Product Number (PPN) and the National Trade Item Number (NTIN) were created, which are generated from the eight-digit PZN. The pharmaceutical company can choose between two above-mentioned product numbers while taking into account the respective licencing conditions. Databases and software systems can algorithmically generate a PZN from the PPN/NTIN or a PPN/NTIN from the PZN. For the retail segment, the PZN will remain the relevant product number and it will continue to be used for reimbursement. As a result, existing processes will be preserved without change.

The two-dimensional Data Matrix Code in accordance with ISO/IEC 16022 must be used for the data container. It has excellent characteristics regarding data density, data volume, geometric scalability and robustness. Additional rectangular versions of the Data Matrix Code in accordance with ISO/IEC 21471 (see http://www.eurodatacouncil.org/de/dmre) make the packaging design easier. Pursuant to Article 5 of the Delegated Act, the coding rules generated by securPharm allow coding of information in compliance with the ASC format described in the IFA specification as well as the format of GS1. Both formats are in accordance with ISO/IEC 15434 and use the data designators in compliance with ISO/IEC 15418. This ensures an open market for pharmaceutical companies without additional, binding licencing fees.

All necessary details on coding and labelling of pharmaceutical packages are described in the securPharm "Coding Rules". Amongz others, this includes generation of the PPN and NTIN, code content with the associated data designators, code size, and printing quality (see https://www.securpharm.de/codierung/?lang=en). The securPharm Coding Rules contain the current requirements resulting from the Delegated Regulation.

2.3 Use of national product numbers in an international system

Just like the PZN in Germany, national product numbers are also used in other European countries. In this respect, they represent a national standard that could only be modified at great expense to all market participants, and they may even be governed by national law.

Therefore, one can use container systems that envelop the national product number, i.e. preserve it for national use, and provide supplementary data to guarantee international usability. Since only one system was known in the past (NTIN by GS1) and GS1 individually decides on the use of the NTIN for each user nation, securPharm commissioned IFA with the development of its own container system – the Pharmacy Product Number (PPN). Since 2013, it has been globally available free of charge and is based on ISO/IEC. Since then, its applications have been extended from printing/labelling retail packages to tagging outer packaging, pallets and shipments. It can be used for multi-country packs and as UDI-DI for medical devices.

2.4 Coding of samples for physicians

Physicians' samples in accordance with Article 96 of Directive 2001/83/EG must also bear the safety features pursuant to Delegated Regulation (EU) 2016/161 (Articles 2 and 41). The pharmaceutical company also generates the unique identifiers for physicians' samples and uploads them to the database system of the pharmaceutical industry. Before the physicians' samples are passed on by the pharmaceutical company, it deactivates these packages as "samples".

Pharmaceutical companies can produce physicians' samples in three different versions:

- Retail products that are tagged with the corresponding supplementary label to declare them as physicians' samples; or
- Physicians' samples in retail product sizes that come in a specially designed package and with a specially assigned PZN; orr
- As above but in a smaller size than the smallest retail package.

For the two latter options, the pharmaceutical company must request a PZN with Informationsstelle für Arzneispezialitäten GmbH (IFA).

2.5 Coding of pharmaceuticals that are not subject to mandatory verification

Pharmaceuticals that are not subject to mandatory verification, such as OTC products, may also bear the Data Matrix Code as long as it does not contain a serial number (see Chapter 1.1.3). However, apart from the product code (PZN as PPN or NTIN), the code can also include the batch designation and the expiry date.

3. The NMVO – the National Medicines Verification Organisation

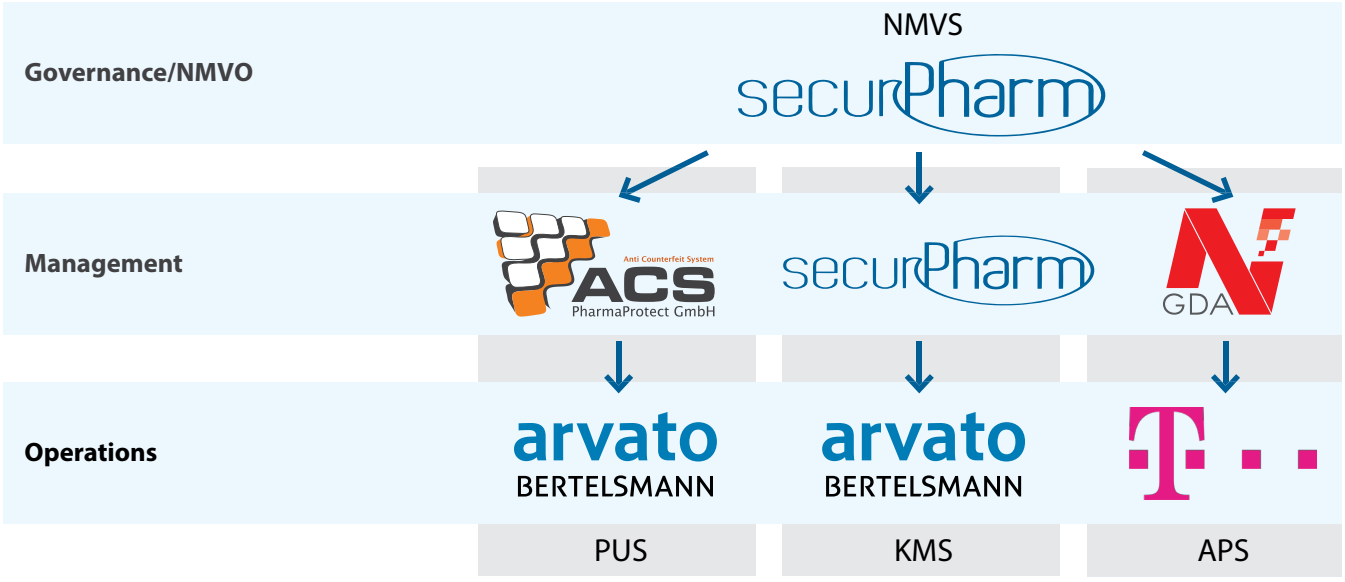
3.1 The tasks of securPharm e. V.

securPharm e.V. is the German organisation for the authentication of pharmaceuticals. In the international context, such an organisation is referred to as a National Medicines Verification Organisation (NMVO). It operates the national system, which authenticates pharmaceuticals based on their unique identifier, in accordance with the legal requirements (Chapter 4). In its function as a platform for the representatives of the stakeholder groups in the supply chain and their monitoring, securPharm ensures that the requirements of the securPharm system take into account the concerns of all market participants. Furthermore, securPharm supports the authorities in charge in the investigation of cases of suspected falsification. For this purpose, it provides the authorities with predefined reports from the securPharm system, e.g. the so-called testing path which contains the data from the securPharm system regarding the path of a package through the supply chain (Chapter 5.2 and 7.2).

3.2 Organisational structure

The Delegated Regulation addresses the responsibility for establishing a national organisation for the authentication and the set-up of a data repository and retrieval system to the stakeholders. As early as 2012, the ABDA, BAH, BPI, PHAGRO

Governance of securPharm System



and vfa established the non-profit securPharm e.V. organisation in order to set up the German verification system (the securPharm system) and to demonstrate how the verification requirements for the new safety features can be implemented in an efficient, industry- and pharmacy-friendly manner that is also viable for all parties involved in the pharmaceutical market.

securPharm acts as the umbrella organisation that stipulates the rules and structures for setting up and operating the securPharm system. In this respect, the securPharm system consists of three connected partial systems. The operation of two partial systems was assigned by securPharm e.V. to different operators in order to ensure data separation and data privacy, not just from a legal but also from an organisational and technical standpoint (see diagram). This modularisation also results in higher efficiency, since both partial systems can specialise in the requirements of their respective user groups. securPharm e.V. as the NMVO also monitors and controls the operating companies' compliance with the stipulated requirements.

The database of the pharmaceutical industry (MAH system) is operated by ACS PharmaProtect GmbH (ACS) (see Chapter 4.2.1). Pharmaceutical companies with products subject to mandatory verification (Chapter 6.3) are connected to the national system for authentication via the MAH system of ACS.

The pharmacy system (PH system) is operated by NGDA - Netzgesellschaft Deutscher Apotheker GmbH (NGDA) (see Chapter 4.2.2). Via NGDA, verifying entities such as pharmacies (Chapter 6.5), pharmaceutical wholesalers (Chapter 6.4), healthcare institutions (Chapter 6.6) as well as compounding manufacturers, industrial blistering companies and the centralised federal procurement entities (Chapter 6.7) are connected.

The authorities' portal is operated by securPharm e.V. itself. Via the authorities' portal, the national authorities in charge connect to the securPharm system.

In this respect, the operators act as contractual partners of the system users and serve as contact for technical and contractual questions regarding connection to the system. They provide the system users with different aids such as starter kits, checklists and guidelines, etc.

3.3 Quality management system

For an organisation like securPharm, a quality management system is a foregone conclusion. Transparency to the inside and outside, legal certainty and conformity with applicable laws must be ensured. The set-up and realisation of a quality management system is oriented on DIN EN ISO 9001. Due to the relevance of the information in the securPharm system, the DIN EN ISO/IEC 27001 standard is additionally implemented in order to take into account the requirements of the Delegated Regulation. securPharm had set for itself the objective of receiving certification in accordance with DIN EN ISO 9001 and DIN EN ISO/IEC 27001.

4. The NMVS – The National Medicines Verification System

Following the requirements of the Falsified Medicines Directive, the securPharm system is based on the end-to-end principle during which both ends of the supply chain help ensure safety. The one end is the marketing authorisation holder who markets pharmaceuticals. The other end represents the dispense of pharmaceuticals to patients, i.e. at a community pharmacy. The national verification system is embedded in a European network in order to also safeguard patient protection across national borders.

4.1 Data ownership and privacy

Experience from other projects has shown that special attention must be paid to data ownership. Based on this experience, the concerns regarding data use by unauthorised market partners and the knowledge that data are already being used for advertising in other EU countries have prompted the founders of securPharm e. V. to physically store and manage the data of the pharmaceutical companies, the pharmacies and wholesalers as well as other verifying entities in separate databases (Chapter 3.2). As a result, data ownership is clearly assigned and organised in a manner that is understandable for everybody.

4.2 The pharmaceutical verification process

During the production process, the marketing authorisation holder equips each pharmaceutical pack that is subject to mandatory verification with both safety features. The unique identifier contains a product code, a unique serial number in the context of the product code, the batch designation and the expiry date. This information is affixed to the pack in the form of a Data Matrix Code. In parallel, these data are uploaded to the MAH system by the marketing authorisation holder via the European hub (Chapter 6.3). An unique identifier (product code and serial number) uploaded this way is termed active (Article 11 of the Delegated Regulation).

Each pharmaceutical company reports to IFA the pharmaceuticals that bear the Data Matrix Code and must be verified in pharmacies. Based on the labelling in the IFA database, pharmaceuticals subject to mandatory verification and existing merchandise that was released prior to the effective date of 9 February 2019 can be distinguished. This information is available to the pharmacy software and can control the processes in the merchandise management systems this way.

To verify the authenticity of a product package, the pharmacy staff scan the Data Matrix Code of a package before dispensing it to the patient. The verification of the unique identifier against the MAH system is running in the background. The verification inquiry of a verifying entity is bundled via the centralised PH system and addressed to the MAH system in anonymised format. The package status as it is stored there is reported back to the pharmacy. If the assigned status is active, the package can be dispensed and the package status is simultaneously changed in the database to "dispensed" or inactive. If the data check shows that the unique identifier is either not found in the database or has already been marked as dispensed, the pharmacy receives a corresponding warning, so that the necessary measures can be taken (Chapter 5). This will prevent a negatively verified and possibly falsified pharmaceutical from being dispensed to the patient.

4.2.1 The operating company of the database system of the pharmaceutical industry (MAH system)

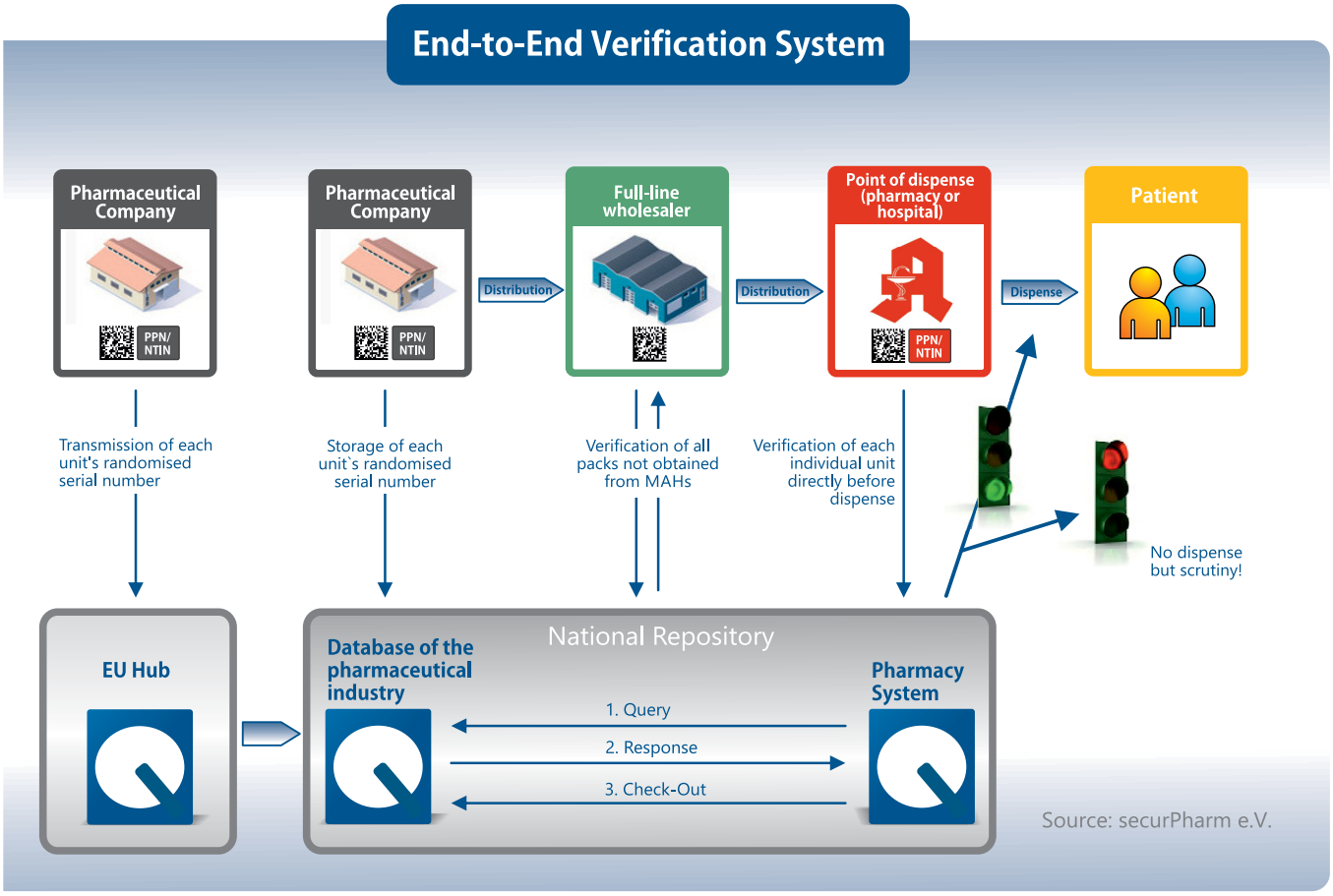
The operating company of the database system of the pharmaceutical industry (MAH system) is ACS PharmaProtect GmbH (ACS) based in Berlin. The managing partners are BAH, BPI, vfa and Pro Generika. In addition, the Board of Directors consists of representatives from the pharmaceutical companies.

4.2.2 The operating company of the pharmacy system (PH system)

The pharmacy system is operated by Netzwerkgesellschaft deutscher Apotheker GmbH (NGDA) based in Eschborn. NGDA is a wholly owned subsidiary of AVOXA – Mediengruppe Deutscher Apotheker GmbH.

4.3 Developers of third-party software for system users

Technical access for system users to the securPharm system is made via an interface. The interfaces and interface specifi-



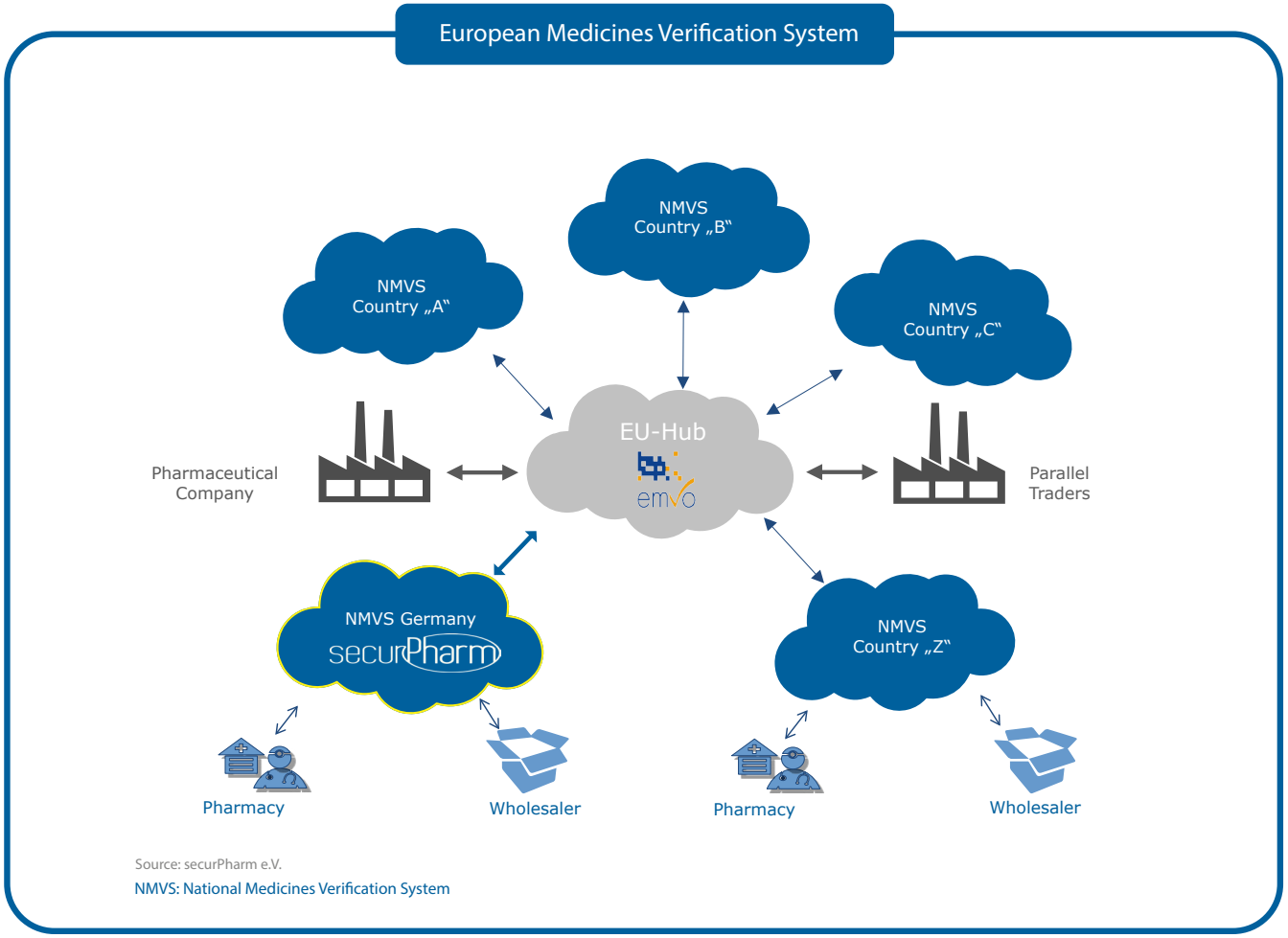
cations are provided by the operating companies. The technical connection between the interface of the securPharm system and the software system of a user is programmed by the user's software provider. The implementation guidelines of ACS and NGDA regarding the use of the interface also contain recommendations for so-called convenience functions, which can e.g. make the capture of the serial number and product code easier during disruptions. securPharm and the operating companies have no influence on the implementation of the recommendations.

4.4 Integration into the European network EMVS

Like the national verification systems of the other member states of the EU and the EEA, the securPharm system is connected to the European hub as the central data router. The European Medicines Verification Organisation (EMVO) is responsible for the European hub. This way, the different so-called National Medicines Verification Systems (NMVS) and the European hub become the European Medicines Verification System (EMVS). The interface of the securPharm system to the hub is created via the MAH system and is specified by the EMVO. This connection is continuously improved and adjusted to the experience and insights from ongoing operations. Furthermore, the European hub serves as a centralised access point for pharmaceutical companies. They can upload the pack data via the EU hub, which routes the data to the corresponding national system.
Based on the networking of the national verification systems, any pharmaceutical pack equipped with the safety features can be verified in any pharmacy in Europe.

4.5 Centralised management of national master data

The securPharm system identifies pharmaceuticals with the help of the master data from Informationsstelle für Arzneispezialitäten GmbH (IFA), a joint company of the trade as-



Source: securPharm e.V.
NMVS: National Medicines Verification System

sociations of the pharmaceutical industry, wholesalers and pharmacists in Germany. The "Pharmazentralnummer" (PZN) assigned by IFA is used without exception by all market participants handling pharmaceuticals. The centralised and uniform assignment of the PZN and ongoing quality assurance guarantee the unambiguousness of the key and the quality of the assigned master data. In addition, the IFA Coding System guarantees the international operability of the PZN in accordance with ISO standards.

5. Handling of system notifications

The Falsified Medicines Directive requires system users to verify both safety features (comp. Chapter 1.1.3). The unique identifier is verified through the use of the securPharm system. Following the rules of the Delegated Regulation, unsuccessful verifications of the unique identifier are captured in the securPharm system and a so-called alarm is generated. This alarm is assigned a unique alarm ID, so that each alarm can be unambiguously referenced. An alarm can have different causes. Therefore, alarms are distinguished based on certain alarm levels. Only if an alarm reaches or exceeds a certain level will an investigation become necessary. This is done in multiple steps, some of which proceed in parallel.

5.1 Warning of the participants: Immediate measure and investigation

First, the alarm is displayed to the system user who caused the alarm. Based on the requirements of the Delegated Regulation, said user must separate the package from the product inventory. With a few exceptions, a package bearing a deactivated unique identifier may not be distributed or supplied to the public, according to Article 12.

To facilitate correction of the cause of the alarm, the marketing authorisation holder responsible for the product also receives the alarm. For this purpose, the alarm ID is sent from the securPharm system to the EU hub and from there to the connected onboarding partner to whom this product is assigned in terms of data technology. Internally, the onboarding partner has clarified with the responsible marketing authorisation holder who will be internally in charge of further tracing the alarm. Depending on the constellation in question, this can be the onboarding partner, the marketing authorisation holder or another company within the same group of companies. He then has seven calendar days to analyze the case and qualify it accordingly (see example).

For example:
Conflict arises on Tuesday, 2 April 2019, 1:00 p.m. Maximum investigation period expires the following Tuesday, 9 April 2019, 12:00 a.m.

If he can ascertain during this time period that the alarm is due to an internal handling error, e.g. an incomplete upload of the pack data to the securPharm system, the incident can be rated a false alarm and the corresponding entry can be made in the securPharm system. For this purpose, he uses the portal of the MAH system, which provides him with the corresponding functions. An alarm rated a false alarm is not subject to mandatory reporting. If the time period of seven calendar days expires without the marketing authorisation holder providing the corresponding feedback to the system, the conflict is automatically rated a suspected falsification and the reporting obligations apply.

5.2 Reporting obligations and pathways

The reporting obligation when a case is rated a suspected falsification applies both to the marketing authorisation holder and the system user with whom the alarm occurred. In this respect, the previous reporting pathways of the individual market participants remain in effect, i.e. the report goes to the respective supervisory authority in charge. The various reports regarding a suspected falsification can be classified by the authorities via the unique alert ID on a Europe-wide scale.

To ensure that a verifying entity is informed that an alarm qualified as either a false alarm or a case of a suspected falsification, it is planned to expand the securPharm GUI by the corresponding function. For a justified suspicion of falsification, the previous reporting obligations will continue to apply.

Based on the Delegated Regulation, one reporting pathway is added: As soon as an alarm has been classified as a suspected falsification in the securPharm system, the securPharm system automatically informs the Federal Institute for Drugs and Medical Devices (BfArM) via the authority portal. Together with the Paul Ehrlich Institute (PEI), the Institute coordinates these cases, registers them in its own official database of falsifications and informs the supervisory authority in charge of the affected marketing authorisation holder. As a result, the reporting obligation for cases of suspected falsification pursuant to Article 37 of the Delegated Regulation and Section 96 of the German Medicinal Products Act (AMG) is met. The previous reporting obligations of the market participants remain unaffected by this additional report.

6. System users and system connection

6.1 System users

From securPharm's perspective, the users are the market participants in German pharmaceutical care, who implement the provisions of the Falsified Medicines Directive and the Delegated Regulation and must connect to the national authentication system for this purpose. According to the German Medicinal Products Act (AMG), this also includes the supervisory authorities in charge.

6.2 Legitimation of system users

According to Article 37 (b) of the Delegated Regulation, each legal entity that sets up and manages a data repository and retrieval system must ensure that only those users can have access to the data repository whose identity, role and legitimacy has been verified. securPharm has developed the requirements for a safe, reliable and appropriate procedure for the authentication and legitimation of the user groups. This set of rules is the guideline for the operating organisations that check the legitimation of their user groups to be connected.

6.3 Pharmaceutical industry

6.3.1 The role of the pharmaceutical companies

During the production process, the marketing authorisation holder equips the pharmaceutical package with two safety features. He uploads the dataset of the unique identifier to the MAH system. This is the prerequisite for these data to be available in a timely manner e.g. in a community pharmacy at the time of dispense. The anti-tampering device is affixed to the pack in accordance with DIN EN 16679. Pharmaceuticals that are subject to mandatory verification and have been released by the marketing authorization holder from 9 February 2019 onwards can only be sold if they bear these safety features

6.3.2 Connection to the system

Pharmaceutical companies that are marketing pharmaceuticals in Germany and are affected by Directive 2011/62/EU must conclude an agreement with ACS in order to connect to the securPharm system. As soon as the agreement is concluded, they receive access to the MAH system. The contractual partner of ACS is the company that also registered the pharmaceuticals with IFA as a supplier, which ensures an unambiguous relationship between the individual item (via the Pharmazentralnummer/PZN) and the company responsible for distribution in Germany.

Furthermore, an additional contract with the European Medicines Verification Organisation (EMVO) is required to ensure that the pharmaceutical company can be clearly identified during the data exchange between the MAH system and the European hub (www.emvo-medicines.eu). The contractual partners of the EMVO are typically higher corporate structures like a corporation (onboarding partner). Furthermore, each marketing authorisation holder must conclude an agreement with the national organisation (NMVO) whose market he supplies in Europe.

The data indicated by the pharmaceutical company while connecting to the MAH system are checked against data from the IFA database, among others. Therefore, it is particularly important for pharmaceutical companies to keep their data up to date with IFA and to contact ACS for any questions arising in connection with the necessary proof for the legitimacy check. For details regarding ACS, please go to www.pharmaprotect.de.

securPharm, ACS and the industry associations have informed pharmaceutical companies many times regarding their legal obligations and responsibilities in terms of the Falsified Medicines Directive. In addition, in October 2018, the EU Commission pointed out to the participants in the pharmaceutical supply chain their obligations in implementing the legal regulations.

6.4 Pharmaceutical wholesalers

6.4.1 The role of pharmaceutical wholesalers

Pharmaceutical wholesalers are an important component in the pharmaceutical supply chain. As a result, they serve an important function in securing the supply routes. Pursuant to the Delegated Regulation (Article 20), wholesalers must verify all returns from pharmacies and other wholesalers as well as pharmaceuticals that were not delivered by a pharmaceutical company/marketing authorisation holder or a wholesaler designated by it/him. In addition, wholesalers must check for authenticity and subsequently deactivate each pharmaceutical that

- Is to be distributed outside the EU;
- Is to be returned to the wholesaler and can be entered into non-sellable inventory;
- Is slated for destruction;

- Is in his physical possession and is requested by the authority in charge as a sample;
- Pursuant to Section 6 para. 1a of the German Pharmaceutical Trading Regulation is delivered to individuals, who are authorised and licenced to dispense pharmaceuticals but are not employed at a health care institution or pharmacy, as well as to veterinarians, dentists, the German Bundeswehr, the police, government institutions, universities or other academic institutions.

6.4.2 Connection to the securPharm system

Based on their legal obligations, wholesalers must connect to the securPharm system and conclude a contract with NGDA for this purpose. With this agreement, they receive access to the PH system. The actual connection will be made by the respective software companies, IT service providers or wholesalers themselves. NGDA offers these companies the necessary technical support. Additional information and contacts are available at the partner portal of NGDA at https://ngda.de/.

In 2017, securPharm informed the holders of a pharmaceutical wholesaler's license listed in the DIMDI list regarding their legal obligations and responsibilities in terms of the Falsified Medicines Directive. In addition, in October 2018, the EU Commission pointed out to the participants in the pharmaceutical supply chain their obligations in implementing the legal regulations.

6.5 Pharmacies

6.5.1 The role of pharmacies

When it comes to discovering falsified pharmaceuticals, pharmacies play a key role, since they verify the authenticity of a pharmaceutical at the end of the supply chain. Pharmacies must check both safety features before a pharmaceutical is dispensed to the patient. Checking the anti-tampering device for package integrity is done by simple visual inspection. The unique identifier is captured by scanning the Data Matrix Code and verified via the securPharm system (see Chapter 4.2).

6.5.2 Connection to the securPharm system

Based on their legal obligations, community pharmacies must connect to the securPharm system and conclude a contract with NGDA for this purpose. In accordance with securPharm's requirements, NGDA also ensures the unique electronic identification of the market partners via the N-Ident procedure. Following the successful legitimation, an N-ID (an electronic certificate) is issued. The actual connection will be made by the respective software companies, IT service providers or market partners themselves. NGDA provides these companies with the required technical support. Additional information and contacts are available at the partner portal of NGDA at https://ngda.de/.

securPharm, NGDA and the ABDA as well as their membership organisations have informed pharmacies regarding their legal obligations and responsibilities in terms of the Falsified Medicines Directive. In addition, in October 2018, the EU Commission pointed out to the participants in the pharmaceutical supply chain their obligations in implementing the legal regulations.

6.6 Connection of hospital pharmacies and pharmacies supplying hospitals

Based on their legal obligations, hospital pharmacies and pharmacies supplying hospitals must connect to the securPharm system. In this respect, each owner bears the responsibility for implementation in compliance with the law. The contact regarding connection, conclusion of the contract and legitimation is NGDA. Following the successful legitimation, an N-ID (an electronic certificate) is issued. The actual connection will be made by the respective software companies, IT service providers or market partners. Additional information and contacts are available at the partner portal of NGDA at https://ngda.de/.

In November 2017, securPharm wrote to all hospitals and provided the required information for connecting to the system. In October 2018, the EU Commission also pointed out once more to the participants in the pharmaceutical supply chain their obligations in implementing the legal regulations.

6.7 Connection of additional user groups

In addition to the aforementioned user groups, other participants who regularly and legitimately obtain merchandise from the market must also be connected. These include e.g. blister pack companies, compounding manufacturers as well as centralised procurement entities. These user groups must also legitimise themselves prior to usage of the securPharm system. The contact regarding connection is NGDA. Following the successful legitimation, an N-ID (an electronic certificate) is issued. The actual connection will be made by the respective software companies, IT service providers or market partners. Additional information and contacts are available at the partner portal of NGDA at https://ngda.de/.

Through their stakeholders, securPharm has informed these user groups regarding their legal obligations and responsibilities in terms of the Falsified Medicines Directive. In addition, in October 2018, the EU Commission pointed out to the participants in the pharmaceutical supply chain their obligations in implementing the legal regulations.

7. National authorities: Supervision, system access and information

The legislature has stipulated that the corresponding national authorities are to be in charge of supervision and system access to the national verification systems in question.

In Germany, several authorities are in charge of pharmaceuticals: On the one hand, the Paul Ehrlich Institute (PEI) and the Federal Institute for Drugs and Medical Devices (BfArM) for regulatory approval and the coordination for clarifying suspected cases of falsification and, on the other hand, regional supervisory authorities for monitoring the market participants.

7.1 Supervision and monitoring of securPharm

The national authorities in charge are responsible for monitoring securPharm e. V. and the securPharm system.

The Detmold district government performed the initial inspection of securPharm e. V. in terms of the implementation of the Delegated Regulation on 18 November 2019. This was the first inspection of an NMVO in Europe.

As a basis for inspections of the National Medicines Verification Organisations, the expert group regarding the "Delegated Act on Safety Features for Medicinal Products for Human Use", which consists of participants from the EU Commission and the member states, has published the following documents:

- The NMVO Assessment Questionnaire of 7 September 2018 (https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/2018_nmvo_assessment-questionnaire_en.pdf);
- the AIDE MEMOIRE FOR INSPECTION of 20 September 2018 (https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/2018_inspection_aidememoire_en.pdf

The preliminary result of the inspection did not result in any major deviations and only a few conspicuities, according to the compliance rating of the inspection report (https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/inspectionreport_en.docx.

Pursuant to Article 44 para. 5 of the Delegated Regulation, authorities can participate in the Steering Committee of securPharm. The authorities have agreed upon that the Federal Institute for Drugs and Medical Devices (BfArM) will fill this position.

7.2 Access of the national authorities

The legislature has governed for what purposes the authorities in charge could gain access to the securPharm system. This way the authorities will have access to available data for the clarification of suspected cases of falsification. In addition, they could use the data of the securPharm system for monitoring and for purposes of pharmacovigilance or pharmacoepidemiology. The concept for the reports to be made available was developed at the European level between the EMVO and a working group of the European Commission and the member states and finalised at the end of 2018. The technical implementation is currently being worked on.

Pursuant to Art. 37 lit b) of the Delegated Regulation, only legitimised authorities will obtain access to the securPharm system. The legitimation is based on the directory announced by the German Ministry of Health pursuant to Section 13 of the General Administrative Ordinance for the Implementation of the German Medicinal Products Act (AMGVwV) for the execution of the AMG address directory. It contains the addresses of all authorities in charge of implementing the German Medicinal Products Act (AMG). securPharm has informed the authorities named in this directory regarding the necessity of legitimation as a prerequisite for system access and has provided the required documents. Agreements regarding system usage of the authorities are being prepared.

7.3 Exchange and collaboration with authorities

For the operation of the securPharm system as part of the implementation of the Falsified Medicines Directive in Germany, it is important to address any arising questions to the authorities in charge. Therefore, securPharm maintains a regular exchange with representatives from the so-called "Working Group on Pharmaceuticals, Pharmacies, Transfusions and Narcotics" (German: AG-AATB) on current issues regarding the operation of the securPharm system. The AG-AATB primarily includes representatives from the state ministries and the superior federal authorities are also participating. In the Federal and State Working Group on Falsified Pharmaceuticals (German: BLAG), securPharm also reports on the degree

of implementation and current issues. The BLAG is coordinated by the Federal Ministry of Health. State ministries, supervisory authorities and the superior federal authorities send delegates to this round. The pharmaceutical expert circles are represented as well. As part of various events of the superior federal authorities and contributions to the Pharmaceutical Working Conference, the current status of the system was presented and questions and answers of the authorities' representatives were discussed.

securPharm e. V. is also planning to establish an advisory board in order to provide a platform to the user group of authorities.

8. Exchange of information

8.1 Information of the market participants

Through events and publications, securPharm and its members have regularly informed the participants in pharmaceutical care that are affected by the Falsified Medicines Directive on the progress of system set-up, the status of regulatory implementation and the necessity of connecting to the system. Since 2012, a total of 38 events and webinars have been conducted for the pharmaceutical industry alone. In addition, there were events held by the professional organisations for pharmacists at the state and federal level. These events addressed not only the connection to the system but also discussed and gathered open questions regarding the implementation of the Falsified Medicines Directive within the pharmacies.

In addition, securPharm has supplied information in the form of press releases and author contributions to specialist publications. Since 2013, a status report has annually documented the implementation progress. Furthermore, the user groups (Chapter 6) were informed about the connection to the securPharm system, which is required for the implementation of the Falsified Medicines Directive. With its website, securPharm has provided a platform where important information on system connection and the implementation of the Delegated Regulation and the Falsified Medicines Directive was made available to all market partners. The knowledge of the securPharm members was presented in checklists and Q&A catalogues. Current developments were addressed in the News section. The securPharm members provided information on their websites as well. The large number of contract partners from the pharmaceutical industry as well as the wholesale and pharmacist segments have shown as of the effective date of 9 February 2019 that securPharm's messages have reached the market participants. securPharm e. V. provides information on system availability on its website. In addition, the operators of the partial systems publish information on current developments and system maintenance or system impairments, if applicable, through webinars and mailings. securPharm and the operating companies will also use these measures for knowledge transfer in the future.

8.2 International collaboration

All member states affected by the Directive face the challenge of establishing an international and functional verification system that does not obstruct the movement of goods and safeguards patient protection. It is for this reason that securPharm pursues a lively exchange with the NMVOs of other European countries. Typically, discussions revolve around questions of system development and improvement, on interacting with each other and with the EMVO. The roundtable of project managers established at the European level by the EMVO is a key factor in this respect and is supplemented by various working groups from the areas of project management, technology and quality assurance. Since Day 1, securPharm has been active in this international exchange and is an important member of this community.

In order to monitor progress in the member states regarding the implementation of the Falsified Medicines Directive and to clarify additional questions, the European Commission organises regular meetings with the member states. For Germany, these are attended by the Federal Ministry of Health (BMG).

9. The 2019 operating year

9.1 System start on 9 February 2019

The securPharm system went live on time on 9 February. Since then, patient protection has been comprehensively guaranteed by the securPharm system:

- Packages equipped with the safety features are checked by the system users. The unique identifier of the packages is verified for authenticity in the process.
- Negative testing results are indicated to the system user and he can subject the pharmaceutical package to additional testing.
- Each action and each alert is saved and a corresponding testing path can be provided to the authorities in individual cases.

9.2 User connection

As of the system start, 98 percent of system users were fully connected. The number of valid operating permits and marketing authorisations issued serves as the basis for the

number of expected users. Deviations from these expected numbers are due to the market dynamics with companies shutting down and getting newly established. The only exception: Regarding the issued wholesale permits, there is no reliable survey regarding the number of wholesale businesses that are affected by the implementation of the Falsified Medicines Directive.

As of 31 December 2019, the number of system users was as follows: 386 pharmaceutical companies, 945 wholesalers, 19,330 community pharmacies, 408 hospital pharmacies, 35 industrial blister companies, 37 compounding manufacturers and 22 centralised procurement departments. The number of users varies according to market dynamics and depends e.g. on mergers, closures, etc.

9.3 Upward trend regarding transactions and the unique identifier

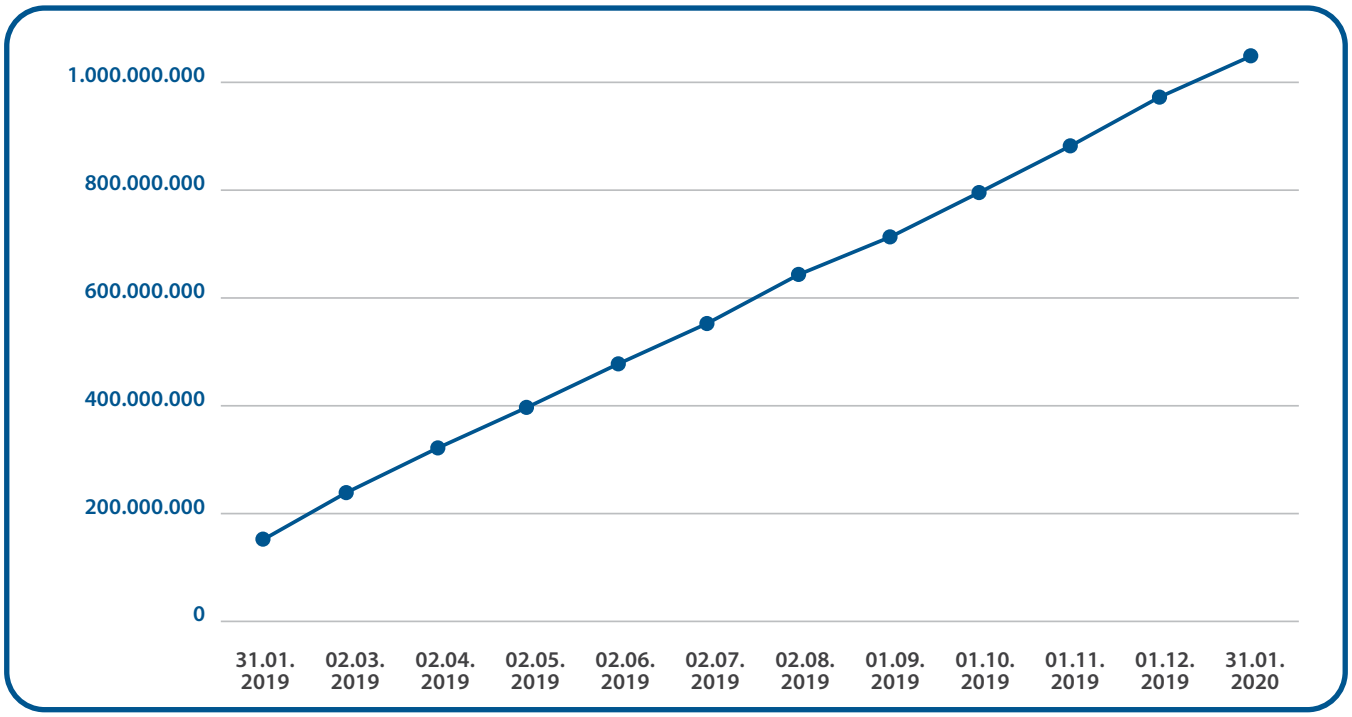
Over the course of the reporting year, the share of new serialised packages grew faster than expected. As of 31 December 2019, there were 1,050 million unique identifiers uploaded to the securPharm system (previous year: 65 million). This means that the share of existing merchandise not subject to mandatory verification is correspondingly decreasing in the market. This trend is also becoming apparent on the dispensing end. As of 31 December 2019, the number of transactions in pharmacies and at wholesalers with the unique identifier recorded in the system was 6.2 million per day.

9.4 System performances

In Article 35 lit. f, the Delegated Regulation stipulates the requirements for the speed of the data repository with which the query regarding the authenticity of a pharmaceutical must be made. This speed must enable wholesalers, pharmacists and other verifying entities "to operate without significant delay". The performance of the overall system is based on the efficiency of the MAH system and the PH system, the software of the system user (third-party software) and the connection pathways between these systems. The securPharm system safely complies with the legal requirement of 300 ms in normal operations.

However, the response time from the users' point of view is also impacted by the data connection between a verifying entity and the pharmacy system and the internal infrastructure within the verifying entity, so that the overall duration of the query can exceed 300 ms.

Number of unique identifiers uploaded in Germany



9.5 System availability

Another critical aspect of the securPharm system's everyday usability is its availability. For smooth pharmacy operations, the system must be consistently available at all times, since verifications must be possible even during night and weekend hours. As a result, the system must be available around the clock, 365 days a year.

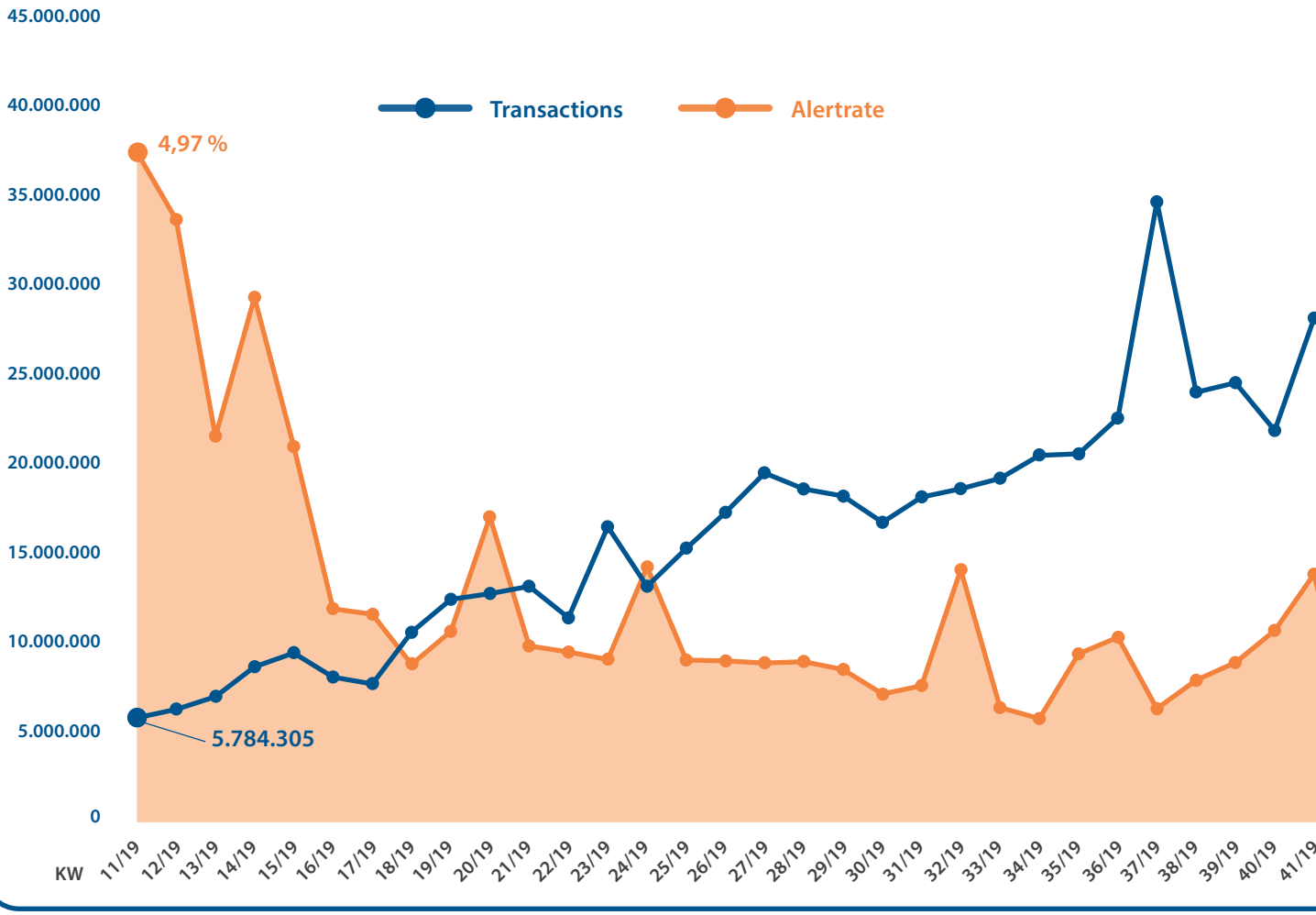
During the time period from 9 February 2019 until 31 December 2019, there were system disruptions with mostly short-term performance bottlenecks and just a few days with outages with complete system non-availability. It is the objective of securPharm to significantly reduce system disruptions.

In order to create transparency regarding availability, securPharm provides an overview of current system availability at www.securPharm-status.de. Information on any system impairments is communicated on the securPharm website and by the operators of the partial systems. It is the objective of securPharm to inform system users quickly and reliably.

9.6 Alarms: Number, cause, measures

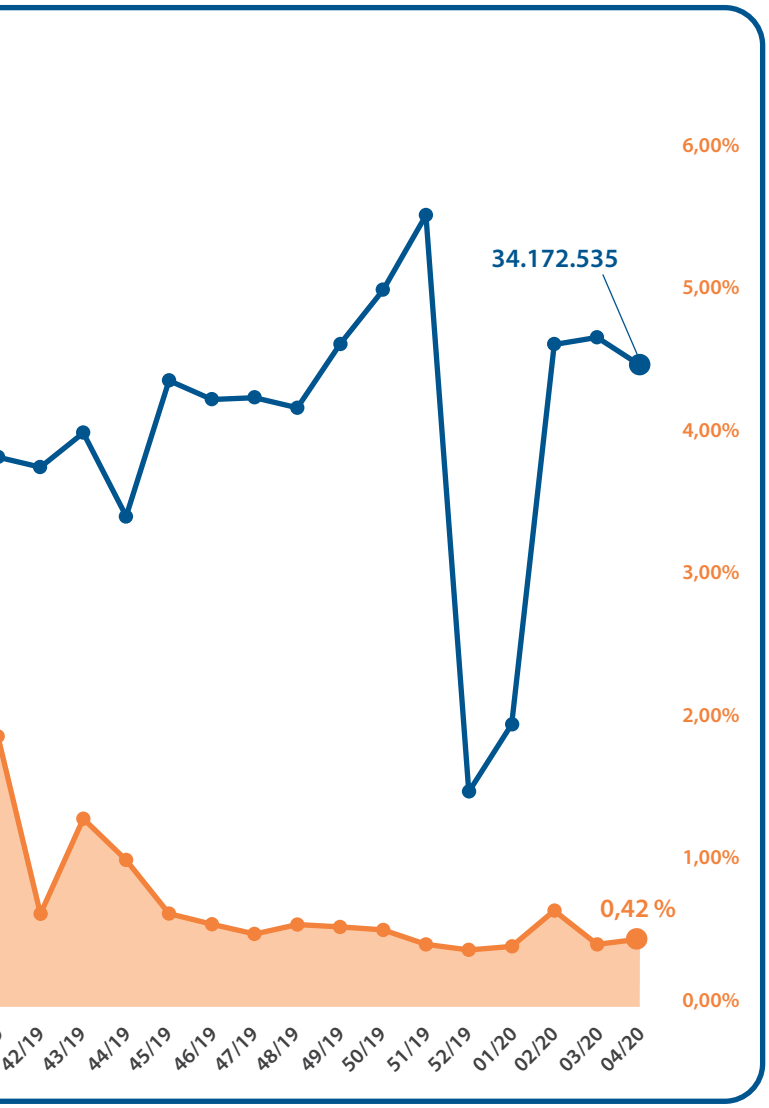
If the securPharm system ascertains a deviation while scanning a package, an alarm is triggered (see Chapter 5). The alarm rate designates the faults per query made to the securPharm system. It is an indicator of the maturity of the securPharm system and its use by the market participants. In February 2019 (week 11/19), 4.97 percent of scans resulted

Transactions und alertrate per week



in an alarm (compared to 6.64 percent for all of Europe). By January 2020 (week 3/2020), this number was lowered to an alarm rate of 0.42 percent (compared to 0.79 percent for all of Europe) while the usage intensity increased at the same time. While this is a considerable development and a good value in a European comparison, the absolute number of alarms is still too high.

Therefore, dealing with alarms and eliminating their cause takes priority for securPharm. As a result, securPharm has established a working group that is concerned with root cause analysis, defines measures and forwards them to the entities causing the alarms for rectification. The search for errors turns out to be complex, since impacts due to actions in other national systems must also be taken into account in an internationally networked system.



9.6.1 Causes of alarms

Dealing with the causes of alarms has revealed that a significant part of alarms can be attributed to handling errors or technical errors in third-party software. Specifically, the following causes of alarms were identified:

- Handling errors by system users
- Unpredicted system behavior due to high complexity
- Missing or incomplete data upload
- Faulty printing of packages
- Bugs in participating systems (EMVS, NMVS, user software)
- Faulty configuration in the participating systems

9.6.2 Measures by securPharm for reducing alarms

Apart from root cause analysis and directly addressing the originators of alarms, securPharm has also implemented technical solutions for alarm reduction in selected cases. This concerns e.g. merchandise released prior to 9 February 2019. The Delegated Regulation provides that this merchandise remains marketable until its expiry date (Article 48). However, if this merchandise bears an affixed Data Matrix Code, the securPharm system can reactwith an alarm, either because coding was incomplete or the data were not uploaded to the MAH system. In this case, the securPharm system behaves technically correctly but generates a so-called false alarm. To ensure that false alarms do not result in a market impairment, securPharm has defined central filter rules, which interrupt the automatic escalation of reports to the authorities in these cases. The information about these packages is stored, so that it can be consulted by the authorities. As merchandise subject to mandatory verification is increasing, the share of these false alarms will decrease.

Prior to 9 February 2019, securPharm has published the corresponding options for action for verifying entities at www.securpharm.de/downloads/.

In addition, securPharm and NGDA provide verifying entities with a scanner test that can be used to verify if a scanner is configured in such a way that it reads the codes in a system-compatible manner. securPharm continues to recommend scanning merchandise at goods in process. When returning merchandise to wholesalers, it must not be deactivated in the securPharm system if it is to remain marketable. securPharm, the members of securPharm and the operating companies have also intensified their communications (updates of the FAQs, circulars) regarding the causes of alarms.

10. Conclusion and outlook

securPharm e. V. successfully launched the German protective system against falsified pharmaceuticals in 2019. The system is available and the users are connected. With over one billion unique identifiers, which were uploaded to the securPharm system by pharmaceutical companies, and more than six million scans by the verifying entities every day, the positive trend has continued. However, future activity areas have also emerged over the course of the year. There were system disruptions all the way to outages, which has resulted in an impairment of authentication operations. Therefore, securPharm and the operating company are intensively dealing with the expansion and stabilisation of the system, both domestically and in an international context. Of course, the objective is creating availability 24/7.

On the users' side, it has also become apparent that many things are already working well. The system and its significance for patient protection enjoy a high level of acceptance and the users were well prepared and got connected in a timely manner. At the same time, it became apparent that numerous alarms occur due to handling errors or faulty coding. Third-party software has also proven to be an important factor for successful performance, but it is one that securPharm cannot influence. securPharm, the operating companies and the securPharm members will therefore intensify the information of system users in 2020.

11. Important links

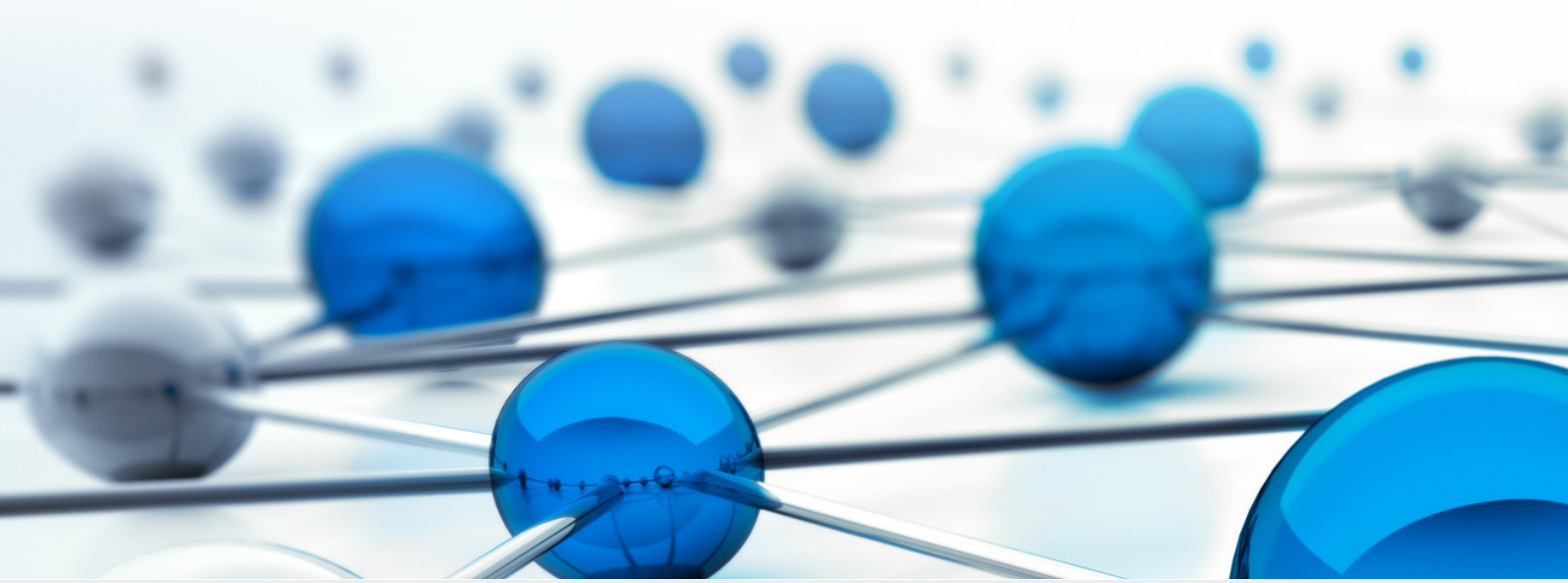
11.1 Legal Principles

Falsified Medicines Directive 2011/62/EU
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2011_62/dir_2011_62_de.pdf

Delegated Regulation (EU) 2016/161
https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2016_161/reg_2016_161_de.pdf

Questions & Answers of the EU Commission on the Delegated Regulation: Version 17, February 2020
https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/qa_safetyfeature_en.pdf

Website on EU measures for the protection of patients against falsified medicines in the legal supply chain:
https://ec.europa.eu/health/human-use/falsified_medicines_en



11.2 System for the authentication of pharmaceuticals

securPharm e.V. – the German organisation for the authentication of pharmaceuticals
http://www.securpharm.de

ACS PharmaProtect GmbH - The operating company of the database system of the pharmaceutical industry at securPharm
http://www.pharmaprotect.de

NGDA – Netzwerkgesellschaft Deutscher Apotheker mbH - The operating company of the pharmacy system at securPharm
http://www.ngda.de

EMVO – European Medicines Verification Organisation - The operating organisation of the European hub
http://www.emvo-medicines.eu

11.3 securPharm members as of 31 December 2019

ABDA – Bundesvereinigung Deutscher Apothekerverbände e.V.
http://www.abda.de

Avoxa – Mediengruppe Deutscher Apotheker GmbH
http://avoxa.de

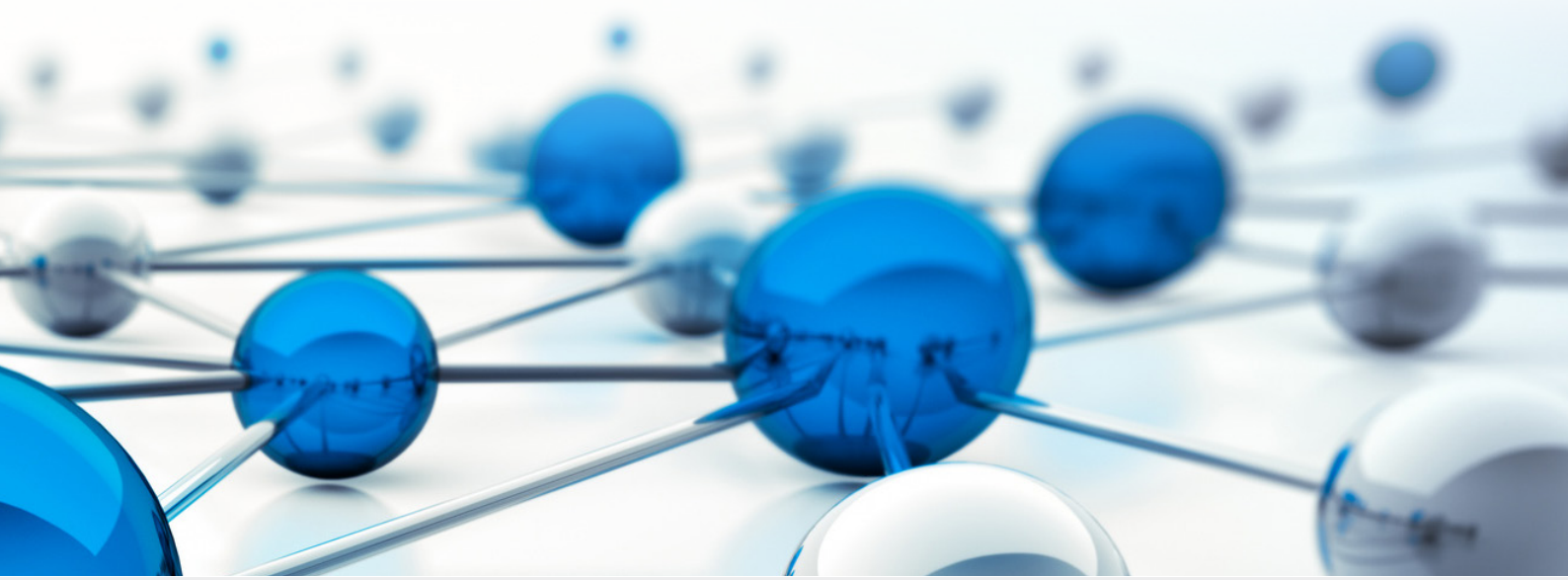
BAH – Bundesverband der Arzneimittel-Hersteller e.V.
https://www.bah-bonn.de

BPI – Bundesverband der Pharmazeutischen Industrie e.V.
http://www.bpi.de

IFA – Informationsstelle für Arzneispezialitäten GmbH
https://www.ifaffm.de

PHAGRO – Bundesverband des pharmazeutischen Großhandels e.V.
(German Association of Pharmaceutical Wholesalers)
http://www.phagro.de

vfa – Verband Forschender Arzneimittelhersteller e.V.
(German Association of Research-based Pharmaceutical Companies)
https://www.vfa.de



2020 Status Report
As of February 2020

This status report is available in German and English
for downloading at www.securpharm.de.

www.securpharm.de

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