EU POLICY AGAINST FALSIFIED MEDICINES: OPTIONS FOR FURTHER DEVELOPMENT

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Abstract: The globalization of trade and internet access significantly increased the health risks associated with falsified medicines. International organizations, pharmaceutical companies and national governments developed a wide variety of measures to combat their pervasive penetration into the legal supply chains. However, the lack of harmonization, broad acceptance and legally bound enforcement obstructed their endeavours. The unsatisfying outcomes resulted in enhanced supranational cooperation focused on strengthening the pharmaceutical regulatory frameworks and the improvement of patient protection.

In 2011 the European Union joined the global fight with the adoption of Directive 2011/62/EU that became known as the Falsified Medicine Directive. It is legally binding for Member States and amends the fundamental for the pharmaceutical sector Directive 2001/83/EC. The objective of the present paper is to verify if it represents a comprehensive tool for effective prevention of the access of falsified medicines in the European legal pharmaceutical supply chains. The results revealed that although it is rather detailed, there are areas that could be further developed and improved when compared to analogical policies and initiatives.

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Introduction

Falsified medicines pose serious threat to health systems, industry and society and the adoption of supranational coherent pharmaceutical policies focused on prevention, control and prosecution became an imperative step to eliminate their uncontrolled pervasion. In 2011 the European Union (EU) joined the global fight with Directive 2011/62/EU or as it became known – the Falsified Medicine Directive (FMD). It is a result of long-term negotiations between the various participants in the complex pharmaceutical network – regional and national authorities, manufacturers, wholesalers, international industrial and patient organizations, etc. The Directive is the formal proof that when facing a life-threatening problem of such magnitude a common understanding could be achieved with respect to the measures aimed at its containment. However, harmonizing the interests of a diverse network of actors often requires compromises that might result in limitations of the regulations and create opportunities that criminal organizations would eagerly seize and exploit.

Research Methodology

The present research has two interconnected goals. The first one is to determine if FMD represents a comprehensive tool that could effectively fight the problem. The second is to reveal if there are options for its improvement and development that could result in further increase of supply chain security and patient protection.

The selected research methods - comparative and content analysis, correspond to the qualitative nature of the goals. The first one is performed by the means of especially designed conceptual framework inspired by Max Weber's "Ideal Type" theory. It combines five elements that are defined by a world renown organization as fundamental for the development of comprehensive and effective policies against falsified medicines. The content analysis is conducted on the basis of formal sources – directives, delegated acts, guidelines and regulations, as well as on institutional and academic publications dedicated to the problem.

Results and Discussion

Legal and Regulatory Scope

Two research questions were formulated with reference to the analysis of FMD's legal and regulatory scope. The first one addresses the types of problematic medicines that the Directive is intended to regulate. It arises from their diversity (Newton et al., 2011; Mackey and Nayyar, 2017) and the various health risks they pose to the patients – falsified, counterfeited, illegally diverted, substandard, unlicensed/unregistered. If the regulations focus only on one or few of them this could create

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prerequisites for the criminal organizations to redirect their activities to the less regulated and prosecuted types.

Figure 1: Conceptual framework for analysis of policies against falsified medicines

Source: Adapted from Committee on Understanding the Global Public Health Implications of Substandard, Falsified, and Counterfeit Medical Products (2013) and World Health Organization (2017)

The very title of Directive 2011/62/EU specifies that its scope is limited to the falsified medicines. But what happens to the other types and why they are not included? Corresponding national pharmaceutical laws include much broader definitions and regulations. For example, in Title II of the Drug Quality and Security act in USA (Drug Quality and Security Act, 2014) the definition “illegitimate product” is adopted. It covers all major types of problematic medicines: illegally diverted or stolen medicines, counterfeit - that infringe the intellectual property rights, substandard and unlicensed. In the Russian Federal Law on Circulation of Medicines (Federal Law 61-FZ, 2010) three main types of problematic medicines are specified – falsified, counterfeit and substandard.

The decision of the European Commission (EC) to limit the scope of the Directive could be explained with the presence of previously adopted measures. They include regulations for the other types of compromised medicines that are set in the fundamental Directive 2001/83/EC and separate legislative measures concerning the intellectual property rights. However, such differential legislative approach could be confusing since one European policy or regulation is often transposed by the Member States in few different national laws and bylaws. This requires the involvement of various institutions and enhanced communication between all participants that are often rather difficult to be achieved. Although fragmented, it can be concluded that on the EU legislative level measures exist against the main types of compromised medicines and no opportunity for further development is identified.

The second research question concerns the two major legal types of medicines that FMD applies to – prescription (Rx) and over-the-counter (OTC). As per art. 54a of the Directive and the Commission Delegated Regulation (EU) 2016/161 the main focus of the regulations is on Rx medicines with some specifically defined exceptions. They could also be applicable to OTC products, but only to those with proven increased risk of falsification as at present only one such medication is included in the respective annex to the Delegated regulation.

The focus on increased regulation of Rx medications might be predetermined by the fact that many prescription medicines are generally reimbursed by the national health funds. Any problems regarding their quality, safety and efficacy directly reflect in financial losses for the state governments. At the same time there is a significant rise in self-medication practices (Noon and Blanchette, 2017) that lead to increased use of OTC products. Self-medication plays an important role (Boxtel, Santoso & Edwards, 2008) in enhancing accessibility to health care services and reduction of national healthcare budgets, but also might pose serious threat to the patents’ health. For example, drug abuse, especially by

teenagers, is one of the biggest challenges for the European drug market since almost one in eight adolescents, or almost 12%, abuse with OTC cough syrups (Modor Intelligence, 2018).

If OTCs are left outside the strict FMD regulations this would create a serious imbalance between the scope of legally protected medicines and the pursuit of higher protection of public health. They would become more attractive for the criminal organizations that might redirect their illegal activities from the expensive but risky Rx medications. The volumes of OTC medicines are much higher and despite the relatively low prices, the profits could be generated by the turnover. The first possible option for further development of the Directive is therefore to include OTC medications in its scope as a next step for policy upgrade. This would result in a higher level of public health protection and would significantly limit the options for illegal activities.

Supply Chain Integrity

The second key element of an effective policy against falsified medicines is the supply chain integrity in terms of defining and engaging all participants in comprehensive prevention, detection and response activities. However, the identification of all engaged parties is a difficult task since the modern pharmaceutical supply chain is far more complex than it used to be (Committee on Understanding the Global Public Health Implications of Substandard, Falsified, and Counterfeit Medical Products, 2013): medicines are made from ingredients originating in different countries; packaging, repackaging and sale can happen in different places under sometimes vague conditions; medications change ownership many times, and each transaction allows falsified products to penetrate the market.

The participants in the modern pharmaceutical supply chain are multiplying, new categories emerge, and the regulations should be updated in adequate and timely manner. The content analyses of FMD reveals that it introduces to the main Directive 2001/83/EU many novelties in this direction. A new category of participants is defined - the so-called "brokers" who carry out intermediary activities, and specific measures to regulate their operations. For the first time in the European pharmaceutical legislation special regulations targeting wholesalers of active substances (APIs) are adopted. Parallel traders are required to align their operations with regulations that were once applicable only to manufactures. New requirements for online sale of medicines are applied since the increased access to internet made it rather easy for the criminals to effectively elude the regulatory barriers.

The analysis confirmed that FMD successfully filled in the existing gaps in Directive 2001/83/EC with reference to defining and engaging all participants in the legal pharmaceutical supply chain. This however is not sufficient to achieve full integrity in the digital era. The pharma industry has designed and applied different technologically based methods for detecting compromised medicines through the years but it is only in the last decade that all stakeholders reached a consensus on the adoption of track-and-trace systems based on serialization. They have already proven its effectiveness in other industries and are now regarded as the new "blockbuster drug" (Ozkaya, 2017) that will enhance significantly the quality and integrity of the pharmaceutical supply chains.

The implementation of traceability technologies is the most up-to-date focus of the pharma business. These systems have two main variations (WHO, 2016): the first is known as "full" track-and-trace system where all actors in the supply chain are required to enter product movement information into a common database by the time it reaches the patient. The other one is called "end-to-end" track-and-trace system because participants involved in the wholesale and distribution are exempt from providing information on medications' movements. Medicines are subject to obligatory authentication check only prior to their disposal to patients.

While countries like Russia, USA, and China chose the full version, EC decided on a third option that is combination of the two basis types. It requires wholesalers (WHO, 2016) and distributors to authenticate only medicines with higher risk of falsification. This saves time, efforts and guarantees better efficiency of the supply chain but at the same time creates a potential opportunity for criminals to infiltrate the system at distribution level. As Albin (2017) notes falsified medicines could enter the supply chain with copied valid unique serial numbers and reach the patient before the original. This is a quite possible scenario as most medicines are not fast-moving consumer goods and sometimes it takes up to 6 months before reaching the distribution endpoint.

The possible future upgrade of the system to full version is the second identified option for further development and improvement of the EU pharmaceutical regulations against falsified medicines.

Although the chosen track-and-trace solution for the EU territory saves time and money, the full version is expected to provide more benefits for the supply chain. It would result (WHO, 2016) in a higher level of protection by fully engaging all participants, the compromised medicines would be detected much faster in real time, their effective and immediate withdrawal will be guaranteed and better control of stocks and quality would be achieved.

Multi-stakeholder engagement

The engagement of all participants in the supply chain is the third key element that constitutes an effective policy against falsified medicines. For the purpose of the research they are divided in two groups – interested (stakeholders) and affected parties. Although both groups would benefit from such regulations, they sometimes have different and even controversial interests when it comes to their implementation.

The first group - the stakeholders, includes supranational and state regulators as well as importers and manufacturers of APIs and medicines. They are usually among the leading initiators and most often the largest beneficiaries from such policies since they would lead to increased security of medications and health protection and consequently reduce multimillion financial losses. The second group – wholesalers, distributors, pharmacists, healthcare professionals and consumers, are those actors who are directly engaged in the policy implementation and make it “happen”. Without their active participation a comprehensive policy would remain a well written document with limited or no impact at all. The problem is that not all affected actors are interested, or at least not consciously, in the development and implementation of policies against falsified medicines. The stakeholders need to invest time and efforts to educate and engage them at an early stage so as to minimize any future conflicts that may derive from lack of understanding or disagreement.

To verify if FMD adequately engages the representatives of both groups, an in-dept content analysis was conducted of the Directive’s text. Table 1 presents a short excerpt that illustrates the key research points and reveals some of the measures adopted as per each of the participants in the pharmaceutical supply chain.

Table 1: Multi-stakeholder engagement as per FMD (excerpt)		
Participants	Binding articles as per FMD	Corresponding activities
Supranational regulator: EU institutions	Art.47 par.3 &4; Art. 54 a; Art. 52 a; Art.40 par.4., etc.	Adopt delegated acts and detailed guidelines, perform registration and inspections, support databases, etc.
National authorities	Art. 52 a; Art. 40 par.4; Art.117 a; Art.118 a, etc.	Perform registrations, send information to databases, implement systems for protection, impose penalties, etc.
Importers/Distributors of active substances and excipients	Art.52 a; Art. 46 b & 47 (3), (4), etc.	Mandatory registration and certification, new obligations, etc.
Patients/ End users	Art.85 d;	Information campaigns

Source: Directive 2011/62/EU

The analysis confirms that FMD includes measures that more or less engage all participants in the pharmaceutical sector – from importers of API and manufactures of medicines to end users. Particularly important are the new measures adopted for the control of APIs since they are defined as the “backbone” of each drug (European Commission, 2011). If their quality is compromised, the final product would not meet the criteria for quality, safety and efficiency. Based on this new regulation, it can be concluded that FMD also targets the problem with the substandard drugs by eliminating the most common causes for their occurrence - the use of low-quality ingredients.

Education and awareness

A major factor that facilitates the uncontrolled spread of falsified medicines is the lack of awareness among consumers about the serious health risks they pose. Among the factors that contribute to such risky behavior (IRACM, n.d) are the lack of doubt about the quality of medicines, the desire to bypass regulations, restricted or limited access to certain medical products, the increased self-medication practices and the broad access to Internet.

FMD imposes significant changes in the pharmaceutical sector that affect all participants. If national governments and pharmaceutical manufacturers are the main initiators and are therefore fully aware of their necessity, this might not be the case with some of the other participants. This is a reason why in art. 85d of the Directive promotion of awareness campaigns for the general public is required. Do such campaigns are undertaken, what is their purpose and are they broadly accessible by the society are the main research questions concerning this policy element. Research was conducted of the web portals of three major European institutions – EU, Council of Europe and the European Medicine Agency (EMA) as brief summary of the results is presented below.

The survey on the website of the European Directorate for the Quality of Medicine, part of the Council of Europe, showed several freely accessible guides on the topic. They include comprehensive information for the general public and groups at risk, for example: “Open minds, free minds: Psycho-pedagogical concept guide for teachers” issued in 2015 and “A strategic approach to assist states in protecting the health of their citizens” from 2013. Also, numerous publications were found regarding the Medicrime Convention – the second major European policy against falsified medicines that unlike FMD is not obligatory for the EU Member States and is open for ratification on a global level.

The second web portal is that of the EU where a document from 2015 - "Guidelines for the Falsified Medicines Campaign", was accessible. It contains a set of communication products that are modular – poster, flyer, presentation, social media content, etc., and could be adapted for use by any of the Member States. Their goal is to raise the awareness of the general public on the problem and introduce them to the special logo for authorized online retailers in the EU.

The EMA is the third institution that plays a significant role in the fight against falsified medicines. On its website information was available on the topic, but no specific communication materials for the general public were found. This might be due to the fact that the agency operates at a specialized level and its communication activities and initiatives are primarily targeted to national competent authorities and specialists.

The identified communication materials confirmed that the EU institutions are committed to develop educational resources for the society regarding the risks of falsified medicines. However, these materials are available mainly on their web sites. The question is whether the general public is motivated to specifically visit them since the majority of the European consumers had little or no information regarding the existence of the problem (IFPMA, n.d). Therefore, the third option for further improvement of FMD is for the creation of a single, specialized and easily accessible European electronic portal dedicated to the problem. It could be advertised to the general public by mass communication channels and social networks following the example of similar portals like the one of the campaign “Fight the Fakes” that uses Facebook, Twitter, Linked In, You tube, Flickr and Pinterest.

Multilevel cooperation

Falsified medicines recognize no boundaries and therefore synchronized measures against them should be adopted on global, regional and national levels. Although the harmonization process is rather time-consuming, the stakeholders are much more eager to reach consensus when facing transnational threats of such magnitude. In Directive 2011/62/EU the collaboration between EU institutions, renowned international organizations and national states is insistently promoted and how it is implemented is the main focus of the following analysis.

At a global level the research focuses on the key areas and forms of cooperation between EU institutions and three of the leading international organizations in the fight against falsified medicines – the World Health Organization (WHO), the EMA and EUROPOL. The results confirm that there is a high level of collaboration through various initiatives: agreement between the WHO, EC and EMA on improving the quality and safety of medicines, confidentiality agreements between the EMA and third country regulatory authorities (Canada, Japan, USA, etc.), joint actions of INTERPOL and EUROPOL against illicit pharmaceuticals trade (PANGAEA, OPSON).

PHARMACRIME is a regional cooperation initiative between the EU and the international Institute of Research Against Counterfeit Medicine (IRACM). It is financially supported by the EC and represents an informal network of European partners that since 2009 introduces new international pharmaceutical crime projects, implemented by EUROJUST in partnership with several European authorities (IRACM, n.d.). EMA is another key institution that actively promotes and coordinates regional cooperation

incentives between the Member States. It unites the national regulatory authorities into a single regulatory network known as the European Medicines Regulatory Network (EMA, 2019) that brings together resources and expertise all across EU and provides the agency with access to thousands of European scientific experts.

The collaboration between national drug agencies, police and customs as well as the interaction between professional and consumer associations and the pharmaceutical industry (WHO, 1999) can significantly contribute to the early identification of falsified medicines circulating in the legal supply chains. Such cooperation is encouraged by FMD but its organization is left to the competent authorities of each Member State and no specific guidelines on how to implement it are provided. Medicrime Convention offers an adequate solution for the local governments (EDQM and Council of Europe, 2016) based on the creation of Single Points of Contact (SPOC) that form a cooperation network and facilitate information exchange regarding pharmaceutical crimes.

The results of the research confirm that there is a high level of cooperation at international and regional levels between the European institutions and leading global and regional organizations in the fight against falsified medicines while at the national level it remains the obligation of the state authorities. A further option for development of coherent local cooperation is the ratification of the Medicrime Convention that could significantly contribute to the increase of health protection by expanding the scope of FMD and help authorities to more effectively prosecute criminal offenders in the pharmaceutical sector.

Conclusion

The primary objective of each policy against falsified medicines is to ensure and guarantee the well-being of society. The present analysis confirms that Directive 2011/62/EU represents a comprehensive legal instrument to increase the level of protection in the EU Member States as it combines all five elements that are defined as key for its effectiveness. The adopted measures form a coherent regulatory framework and if the identified options for its further development are considered in future reviews of the policy, this could significantly enhance the legal barriers in front of criminal organization and increase the public awareness of the problem.

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