securPharm

STATUS REPORT 2018

Status of the project to implement the
Falsified Medicines Directive

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 a nonprofit stakeholder organisation that develops the authentication system for prescription drugs in Germany 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 has the goal of providing a system by the due date of 9 February 2019 that can be used by all market participants. securPharm sees itself as the German component in an EU-wide network working against falsified medicines.

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

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

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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. With the publication of the Delegated Regulation (EU) 2016/161 on 9 February 2016, which includes the technological, organisational and timeline requirements for implementing the Falsified Medicines Directive, the legislative process has come to an end. Pharmaceutical companies, wholesalers, pharmacies and hospitals now largely have clarity regarding the technical and organisational details they will face during the implementation of the directive as well as the mandatory time horizon for implementation. In this respect, the Delegated Regulation confirms securPharm in its key cornerstones.

The German stakeholders have prepared for the implementation of the Falsified Medicines Directive early on. As early as 2012, the ABDA, BAH, BPI, PHAGRO and vfa established the securPharm e.V. organisation in order to set up the German verification system and to demonstrate how the verification requirements can be implemented in an efficient, industry- and pharmacy-friendly manner that is also viable for all parties involved in the pharmaceutical market.

1.1 Project context and limits

It is the objective of securPharm to provide a national verification system that can be used by all market participants in Germany. Since 2013, pharmaceutical companies, wholesalers and pharmacies have been able to use securPharm and practice their own processes. The securPharm project operates under real-life conditions of the German pharmaceutical market and takes into account the diversity of pharmaceutical companies, pharmacy software and pharmacy supplier relations.

The system, which was started five years ago as a pilot project, has been continuously improved and expanded since then. In this phase, the participants in the pharmaceutical supply chain can practice and further optimise their own processes, thereby optimally preparing for 9 February 2019, which is the date on which the requirements of the Delegated Regulation shall apply.

1.1.1 Delegated Regulation

The EU Commission submitted the final version of Delegated Regulation (EU) 2016/161 amending Directive 2001/83/EC to the European Parliament and the Council in October 2015 (referred to in abbreviated form as the "Delegated Regulation" in the text below). On 9 February 2016, it was published in the Official Journal of the European Union. As a result, the legislative process for the Delegated Regulation is concluded. The date of publication also started the implementation period of three years. At that time, the requirements of the Delegated Regulation must be fully implemented.

Starting 9 February 2019, only prescription drugs bearing a unique identifier and whose integrity is visibly recognisable may 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.

Following an intensive review of the Delegated Regulation, we find securPharm well prepared. Overall, the Delegated Regulation confirms the securPharm system in its key cornerstones, such as implementation by a stakeholder organisation, end-to-end verification with risk-based checks by wholesalers, the Data Matrix Code as data carrier, parallel usage of two coding variations and separate databases for pharmaceutical companies and pharmacies.

The content of the Delegated Regulation creates clarity in a variety of respects as to how pharmaceutical companies, wholesalers, pharmacies, hospitals and possibly other health institutions must implement the requirements. However, there are still some unclarified details. In its dialogue with market participants and in the Q&A with the national and international authorities, securPharm makes a key contribution to clarifying open questions.

With expert publications, securPharm accompanies the implementation of the Delegated Regulation and therefore promotes knowledge transfer between the parties involved.

1.1.2 Required safety features

The Delegated Regulation requires two safety features for all pharmaceuticals subject to verification and marketed after 9 February 2019 that are to be sold in the EU member states. The unique identifier represents the basis for authentication. It 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.

Furthermore, the Directive requires an anti-tampering device, which facilitates verification as to whether the outer packaging of a pharmaceutical was manipulated. This safety feature must be implemented independently by each pharmaceutical entrepreneur. In order to create a joint and reliable basis for the manufacturing industry, specialists 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.

1.1.3 Extension of the scope of the security features

The member states can extend the scope of the two security 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 bear such a security feature.

A mandatory extension of the unique identifier is not planned for Germany. Regardless of this fact, all products may bear a Data Matrix Code, as long as it is not serialised. Therefore, e.g. OTC products can also bear the new code, which will include the information of the product code (including the PZN), the batch designation and the expiry data in machine-readable format.

1.1.4 Regulatory information for affixing the security features

The Falsified Medicines Directive imposes significant requirements on the pharmaceutical companies, including those of a regulatory nature. Affixing the security features to the outer packaging of pharmaceuticals subject to mandatory verification is required in terms of the labeling and regulatory approval provisions of Section 10 para. 1c of the German Medicinal Products Act (AMG). As a result, the pharmaceutical company cannot "simply" affix the security features as a piece of information relevant for marketing authorisation, but he must also inform the regulatory agency in charge of this fact. Of course, this also applies to pharmaceuticals that have already received marketing authorisation.

Until 9 February 2019, the pharmaceutical companies can use a regulatory process at regular intervals concerning informative texts for this purpose. For example, applications for extensions and variations could be used to indicate to the authority that the safety features will be affixed.

1.2 Key factors for project success

1.2.1 Stakeholder associations

It is the task of stakeholder associations to represent the interests of their members to the political arena and the public. As a result, they take opposing positions towards each other at times. The key insight is that opposing interests are inappropriate in view of the significance of patient protection and the scope of the task at hand. What is important is to prove to both the public and the political arena that the associations can and will jointly assume responsibility for a safe pharmaceutical supply.

Upon closer scrutiny, it becomes apparent that it is not just pharmaceutical companies, wholesalers and pharmacists who are affected by the Directive but also a variety of others who are involved in the handling of pharmaceuticals. Therefore, it is necessary to describe their tasks precisely as well and to take into account their interests. In forming a stakeholder association to implement the Falsified Medicines Directive, the middle ground between the involvement of all stakeholders and everybody's ability to work must be found. Stakeholder associations that are not a member of this organisation must be credibly assured that their interests will be taken into account through the establishment of appropriate working groups.

1.2.2 Sequence of steps

The sequence of steps chosen by securPharm is tried and tested:

- Establishment of the securPharm stakeholder organisation as a non-profit organisation;
- Attraction and involvement of experts;
- Agreement on objectives and rules as part of a memorandum of understanding;
- Development of a working plan and budget, including start-up funding;
- Review of national conditions, including the
  - Availability of master data (see 1.2.5);
  - Availability of an internationally usable product number (see 1.2.6);
- Establishment of operating organisations;
- IT provider selection and implementation of the systems;
- Organisation of the collaboration with the national authorities in charge;
- Reporting operations pursuant to Article 37 (a) of the Delegated Regulation.

1.2.3 Organisational structure

With Directive 2011/62/EU and the associated Delegated Regulation (EU) 2016/161, the European Parliament and the Council have created the framework to be monitored by the national supervisory authorities. Based on this system, the founders of securPharm have decided on a three-level structure.

1. securPharm creates the prerequisites for implementing the Falsified Medicines Directive in Germany, describes the rules, organises the procedures and resolves conflicts. The latter includes that securPharm will operate a conflict-managing system (CMS) for documenting and settling any type of unexpected event during the verification of medicinal packs.

2. The operation of certain components is assigned to operating companies. The legal operators of the database of the pharmaceutical industry (ACS PharmaProtect GmbH) and the pharmacists' system (NGD – Netzgesellschaft Deutscher Apotheker GmbH) in turn commission the technical service providers that install and technically operate the required databases.

3. Arvato Systems GmbH has already been commissioned to serve as provider for the pharmaceutical industry database and for the conflict-managing system.

In this respect, the national authorities in charge assume a special role. They are responsible for system monitoring and check for compliance with the requirements from the Delegated Regulation and the Falsified Medicines Directive.

1.2.4 Data ownership and privacy

Experience from other projects such as the electronic patient file has shown that special attention must be paid to data ownership. Based on this experience, the concerns regarding data use for other purpose than the intended one by unauthorised market partners and the knowledge that data are already being used for advertising in other EU countries, the German stakeholders have first addressed the issue of data ownership.

They agreed to store and manage the data of the pharmaceutical companies and those of the pharmacies in physically separate databases. As a result, data ownership is organised clearly and in a manner that is understandable for everybody.

1.2.5 Centralised management of national master data

As early as 1967, the German stakeholder associations decided on the central management of master data for the products in demand at German pharmacies (both pharmaceuticals and non-pharmaceuticals). This marked the birth of today's IFA (Informationsstelle für Arzneispezialitäten). It is the organisation that assigns the classification code known as "Pharmazentralnummer" (PZN), which is without exception used by all market participants handling pharmaceuticals. The centralised assignment of the PZN guarantees its uniqueness as a classification code. If the assignment of product identification numbers is left to the pharmaceutical companies in other countries, the uniqueness of product numbers cannot be guaranteed, at least while there are no centrally stipulated rules and the implementation of rules is not centrally monitored.

Apart from data quality, centralised management of master data that relates to one member state and centralised assignment of product numbers offer another key advantage: While the product number is assigned to one specific product and pharmaceutical company, it need not contain a reference to the pharmaceutical company. This information can be flexibly looked up in a centrally managed database. As a result, a product number can be preserved even if the product's licence is sold. The party subsequently responsible for the old merchandise can be ascertained clearly at any time with the help of the centralised database.

1.2.6 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. For example: The extension of the German PZN from seven to eight digits was only feasible after 10 years of discussions and a technical lead time of three years. The complete exchange of a national product number system must therefore seem futile.

A possible alternative are 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 for medicinal products.

1.2.7 Reporting operations pursuant to Article 37 (a) of the Delegated Regulation

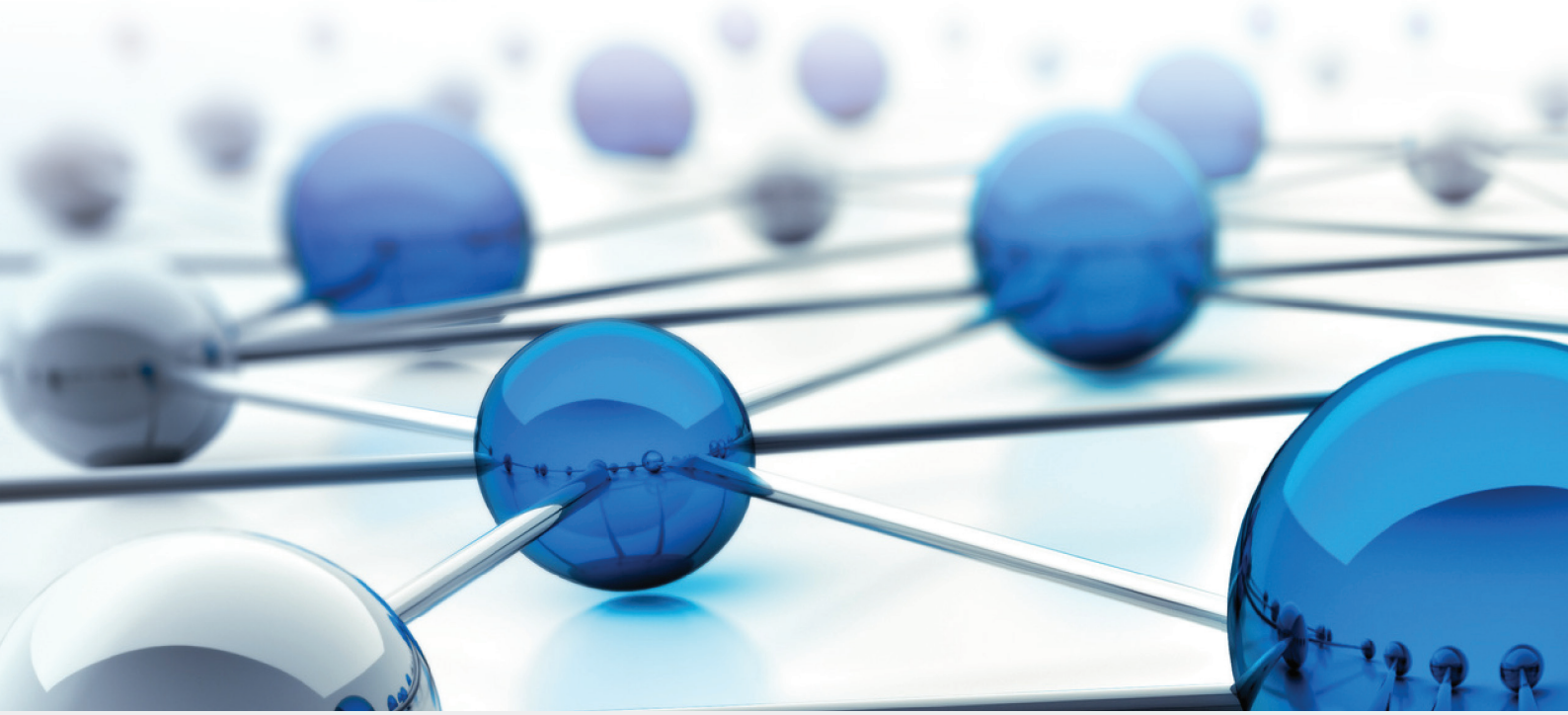
For each EU member state, there must be only one National Medicines Verification Organisation (NMVO) in the future that will establish the respective National Medicines Verification System (NMVS) for the authentication of pharmaceuticals subject to verification and connect it to the EU hub. To the authority in charge, securPharm has declared its intent in terms of Article 37 (a) of the Delegated Regulation to physically set up the repository in conjunction with the systems of the pharmacists and pharmaceutical industry in the territory of the Federal Republic of Germany. This ensured compliance with one of the key reporting obligations of securPharm as the legal entity in charge regarding system operations.

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 of the Delegated Act ("Carrier of the unique identifier") are met.

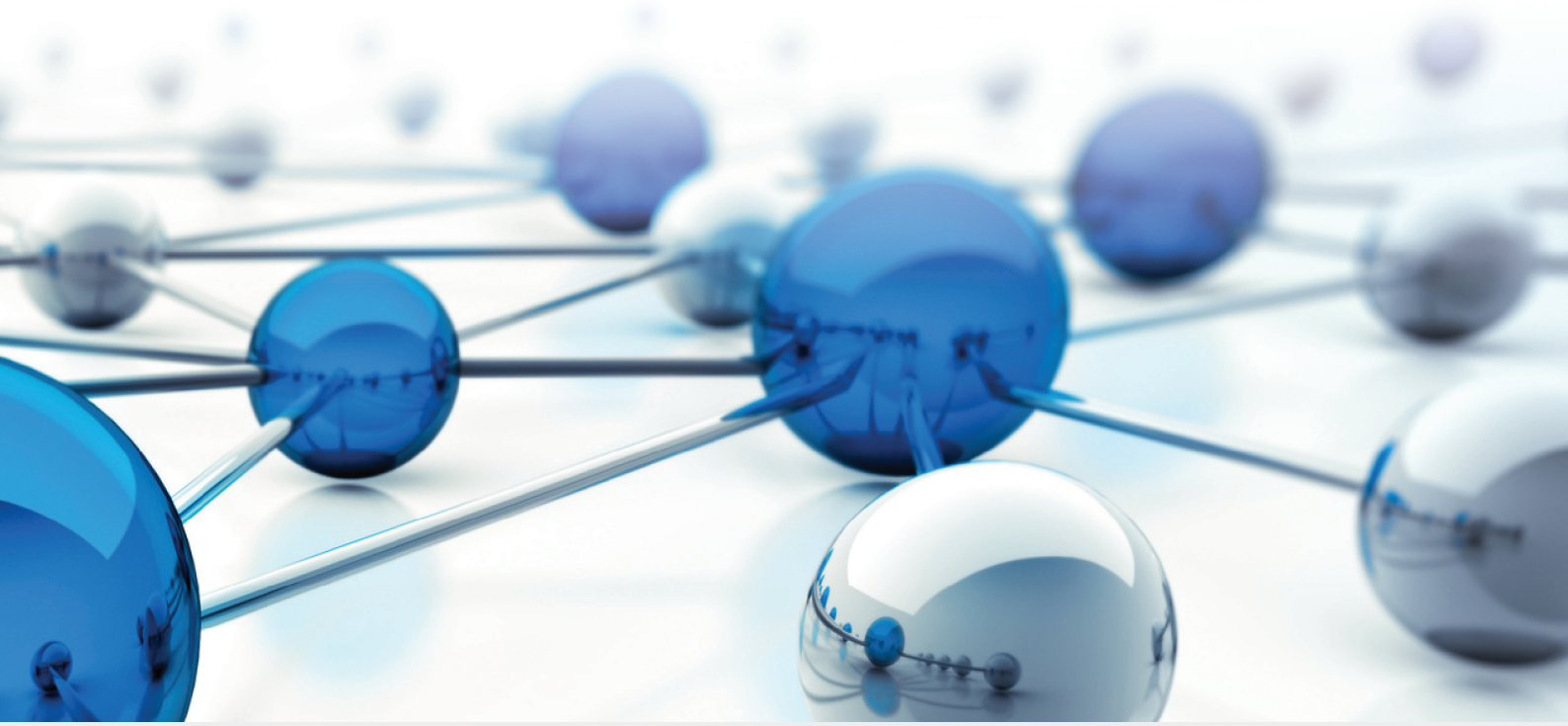
The coding requirements for pharmaceuticals subject to mandatory verification for the German market are stipulated in binding form and specified in greater detail in the securPharm Coding Rules. For the securPharm Coding Rules, please visit www.securPharm.de/kodierung.html.

2.2 Coding rules

For verification within the meaning of Article 4 (d) of the Delegated Act, an unambiguous product code on a Europe-wide scale is needed. To meet this requirement as well, 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. Existing 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 as symbology 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 DIN 16587 (see www.dmre.info) 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". Among others, this includes generation of the PPN and NTIN, code content with the associated data designators, code size, and printing quality (see www.securpharm.de/en/mah/coding.html). The securPharm Coding Rules contain the current requirements resulting from the Delegated Regulation.



2.3 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). This means that 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; or
- 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 (IFA).

2.4 Coding of pharmaceuticals that are not subject to mandatory verification

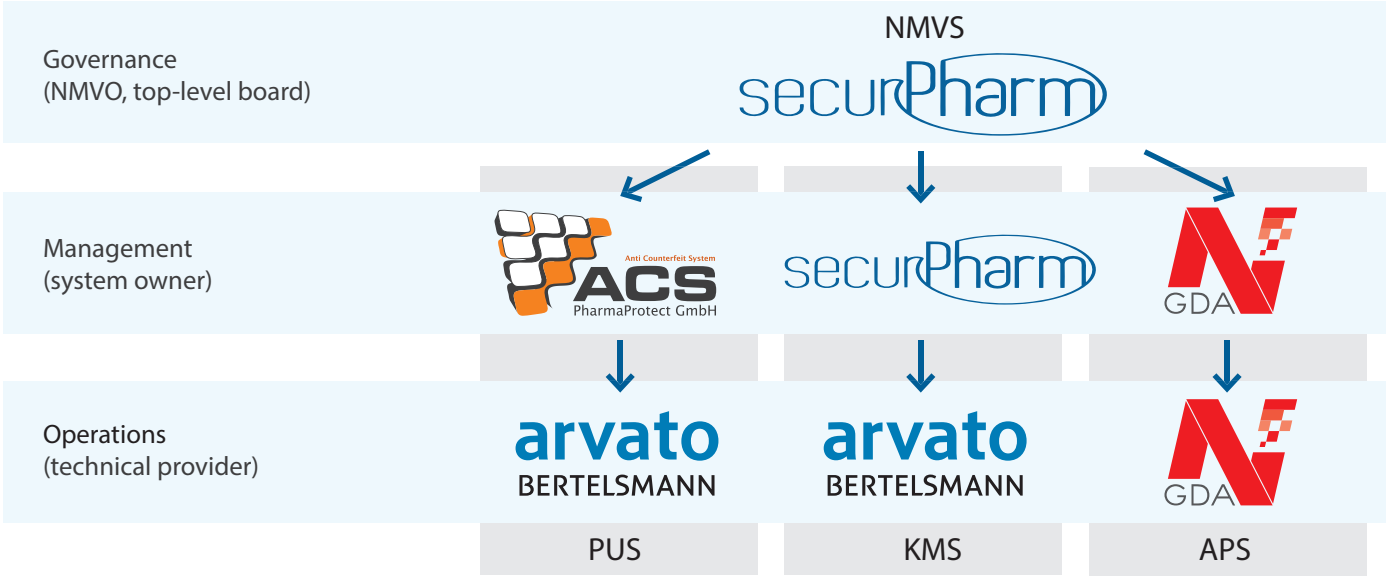
Pharmaceuticals that are not subject to mandatory verification, such as OTC products, may also bear the Data Matrix Code. They are not allowed to be serialised in the same manner required for pharmaceuticals subject to mandatory verification. Apart from the product code (PZN as PPN or NTIN), the code can also include the batch designation and the expiry date.

Various pharmaceutical companies have already announced that they will use this option for their entire product range in order to provide pharmacies and pharmaceutical wholesalers with the opportunity to electronically capture the batch designation and expiry date.

3. The national verification system

Following the requirements of the Falsified Medicines Directive, the German verification system of securPharm 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 verifi-

Governance of the securPharm system



cation system is embedded in a European network in order to also safeguard patient protection across national borders.

3.1 The pharmaceutical verification process

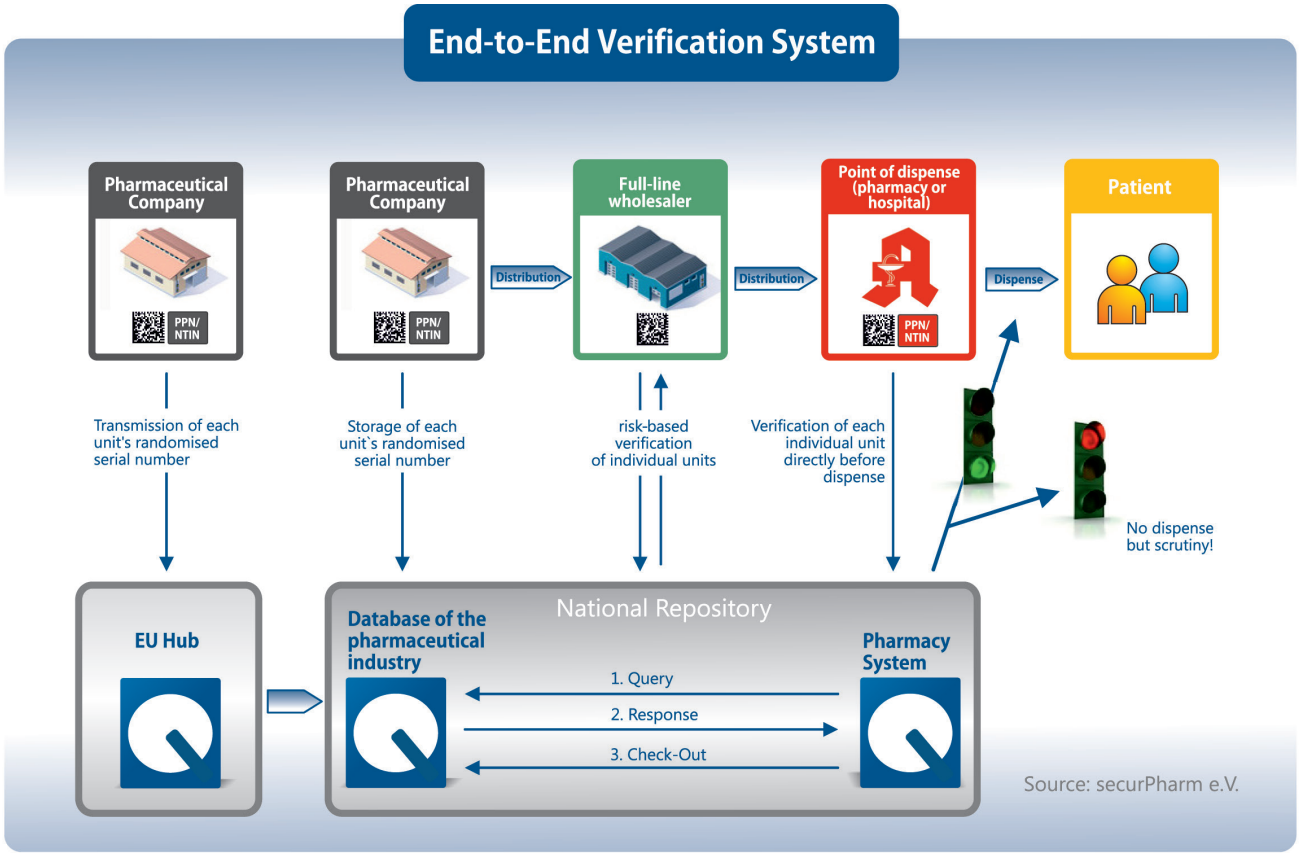
During the production process, the marketing authorisation holder (MAH) equips each pharmaceutical pack that is subject to mandatory verification with the two required safety features. The unique identifier contains a product code (a PZN enveloped in the form of a PPN or NTIN), a unique serial number 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, the pharmaceutical company uploads these data to the central database of the pharmaceutical industry (ACS MAH system).

Each pharmaceutical company reports to IFA the pharmaceuticals that bear the Data Matrix Code and can be verified in pharmacies. Via ABDA information services, the pharmacy software recognises the flag from the IFA database and controls the processes in the merchandise management system of the pharmacy accordingly.

To verify the authenticity of a product package, the pharmacy staff scan the Data Matrix Code of the package before dispensing it to the patient. The verification of the unique identifier (serial number and product code) against the database system of the pharmaceutical industry is running in the background. The package status as it is stored in the database is reported back to the pharmacy. If the status is correct, the package can be dispensed and the package status is simultaneously changed in the database to "dispensed". If the data check shows that the unique identifer 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. This will prevent a negatively verified and possibly falsified pharmaceutical from being dispensed to the patient.

A model with a separate system is used to protect the data of the parties involved (see diagram). Verification inquiries from pharmacies are bundled via the centralised pharmacy system and directed to the database system of the pharmaceutical industry in anonymised form. This modularisation also results in higher efficiency, since both systems can specialise in the requirements of their respective user groups.

Before dispensing, pharmaceutical packages can be additionally verified by others, such as wholesalers or at goods in process at the pharmacy. This allows the verification of authenticity in the chain of distribution even before pharmaceuticals are verified when being dispensed to the patient.



Since retail packages can bear multiple codes and additional two-dimensional codes increasingly appear on packages (e.g. codes with links to URLs), the abbreviation PPN in the Data Matrix Code provides the information that this code contains the data for pharmaceutical verification and must be scanned. The PPN abbreviation stands independent of the above-mentioned "envelope" of the PZN, since the PZN is extracted for merchandise management purposes and the NTIN envelope is transferred into the PPN envelope for verification anyway.

3.2 Integration into the European network

securPharm is the German component in the European shield against falsified pharmaceuticals in terms of the Falsified Medicines Directive. As a result, the securPharm system, which is Germany's National Medicines Verification System (NVMS), has already connected to the European hub, which is the responsibility of the European Medicines Verification Organisation (EMVO). The interface to the hub is the database of the pharmaceutical industry (ACS MAH system). This connection is continuously expanded and adjusted to new circumstances.

In its final version, the European hub will connect the national verification systems of the individual member states with each other. As a consequence, it can be used to verify any pharmaceutical pack equipped with safety features in any pharmacy in Europe. Currently, Germany is still the only country that has successfully connected to the European hub and is actively being used by pharmaceutical companies, wholesalers and pharmacies.

Furthermore, the European hub serves as an additional access point for pharmaceutical companies. They can choose whether to upload the pack data directly via the EU hub, which then routes the data to the corresponding national system. For multinational companies with multiple markets, this certainly is an interesting option. Alternatively, the companies can also directly upload the data of the pharmaceuticals destined for the German market to the national system of ACS. The decision of the pharmaceutical company has no impact on the other participants in the supply chain. Since the data are always stored nationally, patient protection is guaranteed in both cases.

4. Current status of the project

4.1 Structure of securPharm e.V.

securPharm e.V. is the higher-level organisation developing the technical system for the authentication of pharmaceuticals subject to mandatory verification in Germany in accordance with the requirements of EU Directive 2011/62/EU and Delegated Regulation (EU) 2016/161. In this function, it has assigned operation of the two partial systems needed in the Germany arrangement to different operating companies. The database of the pharmaceutical industry is operated by ACS PharmaProtect GmbH (ACS). Via ACS, all pharmaceutical companies whose products are subject to mandatory verification can be connected to the national system for authentication. The pharmacy server is operated by NGDA - Netzgesellschaft Deutscher Apotheker GmbH (NGDA). Via NGDA, wholesalers, retail pharmacies, hospital pharmacies and pharmacies supplying hospitals as well as other healthcare facilities can connect to the system. The operators also serve as contacts for more specific technical issues regarding the connection to the system for authentication. Furthermore, the users are provided with various aids (starter kits, guidelines, etc.) for connecting to the securPharm system.

4.2 Involvement of the pharmaceutical industry

4.2.1 Pharmaceutical companies

As of December 2017, more than 200 pharmaceutical companies are participating in the securPharm project. These include both large, globally active companies with extensive experience in serialisation or coding of medicinal products in other markets (e.g. Turkey, Korea or China), as well as small and medium-sized enterprises from Germany, many of which have been faced with these issues for the first time.

In addition, the participants include parallel importers, who are particularly affected by the EU Directive. They must first go through the EU Hub and into the database system of the country of origin of the merchandise to deactivate the unique identifiers (product code and serial numbers) of the products they have acquired. Subsequently, parallel importers assume the position of the pharmaceutical companies which generate their own unique identifiers and upload these to the database system of the pharmaceutical industry (ACS MAH system) directly or via the European hub, if the merchandise is destined for the German market.

Last but not least, companies manufacturing generic drugs, which will also require safety features pursuant to the EU Directive, increasingly participate in the project with their pharmaceuticals as well.

All in all, the project includes a representative cross-section of the pharmaceutical companies in the overall German pharmaceutical market.

4.2.2 Operating company of the pharmaceutical industry's database

The operation of the database of the pharmaceutical industry was assigned to a separate operating company. The pharmaceutical industry associations established ACS PharmaProtect GmbH (ACS), headquartered in Berlin, for this purpose, which is in charge of specifying, setting up and operating the database system of the pharmaceutical industry in Germany (ACS MAH System). These associations also provide four of the managing directors for this limited liability company. The organisations in questions are the BAH, BPI, vfa and, since March 2017, the newly added Pro Generika e.V. as well. This process goes to show that it is now the entire pharmaceutical industry in Germany that drives the prevention of falsified medicines in the legal supply chain. In addition, the Board of Directors consists of representatives from the pharmaceutical companies.
With arvato Systems GmbH, securPharm and ACS are partnering with a company that develops, implements and operates the ACS MAH system, and processes product data via the interface to the pharmacy system. The company has a proven track record in IT services and demonstrated its efficiency during comparable projects.

Another important concern of ACS is the knowledge transfer in terms of experiences gathered in dealing with serialisation. For this purpose, ACS regularly organises an exchange of experience during which pharmaceutical companies that have already implemented the requirements of the Delegated Regulation communicate their experience to other companies. Furthermore, ACS supports the pharmaceutical companies through webinars, seminars for novices, guidelines, manuals and Q&A catalogs. As a result, pharmaceutical companies can align their processes to serialisation even before the effective date of 9 February 2019 and practice those processes along the entire supply chain.

4.2.3 Connection to the system

All pharmaceutical companies that are marketing pharmaceuticals in Germany and are affected by Directive 2011/62/EU must conclude an agreement with ACS PharmaProtect GmbH to participate in securPharm. As soon as the agreement is concluded, the pharmaceutical companies receive access to the database system of the pharmaceutical industry (ACS 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 hub, whichis operated by the European Medicines Verification Organisation (EMVO), is required to ensure that the pharmaceutical company can be clearly identified during the data exchange between the ACS MAH system and the European hub (www.emvo-medicines.eu). The contractual partners of the EMVO are typically higher corporate structures like a corporation. Furthermore, each marketing authorisation holder must conclude an agreement with the national organisation (NMVO) whose market he supplies.

Pharmaceutical companies can choose from two methods for transmitting their data to the ACS MAH system. The companies can either transmit their data directly to the ACS MAH system or send their data to the European hub, which subsequently routes them to the ACS MAH system.

As part of the connection to the ACS MAH system, the submitted data are checked against data from the IFA database, among others. Therefore, it is particularly important for pharmaceutical companies to always keep their data up to date with IFA and to contact ACS PharmaProtect GmbH for any questions arising in connection with the necessary proof for the legitimacy check.

For details regarding ACS PharmaProtect GmbH or the fee model for pharmaceutical companies, please go to www.pharmaprotect.de.

4.3 Involvement of 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. The Delegated Regulation (Article 20) of the European Commission has specified the wholesalers' obligation to verify packages in terms of a risk-based approach. Accordingly, all returns from pharmacies and other wholesalers as well as all deliveries from other wholesalers that are neither the manufacturer nor the marketing authorisation holder nor a wholesaler who is designated by the marketing authorisation holder must be verified in the future. In addition, wholesalers must check for authenticity and subsequently deactivate each pharmaceutical that

- Is to be distributed outside the EU;mples in retail product sizes that come in a specially designed package and with a specially assigned PZN; or
- Is to be returned to the wholesaler and can be entered into non-sellable inventory;.
- Is slated for destruction; or
- Is in his physical possession and is requested by the authority in charge as a sample.

Furthermore, member states can stipulate in consideration of the specific features of their national supply chain that wholesalers must authenticate and deactivate pharmaceuticals during deliveries to certain individuals or institutions. For Germany, a legal regulation in this respect is still pending. Regardless of this fact, he is authorised to check each pharmaceutical for authenticity.

4.3.1 Wholesalers verify via the pharmacy server

To comply with the aforementioned legal obligations, wholesalers must join the securPharm system. securPharm works with a system of separate databases for pharmaceutical companies on the one hand and wholesalers and pharmacies on the other to ensure the greatest possible data protection for market participants using the securPharm system. Both databases are separate from each other and only exchange data for the verification processes in anonymised form.

Since the start of the project, PHOENIX Pharmahandel GmbH & Co KG with its German subsidiaries has been participating in securPharm, verifying securPharm items in order to test the integration of wholesalers.

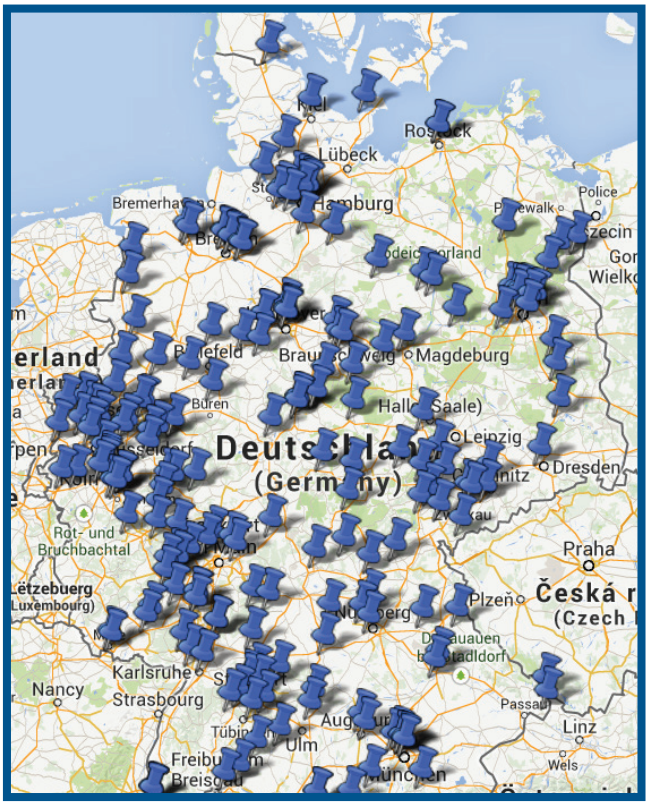
During the process, the securPharm system was tested for its everyday usability and its efficiency during the processing of larger amounts of verifications over short periods of time.

4.3.2 Connection to the securPharm system

To connect to securPharm, wholesalers must contact NGDA – Netzwerkgesellschaft deutscher Apotheker mbH, a subsidiary of Avoxa Mediengruppe Deutscher Apotheker GmbH. securPharm has commissioned the NGDA to serve as the operating company for the pharmacy system, placing the company in charge of the legally required connection as well as the legitimacy check of pharmaceutical wholesalers. 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. For additional information and contacts, please visit https://ngda.de/partner.

In a separate letter to all pharmaceutical wholesalers in October 2017, securPharm has fulfilled its information requirement by informing all holders of a pharmaceutical wholesale licence of their legal obligations and responsibilities in terms of the Falsified Medicines Directive.



Pharmacies connected to the securPharm system

4.4 Involvement of community 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. Before dispensing it to the patient, the pharmacist scans the Data Matrix Code of the pharmaceutical subject to mandatory verification, thereby testing the pack for authenticity. About 400 pharmacies have participated in the pilot operation. Connection is made via the pharmacy server, which is set up and operated by the newly established NGDA – Netzwerkgesellschaft deutscher Apotheker mbH, a subsidiary of Avoxa Mediengruppe Deutscher Apotheker GmbH. In accordance with securPharm's requirements, it also takes care of the unique electronic identification of the market partners via the N-Ident procedure, which is the prerequisite for connecting to securPharm. The actual connection, in turn, will be made by the respective software companies, IT service providers or market partners themselves. NGDA provides these companies with the required technical support. For additional information and contacts, please visit https://ngda.de).

4.4.1 The pharmacy system

The conceptualisation and implementation of the centralised pharmacy system is performed by NGDA – Netzgesellschaft Deutscher Apotheker GmbH. The pharmacy system is a technical solution which, in a first step, renders the verification queries from pharmacies anonymous and then sends them to the database system of the pharmaceutical industry (ACS MAH system). When a positive response is generated by the ACS MAH system, the dispensing pharmacy initiates a second step in the process, which consists of (anonymously) checking the specific package out of the system. Subsequently, the package can be dispensed to the patient. If the pharmacy receives no positive response from the ACS MAH system, the package is not dispensed to the patient but investigated instead. Compliance with the existing reporting protocols is mandatory. Whether a pharmaceutical must be verified or can be dispensed will be automatically shown by the merchandise management system.

Participating companies (abstract)

4.4.2 Machine-readable batch number and expiry date

With the publication of the Delegated Regulation, there is now also clarity regarding the fact that the batch designation and the expiry date must also be part of the Data Matrix Code. This provides pharmacists with the possibility of making their merchandise management more efficient, since the batch designation and expiry date no longer need to be entered manually but can be scanned together with the PZN. Furthermore, they can conduct the authentication as early as during goods in process in order to recognise non-dispensable pharmaceuticals early on and assign them to the supplier in question.

4.4.3 Re-entry of deactivated serial numbers

During the everyday business of a pharmacy, it is possible that a pharmacist books out a pack but does not dispense it. The Delegated Regulation now clarifies that a pharmaceutical - as long as it is in the pharmacist's "physical" possession - can be re-entered for up to 10 days after deactivation.

4.4.4 Pharmacy software providers

In contrast to other countries, there is a variety of different providers for the software used in pharmacies in Germany. The heterogeneity of the pharmacy software market was well represented during the testing phase through the early involvement of five pharmacy software providers with a total of eight merchandise management systems. After just a short time, it became apparent that the securPharm system works reliably, irrespective of what software package is used at the individual pharmacy.

All pharmacy software packages used in community pharmacies will have to offer the verification function through the securPharm system on time, by February 9, 2019, as per the Delegated Regulation. The NGDA provides these companies with the required technical support. Furthermore, the NGDA maintains a close exchange with the ADAS (Association of Pharmacy Software Companies) in order to facilitate the smoothest possible implementation in pharmacies.
In its database, IFA clearly indicates which pharmaceuticals already bear safety features and can therefore be verified at pharmacies. Products are labelled based on the PZN and therefore based on information provided by the pharmaceutical companies to IFA. Using these data, the pharmacy software alerts the dispensing pharmacy employee as to whether the verification for a specific pharmaceutical must be performed or if this is a product that requires no mandatory verification. Through this mechanism, the marketing authorisation holder can also clearly label which pharmaceutical batches he released prior to 9 February 2019.

4.5 Connection of hospital pharmacies and pharmacies supplying hospitals

At the start of 2016, securPharm established a Hospital Project Group. Representatives from hospital pharmacies, community pharmacies that supply hospitals, representatives of the hospital associations and three software companies were to jointly work with securPharm to develop a practice-oriented and practicable implementation of the Delegated Regulation in hospitals.

Since the verification processes at a pharmacy that supplies clinics or hospitals bears only limited comparison to the processes of a community pharmacy, securPharm had planned a six-month hospital pilot starting in the spring of 2017. This pilot tested the specifics of verification in hospitals based on single pack authentication according to the requirements of the Delegated Regulation. As of today, one hospital has connected to securPharm and verified and deactivated successfully. This has proven that the securPharm system basically also works in hospitals.

The large-scale implementation of the Delegated Regulation in hospitals must be collaborative. securPharm provides the verification system for authentication to which the hospitals can connect in order to meet the legal requirements. However, internal preparations for connecting to the securPharm system are the responsibility of the individual hospital. Tasks in this respect include creating the connection prerequisites for the technical system and the planning of internal processes for the authentication in hospitals as demanded by the legislature. In general, the location and time of the authentication must be determined by each hospital.

To meet the legal obligations, hospitals and pharmacies that supply hospitals must connect to securPharm. In regards to the connection, the NGDA - Netzgesellschaft deutscher Apotheker GmbH (the operating company commissioned by securPharm) will serve as contact. This organisation operates the access point for hospitals or hospital pharmacies on behalf of securPharm.

The actual connection will be made by the respective software companies, IT service providers or market partners themselves, who will contact NGDA. The technical and contractual specifications are available at https://ngda.de/Partner or securPharm@ngda.de.

In a separate letter in October 2017, securPharm has fulfilled its information requirement by informing all hospitals of their legal obligations and responsibilities in terms of the Falsified Medicines Directive.

4.6 Involvement of national authorities

The implementation of the Falsified Medicines Directive is new territory as far as the collaboration between the participants in pharmaceutical care and the interaction between securPharm and the authorities in charge is concerned. The legislature has stipulated that the national authorities are to be in charge of supervision and access for the national verification systems in question.

In contrast to the rest of Europe, supervisory duties are fulfilled by several agencies in Germany. One of them is the Paul Ehrlich Institute, the second is the Federal Institute for Drugs and Medical Devices as the highest safety authority. There is also a regional supervisory authority. securPharm is spread out over several locations through its database systems. This is also the reason why - according to the current state of knowledge - one national authority and several regional supervisory authority will be in charge of securPharm and its partial systems.

In a dialogue between the authorities and securPharm, the modalities now have to be settled as to how supervision and access by securPharm and the new processes associated with the authentication of pharmaceuticals can be shaped. The affixing processes for the safety features at the manufacturer as well as the authentication processes in the market follow the GxP rules.

As a new organisation in pharmaceutical care with new tasks, securPharm is subject to supervision by the authorities. So far, the authorities have received reports on suspected falsifications as part of the legal reporting requirement. In the future, securPharm will report additionally. The exact modalities as to how securPharm is to report suspected falsifications and particularly to whom must still be clarified.

Furthermore, the legislature has governed for what purposes the authorities in charge of securPharm can get access to the databases. The authorities have access to all available data when solving cases of suspected falsification but can also use the securPharm system for purposes of pharmacovigilance or pharmacoepidemiology. The exact modalities of data use by the authorities must still be clarified jointly.

4.7 Legitimation

According to Article 37 (b) of the Delegated Regulation, each legal entity that sets up and manages a data respository and access system must ensure that only those users can have access to the data repository whose identity, role and legitimacy has been verified. This means that securPharm as the NMVO for Germany is responsible for the legitimation of all users. As a result, it is indispensable that a safe procedure for the authentication and legitimation of all user groups be set up. The necessary framework and a reliable legitimation procedure have been developed by securPharm. This set of rules serves as a guideline for the institutions that operationally check the legitimation of a future user.

4.8 Quality management system

For an organisation like securPharm, a quality management system is a foregone conclusions. Transparency to the inside and outside, legal certainty and conformity with applicable laws must be ensured. Therefore, another project group dedicated to this task was established. The setup and realisation of a quality management systems will be oriented on the common ISO standards in order to meet the requirements of the Delegated Regulation. securPharm has set for itself the objective of receiving certification in accordance with DIN EN ISO 9001 and DIN EN ISO/IEC 27001 before the year 2018 is out.

4.9 Conflict management process

The analysis of exceptions (to clarify whether a falsification is suspected) means setting up the corresponding conflict-managing system (CMS). securPharm must face this challenge, i.e. handling cases in which a unique identifier cannot be successfully verified. For this purpose, a round of experts was gathered in order to develop a set of rules for handling conspicuities and the core functionalities of a CMS and to compile them in a manual. The focus is the identification, processing,

resolution and documentation of conspicuities (suspected falsifications) that could occur and could be recognized in the securPharm system. This is done in accordance with the requirements of the Delegated Regulation and in coordination with the authorities in charge.

5. International exchange

All nations affected by the Directive face the same 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 stakeholders of other European countries. Discussions typically include questions on system architecture, interactions between stakeholders, coding rules and pricing models. The round of project managers established at the European level by the EMVO is a key factor in this respect and will intensify the exchange between the nations. Since Day 1, securPharm has been active in this international exchange and is also available for bilateral discussions to the organisations in the other countries.

6. Key indicators of the system

6.1 System performance

The Delegated Regulation stipulates requirements for the speed of the repository (Article 35 (f)) at which the query for authentication of a pharmaceutical must be made. This speed must enable wholesalers and pharmacists to "to operate without significant delay".

The overall system performance depends on the performance of the centralised manufacturers' database, the centralised pharmacy database and the individual pharmacy software in use, along with the connections between the various systems. However, naturally, the stakeholders have no influence on the data connection between pharmacies and the pharmacy system. The data packages transmitted during verification are small and therefore using an internet connection with small bandwidth does not represent a problem in terms of system speed. The critical factor for the system's speed in the verification process is how many other processes are simultaneously running via the internet connection. If the connection is at maximum capacity because of other processes (e.g. internet telephony or order processing), this can in some cases lead to verifications being processed within seconds instead of milliseconds.

So far, users are convinced of the system's speed. Deviations with delays in performance can be attributed to the individual pharmacy's implementation of the necessary technical infrastructure for the system. The reaction time of the centralised systems averages 100 milliseconds.

6.2 System availability

Another critical aspect of the securPharm system's everyday usability is its reliability, as expressed by system 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.

So far, the securPharm system has proven robust and reliable overall. To keep availability at this high level, maintenance intervals in regular operations must be covered by redundant systems so that availability is not limited by maintenance activities.

7. Conclusion

After an operating time of more than five years, the securPharm project is well on its way. While a variety of milestones have already been achieved, there will be several more for the project partners. The stakeholder associations have started a

system for the verification of pharmaceuticals that meets the requirements of the EU Falsified Medicines Directives and works under real-life conditions. The Delegated Regulation confirmed the key cornerstones of the project:

- Implementation by a stakeholder organisation;
- End-to-end verification with risk-based testing by wholesalers;
- Data Matrix Code as data carrier;
- Parallel use of two coding variations; and
- Separate databases for pharmaceutical companies and pharmacies.

In view of the significance and scope of the requirements imposed on all stakeholders in the pharmaceutical supply chain by the Falsified Medicines Directive and the associated Delegated Regulation, they have shown that they are the right partners for implementing these important principles for patient protection.

One of the other goals of the securPharm project, namely to realistically represent the heterogeneity of systems and the diversity of market stakeholders, necessitates a significant amount of coordination efforts between the involved parties. Any problems arising during project preparation and implementation were solved jointly and provided valuable insight for the further development of the system by all parties involved.

It was and still is extremely helpful that the stakeholders had agreed early on the basic tenets of their cooperation and the project in general. This has led to the results-oriented and practical resolution of issues (including organisational ones) arising within the project.

Over the past few years, the participating pharmaceutical companies have been able to gather comprehensive experience. At the start of the project, the printing of packages with the Data Matrix Code was a process that was subject to certain variations in quality. These difficulties have now been resolved by the companies and printing is a valid process in most cases. The generation, management and reliable transmission of serial numbers to the database system of the pharmaceutical industry is another challenge that has been solved by the participating companies through the systematic adjustment of IT solutions and processes within the company. The experience the participating companies were able to gather so far also shows how valuable it is to start the implementation early. Almost none of the tasks listed can be solved without the help of external partners such as the manufacturers of cameras, printing and packaging machines, the providers of software solutions and the producers of folding cartons. The only problem is that their capacities are ultimately not unlimited either.

For pharmaceutical companies, it is now a matter of great urgency to address the technical and organisational challenges associated with the implementation of the EU Falsified Medicines Directive. One of the greatest challenges is and will be the conversion of internal company processes, since almost all processes have to be adjusted. It is their responsibility to create the internal prerequisites for the pharmaceutical verification and to connect to the national and European systems for the authentication of pharmaceuticals in a timely manner, to convert the systems for the implementation of the requirements for protection from falsifications, to find and implement the appropriate software and hardware for their company, and to initiate training measures for the employees.

The legislature has set 9 February 2019 as the effective date. Going forward from that date, manufacturers can only release packs that bear the new safety features. The existing merchandise will remain eligible for distribution until the respective expiry date is reached.

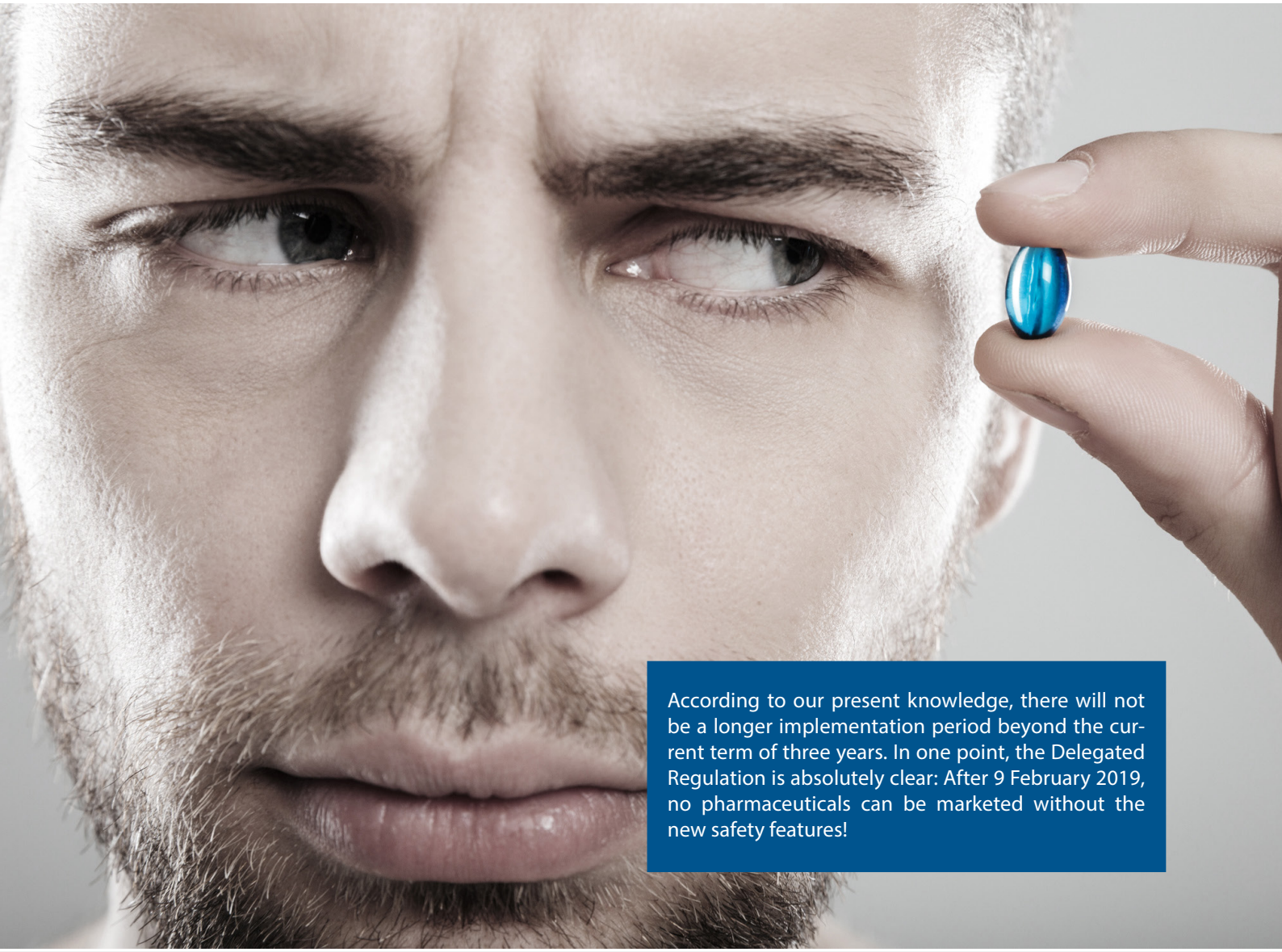
It is now high time that pharmaceutical companies with products subject to mandatory verification connect to the database of the pharmaceutical industry.

All participants in the supply chain have one more year for training their procedures and processes. This is all the more important, since processes run under real-life conditions during the training phase, but any errors that occur will not lead to business disruptions. So there is room for adjustments and corrections.

8. Outlook

The Delegated Regulation confirms essential assumptions of the securPharm project. Nevertheless, the remaining time must be used to continuously analyse and successively implement all details of the Delegated Regulation. This includes the following tasks, among others:

- Integration of additional user groups such as hospital pharmacies and pharmacies that supply hospitals;
- Analysis of exceptions and the systematic expansion of the corresponding conflict management process; Arising exceptions (suspected falsifications) must be solved or clarified according to precisely defined rules and under government supervision in cooperation with the market participants; Discussions with the authorities in charge must be intensified and any open questions must be clarified;
- Efficient representation of international movements of goods and the further integration of the EU hub;
- Connection and integration of the national authorities in charge;
- Systematic improvement of system security;
- Set-up of a quality management system that clearly defines all cross-organisational processes, thereby facilitating smooth, lean business processes and the certification of securPharm. Rendering securPharm fully functional as of 9 February 2019;
- Connection of as of yet unconnected pharmaceutical companies and the entities that dispense pharmaceuticals, i. e. wholesalers, pharmacies and health institutions (hospitals, day clinics etc.).



According to our present knowledge, there will not be a longer implementation period beyond the current term of three years. In one point, the Delegated Regulation is absolutely clear: After 9 February 2019, no pharmaceuticals can be marketed without the new safety features!

9. Important links

9.1 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) 2016/1611
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 9, Februar 2018
https://ec.europa.eu/health/sites/health/files/files/falsified_medicines/qa_safetyfeature_v9.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

Announcement of the BfArM and PEI regarding the anti-tampering device
http://www.pei.de/SharedDocs/bekanntmachungen/2017/banz-vorabveroeffentlichung-bekanntmachung-pei-bfarm-anti-tampering-device.html

9.2 Pharmaceutical verification system

securPharm e.V. – the German Medicines Verification Organisation
http://www.securpharm.de

ACS PharmaProtect GmbH - the operating company of the MAH system at securPharm
http://www.pharmaprotect.de

NGDA GmbH - The operating company of the pharmacy system at securPharm
http://www.ngda.de/projekte/securpharm/

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

9.3 securPharm members

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

10. Expert articles by securPharm

- Pharmind No. 1, p. 45 (2017): Martin Bergen, Thomas Brückner: Status quo von securPharm e. V.
- Pharmind No. 2, p. 194 (2017): Dr. Hermann Kortland: Regulatorische Hinweise zum Aufbringen der Sicherheitsmerkmale gemäß der Fälschungsschutzrichtlinie
- CHEManager 3-4, p. 6 (2017): Dr. Reinhard Hoferichter: Herkulesaufgabe für die Pharmawirtschaft
- Bundesgesundheitsblatt Vol. 60, Issue 11 (2017), p. 1255 (published online on 19. September 2017): Martin Bergen, Dr. Reinhard Hoferichter: securPharm e. V. – der Schutzschild gegen gefälschte Arzneimittel
- Pharmind No. 11, p. 1492 (2017): Martin Bergen, Paul Rupp, Dr. Wolfgang Stock: Best Practice – Hilfe für den perfekten Start zur Serialisierung

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and English at www.securpharm.de

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