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THE FALSIFIED MEDICINES DIRECTIVE AND LEGAL GUARANTEES TO ENSURE AUTHENTICITY OF MEDICINES. THE IMPACT OF DRUG SERIALIZATION ON MEDICINE SAFETY IN THE EU

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Abstract: The aim of this study is to present the impact of the new legal solutions introduced in the so-called Falsified Medicines Directive on medicine safety in the EU. For the purposes of this study, it was necessary to analyze and interpret the provisions of the said Directive and the Delegated Regulation. The guarantees of medicine authenticity, such as a code to be scanned and placed on the medicine packaging (serialization) have been discussed in the paper. These activities are aimed at reducing the market of counterfeit medicines across the EU. The research tool used in the study was the dogmatic and legal method, which made it possible to conclude, that the provisions of the Falsified Medicines Directive increase the guarantee of drug safety. Considering the fact that these regulations are apolitical, one can assume that they will be implemented in other legal systems.

Keywords: medicine safety, counterfeit medicines, medicine serialization, medicine scanning.

1. Introduction

The new European legal solutions lead to discussions about regulations, the aim of which is to ensure that marketing authorization is granted only to authentic medicines. The paper focuses on medicine safety, which has recently been an important issue in the EU and other countries. This issue became particularly significant on February 9, 2019, when the provisions of the Falsified Medicines Directive came into force. Theoretically, these regulations allow for systematic verification of the authenticity of medicines dispensed to the patient. The problem is, that not all medicines are covered by the provisions of the Directive. Its impact can be proved by the fact, that it covers approximately 10 billion packages of prescription medicines dispensed in pharmacies across the EU.

Undoubtedly, the regulation of medicine safety at the EU level is fully justifiable. Its aim is to standardize elementary safety principles. At the same time, individual member states have been given a certain scope of freedom to pass their own regulations in that respect. Awareness of the existence of regulations on medicine authenticity is low, which is due to their considerable diversity.

A research hypothesis has been brought up, that "The Falsified Medicines Directive strengthens the guarantees of drug safety in the European Union".

The research involves the provisions of the Directive and the Delegated Regulation. They have been interpreted teleologically and linguistically. The method used in this study is the dogmatic and legal method.

The aim of this analysis is to better comprehend the EU regulations and make it possible to implement them in other legal systems outside the Union.

2. Sources and methods

The application of the dogmatic and legal method in the research entailed an analysis of the existing EU regulations, such as:

- Directive 2011/62/EU of the European Parliament and of the Council of June 8, 2011, amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products (OJ L 174/74, 01.07.2011),
- Commission Delegated Regulation (EU) 2016/161 of October 2, 2015, supplementing Directive 2001/83/EC of the European Parliament and of the Council, by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use (OJ L 32/1, 09.02.2016).

Introduction of the above-mentioned regulations was motivated by gaps in the medicine safety system, which made it possible to distribute counterfeit medicines on the European market. Since it posed a serious and immediate threat to the health and safety of patients, it was aptly assumed at the EU level, that it was necessary to adopt a comprehensive strategy to counteract the production and distribution of counterfeit medicines. The organization responsible for acting against medicine counterfeiting is the European Medicines Verification Organization (EMVO), which is a joint initiative of the following groups of entities:

- interested parties from the EU representing producers (Medicines for Europe, EFPIA, EAEPC),
- wholesalers (GIRP),
- pharmacists (PGEU).

The work on the implementation of the Falsified Medicines Directive (FMD) was initiated a relatively long time ago (10 years), which eventually led to the adoption of the aforementioned Directive 2011/62/EU.

An effect of the work on the technical details of serialization and verification systems was the Delegated Regulation issued in February 2016, which has been in force since February 9, 2019. Provisions of the above-mentioned EU legal acts enabled the creation of both European and national database systems. These databases have been based on a common model of "plurality of parties interested in counteracting the falsification of drugs". They have been grouped under the five existing basic sectors of the distribution chain:

- innovative producers,
- generic producers,
- parallel importers/exporters,
- pharmaceutical wholesalers,
- pharmacies.

It is important to establish the boundaries of the scope of the Falsified Medicines Directive. It applies in all 28 European Union countries and 4 EFTA members (Norway, Switzerland, Iceland, Liechtenstein). When it comes to the Delegated Regulation, it has a 6-year transitional period for such countries as Greece, Belgium and Italy, which stems from the fact that they have had their own national serialization models.

Undertaking a teleological interpretation of the examined provisions, a reference should be made to the intended purpose of both the Directive and the Delegated Regulation. One should, therefore, have a look at the preambles of these EU acts, which outline their fundamental goals, namely the uniformity and coherence of regulation at the EU level.

Serialization, as a rule, is to encompass prescription medicinal products (medicines). However, the Delegated Regulation provides for specific exceptions, one of them being non-prescription medicines. According to Annex II of the Delegated Regulation, serialization covers all products containing omeprazole in doses of 20 mg and 40 mg in any form (the so-called black list). Annex I of the Regulation excludes from the obligation of serialization the following groups of prescription medicines (the so-called white list):

- Homeopathic medicinal products,
- Radionuclide generators,
- Kits,
- Radionuclide precursors,
- Advanced therapy medicinal products, which contain or consist of tissues or cells,
- Medicinal gases,
- Solutions for parenteral nutrition, having an anatomical therapeutic chemical ("ATC") code beginning with B05BA in the form of solutions for infusion,

- Solutions affecting the electrolyte balance, having an ATC code beginning with B05BB in the form of solutions for infusion,
- Solutions producing osmotic diuresis, having an ATC code beginning with B05BC in the form of solutions for infusion,
- Intravenous solution additives, having an ATC code beginning with B05X,
- Solvents and diluting agents, including irrigating solutions, having an ATC code beginning with V07AB,
- Contrast media, having an ATC code beginning with V08,
- Tests for allergic diseases, having an ATC code beginning with V04CL,
- Allergen extracts, having an ATC code beginning with V01AA.

Article 54a Paragraph 5 of the Directive introduces a special entitlement for Member States. They can decide to extend the scope of application of the so-called anti-tampering device (ATD) to the packaging of medicinal products outside the scope defined in this Directive. The consistency of the analyzed EU acts is confirmed by the fact, that this possibility has also been allowed in Recital 40 of the Preamble to the Delegated Regulation.

Implementation of the Directive entails imposing certain obligations on Member States, which means that the model and tools used for this purpose depend on local legal systems.

A linguistic interpretation of the provisions allows for a statement that the Regulation applies to "medicinal products that have been released for sale or distribution" since February 9, 2019. The interpretation of the phrase "released for sale or distribution" should mean the act of releasing a batch of a given medicinal product. This assumption stems from Article 48 of the Delegated Regulation, which stipulates that medicinal products that have been released for sale or distribution without the safety features in a Member State before the date, in which this Regulation becomes applicable in that Member State, and are not repackaged or relabelled thereafter, may be placed on the market, distributed and supplied to the public in that Member State until their expiry date.

The analyzed Regulation provides for:

1) the characteristics and technical specifications of the unique identifier, that enables to verify the authenticity of medicinal products, as well as identify individual packs,
2) the modalities for the verification of the safety features,
3) the provisions on the establishment, management and accessibility of the repositories system, where the information on the safety features shall be contained,
4) the list of medicinal products and product categories, subject to prescription, which shall not bear the safety features,
5) the list of medicinal products and product categories, not subject to prescription, which shall bear the safety features,

6) the procedures for the notification to the Commission by national competent authorities of non-prescription medicinal products, bearing the risk of falsification, and prescription medicinal products not deemed at risk of falsification, in accordance with the criteria set out in Article 54a(2)(b) of Directive 2001/83/EC,
7) the procedures for a rapid evaluation of and decision on the notifications referred to in Article 54a(2)(f) of the Directive.

Article 23 of the Delegated Regulation highlights the differences in the characteristics of supply chains in the Member States, and thus leaving the exemptions regarding the verification and withdrawal of a unique identifier from the database to national regulation. This obligation has been imposed on wholesalers who supply medicinal products to retailers.

3. Literature review

Considering the fact that the new provisions came into force on February 9, 2019, it is difficult to find up-to-date references in the literature. The scale of drug counterfeiting can be demonstrated by the selected literature presented below. First of all, it is important to refer to a publication, the authors of which present statistical data on the scale of drug counterfeiting in the world (Fijałek, 2009). WHO research shows, that the market share of falsified medicinal products in countries where the control system is the most effective is even around 1%. The world average is 10%, but in some countries, especially the developing ones, where the profits from the sales of falsified medicines are the largest, this share may reach even 30% (Maksim, 2017). It is pointed out in the literature, that it is necessary to implement technological changes, aimed at detecting medicines that are falsified or do not meet the standards. One example is the struggle to fight malaria. 228 million doses of combination therapy are consumed worldwide. According to research conducted in Asia and Sub-Saharan Africa, 1/3 of all drugs are falsified or do not meet the standards (Kovacs, 2014). The problem of drug falsification, as shown by the analysis of legal regulations, occurs on three levels (Hamilton, 2016):

- international – global reporting systems regarding supervision over drug safety,
- national – the importance of creating legal regulations and regulatory bodies supervising the production and distribution of medicines,
- local – trainings and guidelines for health personnel on drug quality assessment and drug registration rules.

The examples selected from the literature clearly indicate that the problem of drug counterfeiting does not only concern the EU, but also occurs outside of Europe.

4. Results

Having applied the dogmatic and legal method, as well as the linguistic and teleological interpretation, the following has been established:

- medicinal products available on the EU market, that have been released for sale or distribution before February 9, 2019, in countries which have adopted the provisions of the Delegated Regulation, provided that they have not been repackaged or relabelled after that date, do not have the safety features within the meaning of the Regulation, because such features were not required before February 9, 2019;
- medicinal products, that were placed on the EU market before February 9, 2019, and that have not been repackaged or relabelled after that date, are not subject to the authenticity verification provided for in the Regulation;
- any medicinal product, which meets the above condition, i.e. exemption of the batches produced before February 9, 2019, and has not been repacked or relabelled after that date, can be dispensed to the patient without the necessity to verify its authenticity.

The most important objectives of the examined regulations are as follows:

- to increase the use of bar codes and automatic data collection in drug dispensing processes in pharmacies and hospitals. This is a vital element in the verification of compliance of prescriptions with medicines dispensed to the patient, with confirmation of their authenticity;
- to harmonize and standardize logistics processes in pharmacies and hospitals through the use of two-dimensional bar codes on the packaging[1], containing all relevant logistics data;
- to use automated methods of obtaining data without having to enter it manually and risking making mistakes when dispensing medicines to the patient. What is important here, is the method of collecting data for the purposes of electronic medical documentation, which aims at improving the quality of that data. It can be achieved by creating solutions compatible with other, more and more common, electronical health services and solutions, such as the electronic prescription or the Integrated System for Monitoring the Sales and Distribution of Medicinal Products;

[1] The unique identifier must be represented in the form of a 2D code and must contain at least:
- Product code (PC): allowing the identification of the name, common name, pharmaceutical form, product strength and packaging size;
- Serial number (SN): being a numeric or alphanumeric sequence of maximum 20 characters;
- Batch or lot number (Lot);
- Expiry date (Exp).

Scanners should meet the following requirements:
- Read 2D Data Matrix codes (ECC 200) and QR codes.
- Read codes from the displays of portable electronic devices (tablets, smartphones etc.).
- Encode the symbol „@" as a prefix for scanners (for pharmacies using the KS Apteka system, e.g. from KAMSOFT).

- to create solutions consistent with good operating practices of ICT systems, by allowing one-time scanning of medicinal products bar codes.

5. Conclusions

Attempts to implement the guidelines provided for in the "Falsified Medicines Directive", made by interested entities (producers, wholesalers, pharmacies, hospitals), are expected to bring about a twofold effect. First of all, the treatment process will be supported and patient safety will be increased. Secondly, internal logistic processes of hospitals and pharmacies will be more efficient. The use of standard bar codes and introduction of changes in ICT systems will undoubtedly allow to achieve a higher level of patient safety and rationalize some of medical processes. It will be possible to achieve by using solutions and modern technologies that have already been tested in other industries.

The rationalization of costs achieved thanks to the application of available methods and tools may contribute to an increase in economic efficiency of the processes carried out. What is more, it may contribute to the improvement of patient's safety.

The issues stemming from the implementation of the Falsified Medicines Directive are broader, as some manufacturers have placed security codes on the packaging of medicines manufactured before this date and then entered them into the European database, which is used to check the authenticity of medicinal products.

However, the conflict occurs in the pharmaceutical system implemented after the entry into force of the said Directive. The system recognizes as authentic only the unique 2D codes, generated after February 9, 2019. The "Code" entered earlier will be deemed as false and generate an alert.

In Poland, the problem is the preparation of the entire system for the implementation of the analyzed regulations. In some Member States, preparations for the entry into force of the Falsified Medicines Directive took a relatively long time (several years), which enabled all the interested entities and the pharmaceutical market itself to function properly from that date. Some countries decided to have a transitional period. In Poland, the changes were implemented without time-consuming tests. Some of the traditional pharmacies obtained the so-called "Access to the system" the moment the Directive entered into force. There are also data management problems affecting the verification of authenticity and the marketing of medicinal products, which occur at the European level, e.g. difficulties with scanning the codes by hospitals and pharmacies.

The issue, particularly important for patients, is the price of medicines. The implementation of serialization is one of the factors affecting the cost of medicine production. The price is affected also by the growing prices of raw materials and utilities, labor costs and the

modernization of technical infrastructure. In the current health and medicine safety policy, the costs that pharmaceutical companies had to incur because of the new regulations seem to have been ignored.

The new medicine safety regulations have been in force for quite a short time; thus, it is impossible to conduct a broader analysis that would show how they work in practice.

References

1. Commission Delegated Regulation (EU) 2016/161 of October 2, 2015, supplementing Directive 2001/83/EC of the European Parliament and of the Council, by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use (OJ L 32/1, 09.02.2016).
2. Directive 2011/62/EU of the European Parliament and of the Council of June 8, 2011, amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products (OJ L 174/74, 01.07.2011),
3. Fijałek, Z., Sarna, K. (2009). Fałszowanie leków i inne przestępstwa farmaceutyczne [Falsification of medicines and other pharmaceutical crimes]. *Problemy Kryminalistyki, 263,* 5-11.
4. Hamilton, W.L., Doyle, C., Halliwell-Ewen, M., Lambert, G. (2016). Public health interventions to protect against falsified medicines: a systematic review of international, national and local policies. *Health Policy and Planning, 10(31),* 1448-1466.
5. Kovacs, S., Hawes, S.E., Maley, S.N., Mosites, E., Wong, L., Stergachis, A. (2014). Technologies for Detecting Falsified and Substandard Drugs in Low and Middle-Income Countries. *PLoS ONE, 9(3),* e90601. https://doi.org/10.1371/journal.pone.0090601.
6. Maksim, I.K. (2017). Fałszowanie Produktów leczniczych – Uwagi na tle Kodeksu Karnego i regulacji poza kodeksowych [Falsification of medicinal products – comments on the Penal Code and other regulations]. *Zeszyty Prawnicze, 17.2,* 39-43.