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Impact of legislative solutions on counterfeiting of medicines at european level

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Abstract. Counterfeit medicines pose a serious threat to health systems, industry and society. Globalization of commerce and the active online environment have significantly increased the health risks associated with counterfeiting medicines.
Considering these alarming issues, the European Parliament and the Council have adopted a legislative framework aimed at combating the entry of falsified medicinal products into the legal supply chain, without affecting the functioning of the internal market for medicinal products for human use.
This article aims to present the impact of the new legislative solutions known as the "Falsified Medicines Directive", by which, in 2011, the European Union took an imperative step in protecting public health, establishing the legal basis by which the falsification of medicines is a criminal law action, which deprives patients of safe and quality medical treatment.

Keywords. European legislation, falsified medicines, internal market for medicines, public health, health systems, serialization

1. Introduction

Counterfeit medicines are a serious threat to health systems, industry and society. The globalization of commerce and the active online environment have significantly increased the health risks associated with counterfeit medicines. Over the past decade, international organizations, pharmaceutical companies and national governments have developed a wide variety of measures to combat their intrusion into legal supply chains.

All these efforts focused on strengthening pharmaceutical regulatory frameworks and improving patient quality of life. The purpose of this paper is to present the impact of the new legal solutions known as the "Counterfeit Medicines Directive", through which, in 2011, the European Union took an imperative step in this fight for public health. The implementation process of this directive had a deadline of February 9, 2019, and theoretically this convention allows the systematic verification of the authenticity of the medicines issued to the patient.

However, harmonizing the interests of a diverse network of "actors" often requires trade-offs that could lead to regulatory limitations and create opportunities for criminal organizations to seize and exploit.

2. Materials and methods

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There is no doubt that the regulation of the safety of medicines at EU level is fully justified. Its purpose is to standardize basic safety principles. At the same time, individual member states have been given some freedom to adopt their own regulations in this regard.

This study involves the provisions of Directive 2011/62/EU and Delegated Regulation (EU) 2016/161, the content analysis is carried out on the basis of formal sources, directives, delegated acts, guidelines and regulations, and the method used is the dogmatic and legal method.

In Romania, the provisions of the Falsified Medicines Directive were transposed into national legislation by Law 95/2006 republished Title XVIII Medicines and starting from 09.02.2019 the provisions of Delegated Regulation 2016/161 come into force on the territory of Romania as well.

The introduction of the regulations mentioned above was motivated by many deficiencies in drug safety, which made it possible to distribute falsified drugs on the European market. The group responsible for the actions against the falsification of medicines is the *European Medicines Verification Organisation*, a joint initiative of the following groups of entities: EFPIA - manufacturers of innovative medicines and EAEPC (generic medicines), GIRP - pharmaceutical and parallel distributors and pharmacists from community pharmacies.

Before presenting the specific objectives and their impact on public health, the definition of falsified medicine is clarified, which is included in Law 95/2006 republished - Title XVIII, Medicines: "Falsified medicine - any medicinal product with a false representation of: (a) its identity, including its packaging and labelling, its name or its composition as regards any of the ingredients including excipients and the strength of those ingredients; (b) its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorisation holder; or (c) its history, including the records and documents relating to the distribution channels used.

The definition does not refer to the violation of "intellectual property" rights, these drugs containing substandard or falsified ingredients, or the lack of active substances, the presence of the incorrect dose, also being a major percolation for public health.

Until recently, the most commonly counterfeited drugs in rich countries were expensive lifestyle-enhancing drugs such as hormones, steroids and antihistamines. In developing countries, they included drugs used to treat life-threatening conditions such as malaria, tuberculosis and HIV/AIDS.

2.1. Objectives

a. Safety features

An effect of the work on the technical details of the serialization and verification systems was the Delegated Regulation issued in February 2016, which enters into force on 9 February 2016. The provisions of the EU legal acts mentioned above allowed the creation of a data system based on a model joint "multiple stakeholders in countering drug counterfeiting". These parties were grouped into the five basic existing sectors of the distribution chain: innovator and generic manufacturers, parallel importers or exporters, pharmaceutical suppliers and pharmacies.

Marketing Authorization Holders are required to place two security features on the packaging of most prescription and non-prescription medicinal products in the European Union: a unique identifier (a 2-dimensional barcode) and a device anti-fraudulent manipulation, in accordance with Commission Delegated Regulation (EU) 2016/161. The annexes to the regulation include the list of medicines subject to this requirement.

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Manufacturers will upload the information contained in the unique identifier for each individual medicine to a central EU register. The register is part of an end-to-end medicine verification system introduced by regulation. Depending on the source of the medicine, distributors will also need to scan the medicine at different stages of the supply chain to verify their authenticity. Pharmacies and hospitals will then scan each medicineat the end of the supply chain to verify their authenticity and check them out of storage before dispensing them to patients. These safeguards will guarantee the authenticity of medicines for the benefit of patients and businesses, and strengthen the security of the medicine supply chain, from manufacturers to distributors, pharmacies and hospitals. In the context of pharmacy practice, these new obligations are introduced into routine settings and can often be time-consuming for community and hospital pharmacy staff. However, it should be noted that, thanks to the solutions proposed by the EU Parliament, the pharmacist's role will increase. In particular, at the time of dispensing the medicine, the pharmacist will be required to scan the unique serial identifier of the packaging in the form of a technologically advanced matrix, allowing them to verify the authenticity of the medicines.

Serialization is usually applied to prescription drugs, but nevertheless the Delegated Regulation also provides for specific exceptions such as medicines or categories of medicines that are released without a medical prescription that present the safety elements: omprezol, gastro-resistant capsule in concentration of 20 mg, respectively 40 mg.

Annex 1 of the Delegated Regulation contains a List of medicines or categories of medicines that are issued on the basis of a medical prescription that do not present the safety elements:

- ✓ Homeopathic medicines
- ✓ Radionuclide generators
- ✓ Radionuclide kits
- ✓ Precursors of radionuclides
- ✓ Gases for medical use
- ✓ Advanced therapy drugs containing or consisting of tissues or cells
- ✓ Solutions for parenteral nutrition with an anatomical chemical therapeutic code (hereinafter referred to as "ATC") beginning with B05BA
- ✓ Solutions affecting electrolyte balance with ATC code starting with B05BB
- ✓ Solutions producing osmotic diuresis with ATC code beginning with B05BC
- ✓ Additives for intravenous solutions with ATC code starting with B05X
- ✓ Solvents and diluents, including irrigation solutions, with ATC code starting with V07AB
- ✓ Contrast media with ATC code starting with V08
- ✓ Tests for allergic diseases with ATC code starting with V04CL
- ✓ Allergen extracts with ATC code starting with V01AA

It is important to set the limits of the scope of the Falsified Medicines Directive. It applies in all 27 countries of the European Union and in the 4 EFTA member states (Norway, Switzerland, Iceland, Liechtenstein). When it comes to the Delegated Regulation, it has a 6-year transition period for countries such as Greece, Belgium and Italy, which have their own national serialization models.

b. Supply chain integrity

The second key element of an effective policy against falsified medicines is the integrity of the supply chain in terms of defining and involving all participants in the prevention and detection of illegal activities. However, identifying all the parties involved has been a difficult

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task since the modern era, the pharmaceutical supply chain being much more complex than it used to be: drugs are manufactured from ingredients originating in different countries, packaging, repackaging and sale are done in different places in terms are sometimes vague, drugs change ownership many times, and each transaction allows counterfeit products to enter the market.

Participants in the modern pharmaceutical supply chain are multiplying, new categories are emerging, and regulations should be updated appropriately and in a timely manner. A new category of participants is defined - the so-called "brokers" who carry out intermediate activities and specific measures to regulate their operations. For the first time in European pharmaceutical legislation special regulations are adopted targeting high active substance (API) traders. In parallel, traders are forced to align their operations with regulations that were once only applicable to produce.

c. Involvement of several interested parties

The involvement of all participants in the supply chain is the third key element that constitutes an effective policy against falsified medicines. For research purposes, they are divided into two groups: interested parties and affected parties. Although both groups benefit from the proposed regulations, they sometimes have different and even conflicting interests when it comes to their implementation.

The first group - stakeholders, includes supranational and state regulatory authorities, as well as importers and manufacturers of APIs and drugs. They are usually among the most important initiators and most often the biggest beneficiaries of such policies because they would lead to increased safety of medicines and health protection and, consequently, the reduction of financial losses of several millions.

The second group - wholesalers, distributors, pharmacists, health professionals and consumers are those actors who are directly involved in policy implementation and make it 'happen'. Without their active participation a comprehensive policy would remain a well-written document with little or no impact. A key problem is that not all those affected are interested, or at least not consciously, in the development and implementation of policies against falsified medicines. Stakeholders must invest time and effort, initiate and get involved at an early stage, so as to minimize any future conflicts that may arise from lack of understanding or disagreement.

In order to check whether the falsified medicinal directive (FMD) adequately involved representatives of both groups, an in-depth content analysis was conducted on the content of the Directive. Table 1 presents a brief excerpt that illustrates the key research points and reveals some of the measures adopted for each of the supply chain participants.

Table 1. Participants in the supply chain

Participants	**Article modified according to Directive 2011/62/EU**	**Corresponding activities**
EU authorities	Art. 40 par. 4 Art. 47, paragraphs 3 and 4 Art. 52 a Art. 54 a;	The Commission adopts, through delegated acts, the principles and guidelines of good manufacturing practice for active substances and for excipients; The commission carries out registrations and inspections and

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		creates supporting databases.
National Authorities	Art, 40 par. 4 Art. 52 a Art. 117 a Art. 118 a	Registration of the activity with the competent authority of the member state where the importers, producers and distributors of active substances are established; Use of a system that registers and manages notifications of suspected falsified medicines. Organization of meetings with patients and consumers to communicate public information regarding prevention and law enforcement initiatives to combat drug counterfeiting
Importers and distributors of active substances and excipients	Art. 52 a Art. 46 b Art. 47, paragraphs 3 and 5	New obligations, mandatory registration and certification
Final consumers/patients	Art. 85 d	Information campaigns

The analysis confirms that the Directive includes measures that more or less involve all participants in the pharmaceutical sector – from API importers and medicines manufacturers to end users. Important are the new measures adopted for the control of APIs, because they are defined as the "backbone" of each medicine (European Commission, 2011). If their quality is compromised, the final product would not meet the quality, safety and efficiency criteria. On the basis of this new regulation, the problem of substandard drugs can also be concluded by eliminating the most common causes for their appearance - the use of low-quality ingredients.

d. The online environment

The new requirements for the online sale of medicines come as increased access to the Internet has allowed criminals to effectively circumvent regulatory barriers.

In this regard, the Directive introduced a mandatory visible logo on the websites of legally operating online pharmacies and approved retailers in the EU. The logo allows patients and consumers to identify authorized online pharmacies and authorized retailers who supply authentic and authorized medicines. A single click on the logo brings up a link to the websites of the national regulatory authority, where all legally operating online pharmacies and approved retailers in the respective countries are listed.

e. Medical education and awareness

A major factor facilitating the uncontrolled spread of counterfeit drugs is lack of awareness among consumers about the serious health risks they pose. Among the factors that contribute to this risky behavior are the lack of doubt about the quality of medicines, the desire to avoid regulations, restricted or limited access to certain medical products and increased self-medication.

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In this context, FMD imposes significant changes in the pharmaceutical sector that affect all participants. If national authorities and pharmaceutical manufacturers are the main initiators and are therefore fully aware of their need, this may not be the case for some of the other participants. This is a reason why art. 85d of the Directive aims to promote awareness campaigns for the general public.

On the website of the European Medicines Agency there is information available on this topic, but there are no specific communication materials for the general public related to the falsification of medicines. This could be due to the fact that the agency operates at a specialized level and its communication activities and initiatives are primarily aimed at competent national authorities and specialists.

The identified communication materials confirmed that the EU institutions are committed to developing educational resources for society on the risks of falsified medicines. However, these materials are mainly available on their websites. The question is whether the general public is motivated to visit them specifically, since most consumers have little or no knowledge of the existence of this problem. Therefore, taking into account the social activity in the online environment, an advertisement for the general public regarding the falsification of medicines and the presence of a major danger to public health could be carried out on communication channels and social networks that have an impact, such as 'Facebook', 'Instagram', 'Youtube', 'Twitter' etc.

3. Result

In the intended purpose of both the directive and the delegated regulation, their fundamental objectives are emphasized, namely the uniformity and coherence of regulation at the EU level. Applying the dogmatic and legal method, the regulation of Directive 2011/62/EU on falsified medicines confirms that there is a high level of cooperation at the international and regional level, between levels of European institutions and leading global and regional organizations in the fight against falsified medicines in while at the national level the obligation of the state authorities remains. The establishment of a community code on medicinal products for human use in terms of preventing the entry of falsified medicinal products into the legal supply chain concerned several stakeholders - distributors, pharmacists, health professionals and last but not least, the patient.

As of February 9, 2019, prescription drugs (with very few exceptions) can only be put into circulation by manufacturers if they carry the new safety features.

The directive aims to increase the protection of public health by expanding the scope and helping the authorities to more effectively pursue criminal offenders in the pharmaceutical sector.

4. Conclusions

The main objective of every policy against falsified medicines is to ensure and guarantee the welfare of society. This article confirms that Directive 2011/62/EU represents a surprising legal instrument for increasing the level of protection in EU member states through the adopted measures.

A coherent regulation is being formed and if the options identified for its further development are taken into account in future policy reviews, it could significantly increase legal barriers to criminal organizations and increase public awareness of the issue.

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