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Research Article

The current state of the pharmaceutical market of Ukraine, quality assurance and falfication of medicines

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Abstract

The aim of our article was the study of the current state of the pharmaceutical market of Ukraine in the context of the quality assurance of medicines and preventing the spread of falsified medicines (FM), the identification of the main problems in the field of circulation of medicines and the ways to solve them. It is established that the dynamic development of the pharmaceutical market and its high profitability cause problem of drug quality, increasing threats to the spread of FM in circulation and require the implementation of effective mechanisms for regulation of quality and safety of medicines. Analysis the annual official statistics of the State Service of Ukraine on Medicines and Drug Control for the period of 2008–2019 on the number of detected FM in circulation showed a steady trend of increasing FM and insufficient implementation of effective measures to combat them. The creation of effective quality assurance system of drugs and preventing the spread of FM need to improve the organization of state control of drug quality, strengthening criminal liability for falsification of drugs and optimization of the system of their detection.

Keywords

authorized drug control authorities, falsified medicines, pharmaceutical market, prevention, quality of medicines

Introduction

The quality and safety assurance of medicines is an integral part of Ukraine's state policy in the field of health care. The current understanding of quality assurance approaches is based on a comprehensive concept that covers the quality assurance of circulation of drugs, from the stage of their pharmaceutical development, laboratory and clinical research, production, quality control, storage, realization and providing information to doctor and patient. According to this concept, reliable guarantees of quality and safety of drugs should be provided at all stages of the life cycle of the drug. According to the World Health Organization (WHO) recommendations, all activities to implement the concept of quality assurance of medicines should be aimed at meeting the needs of citizens (https://www.who.int/medicines/areas/quality_safety/quality_assurance/about/activities/).

The main task of the state, according to the Concept of development of the pharmaceutical sector of Ukraine for 2011–2020 years, approved by the order of the Ministry of Health of Ukraine (MOH), dated 13.09.2010 № 769 (https://zakon.rada.gov.ua/rada/show/v0769282-10), is to ensure the quality, effectiveness and safety of drugs that improve public health, increase the duration and quality of life of the population of Ukraine. Medicines are a group of consumer goods, which accordingly gives them special social significance, because the consumer can not assess the potential health risk.

Today, drug falsification is a global problem that affects countries at different financial levels, from high-income countries to low-income countries, including Ukraine (Barry 2014; Venhuis et al. 2016; Ozava et al. 2018). FM – medical products that deliberately/fraudulently misrepresent their identity, composition or source (https://www.who.int/medicines/regulation/ssffc/definitions/en/). During 2010–2015, national authorized drug control authorities detected more than 9.6 million FM on the pharmaceutical market of Ukraine for a total of over 270 million UAH (Dedishina 2016).

FM are illegal and dangerous products because they may not meet the basic requirements for medicines – in terms of their effectiveness, safety and quality. They can be ineffective (do not contain active ingredients or contain them in inappropriate quantities, or not be bioequivalent), be dangerous (contain unacceptable amounts of toxic impurities or undeclared active pharmaceutical ingredients with other dangerous effects) and / or poor quality are not produced in accordance with the requirements of Good Manufacturing Practice (GMP), there is no certainty about the consistency of their composition and properties, even if the samples of FM formally meet the pharmacopoeial requirements (https://www.who.int/medicines/services/counterfeit/faqs). FM are less common in developed countries with high incomes, where a strict regulatory system is in place to control the pharmaceutical market and national authorized drug control authorities use an effective complex of measures to prevent and combat againts FM, taking into account the market situation, their experience and the significant resources available. As a result, the number of cases of detection of FM in these countries is very small, much less than 1%. In developing countries, the problem of FM is more acute due to insufficiently stringent regulatory requirements (Koczwara and Dressman 2017; Rahman et al. 2018). The circulation of FM is a direct threat to public health, but sometimes in people's lives and leads to significant financial losses for legal manufacturers. The 2006 estimate of falsified medicines by WHO indicated that the prevalence of falsified medicines ranged from less than 1% in developed countries to over 10% developing countries (http://www.who.int/medicines/services/counterfeit/impact/TheNewEstimatesCounterfeit.pdf).

About 50% of medicines for online sale are falsified, about 95% of the 50,000 online pharmacies do not meet the laws and standards (Mackey et al. 2015; Nayyar et al. 2015; Nayyar et al. 2019). That is, in the conditions of active development of the national pharmaceutical market the question of quality assurance of medicines and preventing drug falsification is especially actual (Kovalenko 2018). In different countries have already gained experience in creating and implementing effective mechanisms of quality assurance of medicines. To provide the population with quality medicines in Ukraine, there is a system for regulation and controle of the pharmaceutical market and national regulatory organizations. But in terms of quality standards for medicines, Ukraine still lags behind many countries, and this affects the ability to provide the population with quality and safe medicines. The aim of our article was the study of the current state of the pharmaceutical market of Ukraine in the context of the quality assurance of medicines and preventing the spread of falsified medicines (FM), the identification of the main problems in the field of circulation of medicines and the ways to solve them.

Matherials and methods

The empirical base of the research was the national laws and regulatory legal acts of quality assurance of medicines and possible ways to combat against falsification of medicines, European (EU) directives and WHO recommendations, the State Pharmacopoeia of Ukraine, the European Pharmacopoeia, statistical data from the State Drug Register of Ukraine for 2020, the State Service of Ukraine on Medicines and Drug Control for the period from 2008–2019, the General Prosecutor's Office of Ukraine for the period from 2017–2019, media materials and scientific publications. A literature review was carried out through 2 databases: PubMed and Google Scholar, to identify relevant articles. Search terms included: "pharmaceutical market of Ukraine", "quality of medicines", "falsified medicines" and "combat the spread of falsified medicines". The methodological basis was the complex of general methods of scientific cognition. The method of system analysis and genezalization made it possible to formulate the reasons of the falsification of medicinal products and proposals on ways to improve the system of measures to combat drug falsification, to determine the structure of violations in the field of circulation and their features in Ukraine. The logical and documental methods were used to study the activities of national authorized drug control authorities of state control of drug quality and counteraction to the falsification of medicines and methods of its improvement. The statistical and comparative methods were used for analisis the statistical data of the State Drug Register of Ukraine (http://www.drlz.com.ua), the State Service of Ukraine on Medicines and Drug Control and the General Prosecutor's Office of Ukraine (https://www.gp.gov.ua/ua/index.html): conducted a procedure for collecting and analisis of empirical public information, published on the official website of the State Service of Ukraine on Medicines and Drug Control (https://www.dls.gov.ua/), online newpaper "Pharmacy weekly" (https://www.apteka.ua/) and pharmaceutical portal Pharma.net.ua (https://pharma.net.ua), was analized 440 orders prohibiting the sale, storage and use of FM of the State Service of Ukraine on Medicines and Drug Control in Ukraine for the period from 2008–2019 and the statistical data of the General Prosecutor's Office of Ukraine about registered criminal offenses for the spread of FM for the period from 2017–2019.

Results and discussion

Characteristic of the pharmaceutical market of Ukraine

Ensuring the regulatory quality of drugs is closely related to the trends that characterize the current state and development of the pharmaceutical market of Ukraine. According to the State Drug Register of Ukraine (SDRU), in October 2020 were registered 13664 drugs (Table 1). That is today in the structure of the range of drugs in the pharmaceutical market of Ukraine foreign medicines are more than 70%, and in some ATC classification groups up to 90%. The main importers of medicines to Ukraine are Germany, India, France, Italy, Slovenia and Hungary. Ukraine has virtually no own production of active pharmaceutical ingredients (API's), about 80% of API's are imported from China and India. Today the quality of API's is largely the responsibility of distributors. Distributors that import API's and products "in bulk" independently take samples for laboratory analysis and quality control for compliance with the requirements of the quality specification of drug quality control methods to the registration certificate (or the requirements of the State Pharmacopoeia of Ukraine) and are responsible for quality of these drugs in accordance with the law (https://zakon.rada.gov.ua/laws/show/804-2015-%D0%BF#Text). Laboratory analysis of API's and products "in bulk" is carried out in laboratories for quality control and safety of medicines certified by the MOH.

Table 1. The number of medicines registered in the State Drug Register of Ukraine, 2020.

№	Group of medicines	Ukrainian medicines	Foreign medicines	Total
1	Medicines	3603	7090	10693
2	Active pharmaceutical ingredients	355	1815	2170
3	In bulk	190	422	612
4	Packing with in bulk	53	136	189
5	Total	4201	9463	13664

Given the high import dependence of the domestic pharmaceutical market, the real way to solve this problem is import substitution. Recently, despite the decline in real incomes and a significant increase in prices for imported drugs, there has been a tendency to increase sales of domestically produced drugs. More than 60% of medicines registered in Ukraine are generics, and only 12% are original drugs. Thus, the pharmaceutical market of Ukraine is mainly a generic market, which distinguishes it from the markets of developed economies, where the share of original drugs is much higher. Also, over the past 5 years, domestic drug manufacturers have been increasing exports to Belarus, Kazakhstan, Azerbaijan, Uzbekistan, Moldova and Georgia. Among the main trends in the pharmaceutical market of Ukraine is the increase in the share of Ukrainian enterprises in the structure of production of generic drugs, their share in the domestic market is over 70%, while in the USA – 12%, Japan – 30%, Germany – 35%, France – 50%. Despite the unstable social and economic situation in the country, the domestic pharmaceutical market is growing. The average annual growth of the national market over the past 5 years remains at 15–20%. The volume of the pharmaceutical market of Ukraine in 2019 amounted to 3.4 billion USD (http://www.ukrstat.gov.ua/). Experts predict further growth of the Ukrainian pharmaceutical market given the global trend to increase production and consumption of pharmaceutical products. The increase in the range of medicines on the domestic pharmaceutical market in recent years has led to an increase in problems related to the quality of medicines. At the same time, the volumes of drug sales directly determine the scale of relevant control and supervision measures in the domestic pharmaceutical market. In 2020, 115 enterprises of various forms of ownership carried out industrial production of drugs in Ukraine. It should be noted that recently there has been a downward trend in the number of pharmaceutical manufacturers, which can be explained by fierce competition and production licensing under GMP requirements. But at this time, not all domestic manufacturers have reached the level that meets the GMP requirements. Domestic pharmaceutical companies are trying to change the range in order to meet the needs of customers, improving the quality and range of products every year. Given the financial constraints, the problem of supply of raw materials, domestic pharmaceutical production is directed mainly to the production of generics. In 2020, 401 pharmaceutical distributors were engaged in Ukraine, 17485 pharmacies and 4399 pharmacy points were engaged in the retail trade of drugs. Over the past 15 years, there has been a 1.4 times decrease in the number of wholesale warehouses and a 1.3 times steady increase in pharmacies. The presence of a large number of pharmacies and wholesale warehouses complicates the state control over the circulation of drugs, tracking the distribution of FM on the pharmaceutical market in Ukraine and causes quality assurance problems at the stage of wholesale and retail sales.

Thus, the features of the domestic pharmaceutical market include a wide range of drugs, expansion and renewal of the arsenal of original and generic drugs, a large number of pharmacies and distributors involved in supply chains, the dependence of demand on epidemics, natural disasters and other emergencies situations. The threat of the spread of falsified medicines determines the importance of ensuring the quality and safety of drugs in Ukraine.

The state of the pharmaceutical market significantly affects the organization of quality assurance of medicines in circulation and requires a reliable system of state regulatory and control and constant improvement of mechanisms to ensure the quality of drugs at the stages of their entry into Ukraine, production, transportation, storage, wholesale and retail. Therefore, the role of the national system of state regulation and quality control of medicines acquires special significance.

The national system of state regulation and quality control of medicines

The national system of state regulation and quality control of medicines is built on the principle of centralization with administrative subordination and has three levels: national, regional and microeconomic. The national level includes the Ministry of Health of Ukraine, the State Service of Ukraine on Medicines and Drug Control (SMDC) and the State Expert Center of the Ministry of Health of Ukraine. To the regional level – 27 authorized territorial drug control authorities of the SMDC in the regions and in the city of Kyiv. The third level includes Qualified Persons responsible for ensuring the quality of medicines of pharmaceutical manufacturers, pharmacy and distributors. The MOH is the main organization in the system of central executive authority for the implementation of state policy in the field of production, quality control and sale of medicines. The MOH ensures the circulation of medicines in accordance with the requirements of good practices: laboratory, clinical, manufacturing, distribution, pharmacy, harmonized with the relevant directives and recommendations of the EU and WHO. The State Expert Center of the Ministry of Health of Ukraine is a specialized expert institution authorized by the MOH in the field of laboratory and clinical trials and state registration of drugs. Its the main national authority in the field of pharmacoviligeance, standardization of medical care, medical and pharmaceutical services.

The state regulation in the field of drug quality assurance is carried out by the Law of Ukraine № 123/96 "On Medicines" dated 04.04.1996 (https://zakon.rada.gov.ua/laws/show/123/96-%D0%B2%D1%80#Text) and regulatory legal acts, adopted by the Cabinet of Minister of Ukraine and MOH. According to the current legislation, the main regulatory functions in the field of pharmacy are: the state registration of medicines, licensing of production, licensing of wholesale, retail trade and import of medicines, inspecting manufacturers and distributors for compliance with good manufacturing/ distribution practice standards, state quality control of medicines, pharmacovigilance of drug safety. By implementing these state regulatory functions, the implementation of international quality assurance standards (GxP) at the stages of the life cycle of a medicinal product is ensured.

An important component of the quality assurance system of medicines is the state control over their quality, which directly affects the efficiency of this systeme. According to the Article 13 of the Law of Ukraine № 123/96 "On Medicines" dated 04.04.1996, state quality control of medicines – a set of organizational and legal measures aimed at complying with the requirements of the legislation on quality assurance of medicines by pharmaceutical manufacturers, pharmacies and wholesale warehouses. The special authority of state control over compliance with the legislation of Ukraine in the field of quality of medicines is the State Service of Ukraine on Medicines and Drug Control, the activity of which are coordinated by the MOH. SMDC implements state policy in the field of state control of quality and safety of medicines. The SMDC performs the following tasks: compliance control with legislation of Ukraine on the quality assurance of medicines, compliance control with licensing conditions for economic activity of drug production, of import, of wholesale and retail sale of medicines, import of drugs into the customs territory of Ukraine, compliance control the requirements of standards for manufacturing, transportation, storage, realization and use of medicines. The SMDC carry out state control regarding drug quality assurance in pharmacies and wholesale warehouses through scheduled and unscheduled inspections and laboratory control of drugs in authorized laboratories. Scheduled inspections are carried out according to the plan approved annually for 27 authorized territorial drug control authorities of the SMDC in the regions and in the city of Kyiv by the main control authorities of the SMDC, unscheduled inspections are carried out on complaints of consumers and appeals of law enforcement authorities. During the inspection of pharmacies and wholesale warehouses, specialists of the SMDC take samples of drugs for laboratory control of their quality in authorized laboratories of the MOH and decides to withdraw from circulation and prohibit the production, sale and use of drugs that do not meet the requirements of regulations. First of all, those drugs that are stored, transported, sold in violation of current norms and rules are selected for state quality control. Medicines are also monitored based on consumer complaints about the quality and in case of doubts about the quality of the results of the preliminary visual inspection of medicines carried out by the state inspector. If the inspection revealed FM, the SMDC issues order prohibiting the sale, storage and use of FM, which published on the official website of SMDC for pharmacies and wholesale warehouses. As well as in addition to laboratory tests SMDC conducts investigations into the origin and distribution FM.

In order to strengthen state control over the quality of medicines and combat the production and distribution of FM in Ukraine in accordance with Article 15 of the Law of Ukraine "On Medicinal Products" and the Cabinet of Ministers of Ukraine from 12.08.2015 № 647, permanent working groups were established in the SMDC and 27 authorized territorial drug control authorities in the regions to prevent the import, production and distribution of FM. This groups includes heads and specialists of the SMDC and territorial control authorities, the customs and law enforcement authorities to track the distribution channels of FM. The work programs have been established and approved by the order of the SMDC. The main objectives of the program are to develop a mechanism for the interaction of SMDC with the custom and law enforcement authorities in order to control the sale and import of drugs, to create a system of operational information about the identified FM and the results of combating whith these violations.

The results of the activity of national authorized drug control authorities

The SMDC and authorized territorial drug control authorities carry out state quality control of medicines through planned annual inspections of manufacturers,

pharmacies and wholesale warehouses and laboratory control of drugs in authorized laboratories. According to the results of inspections, every year the SMDC creates a report, which published on the official website of SMDC in the section"Activity" and official website of online newspaper "Pharmacy weekly" (https://www.apteka.ua/article/534946). We analized the "Public report of SMDC on the results of activities for 2019". We determined that 1215 scheduled inspections of manufacturers, wholesale warehouses and pharmacies were conducted regarding their compliance with the requirements and norms of the legislation at all stages of drug circulation. During the inspections 2453 violations of the requirements of the current legislation were established. According to the results of scheduled inspections of manufacturers, wholesale warehouses and pharmacies, 1034 orders were issued to eliminate violations, 432 administrative protocols were drawn up for violations of current legislation. Distributors imported to the customs territory of Ukraine 22026 series of medicines, of which 5230 (23.7%) series of medicines were subjected to laboratory analysis, 34 negative conclusions were issued on the quality of medicines (0.65%). The territorial authorized drug control authorities of SMDC analyzed 2511 series 1565 names of medicines of selected for laboratory control by specialists during inspections of pharmacies and wholesale warehouses. According to the results of laboratory control, the SMDC issued 66 orders prohibiting the sale, storage and use of 78 unregistered medicines (4.9%) and 19 orders prohibiting the sale, storage and use 57 series 18 names of FM (2, 3%). The analysis of violations of the requirements of the legislation on the quality of medicines during 2019 showed, that the tipical violations are: improper storage conditions of medicines in wholesale warehouses and pharmacies, trade of FM, wich are prohibited by the orders of the SMDC, the sale of medicines that are not confirmed by the manufacturer's quality certificate. The sale of medicine are carried out only in the presence of a quality certificate issued by the manufacturer, that confirming the compliance of a batch number of a medicine with the requirements of pharmacopoeial article approved during the registration of a medicine in Ukraine. Also the problem of ensuring the quality of medicines and falsification of medicines in the process of their circulation in Ukrainian pharmaceutical market remains acute. It is found that the scale of drug falsification in Ukraine is significantly affected by the average level of affluence, military conflicts, insufficient work of authorized drug control authorities, imperfect legal system, high level of corruption and limited public access to medicines due to their high cost.

Despite the significant efforts of SMDC and authorized territorial drug control authorities to counteract the falsification of medicines in Ukraine, for the last 10 years there has been a steady trend towards increasing the number of FM in the pharmaceutical market of Ukraine. Therefore, the next stage of our study was to collect and analisis of statistical data of SMDC, prohibiting the circulation of FM, detected and seized in Ukraine for the period from 2008–2019, published on the official website of SMDC in section"Orders" and in pharmaceutical portal Pharma.net.ua (https://pharma.net.ua). Was analyzed 440 orders of SMDC prohibiting the sale, storage and use of FM for the period from 2008–2019 (Table 2).

Table 2. Quantity of detected and seized FM in Ukraine for the period from 2008–2019.

Year	Quantity of series of FM	Quantity of names of FM
2008	21	12
2009	46	28
2010	69	27
2011	34	15
2012	62	39
2013	66	40
2014	117	63
2015	29	20
2016	59	22
2017	16	14
2018	9	7
2019	57	18
Total	578	305

The results of analysis showed, that SMDC detected and seized in circulation 578 series 305 names of FM, which 52% are domestic medicines, 48% are foreign medicines, that is the medicines of domestic manufacturers are falsified more often. It was investigated, that a bigger quantity of FM was detected by indicators "Description", "Packaging", "Labeling" (48%) and "Identification of active pharmaceutical ingredient" (31%), prescription drugs (60%) were falsified more often than OTC drugs. According to the types of dosage form, FM for external use, solid dosage forms and injectable drugs were the most detected.

The conducted analysis of FM according to the ATC classification has shown that there are counterfeits of almost all pharmacotherapeutic groups of medicines in the pharmaceutical market of Ukraine. However, the largest quantity of FM accounts for antibacterials for systemic use, which make up 28% of the total quantity of FM detected and seized in Ukraine for the period from 2008–2019 (Table 3).

Table 3. The ratio of detected FM according to the ATC classification for the period from 2008–2019.

№	ATC code of FM	ATC code name of FM	Number (%)
1	J01	Antibacterials for systemic use	28
2	C01	Cardiac therapy	18.5
3	M01	Anti-inflammatory and antirheumatic products	10.9
4	N02	Analgetics	8.1
5	D01	Antifungals for dermatological use	7.8
6	A	Alimentary tract and metabolism	6.6
7	H	Systemic hormonal preparations, excluding sex hormones and insulins	5.2
8	V	Various	7.6
9	R05	Cough and cold preparations	3.8
10	L01	Antineoplastic agents	3.5

According to the data of SMDC, in Ukraine the circulation of FM is not more than 2%–2.5%. However, the data show only the quantity of FM detected in circulation, and not the quantity of available FM, which is due to the lack of a unified system for monitoring drug circulation

and insufficiently effective mechanism for preventing FM. Also does not take into account the online sales of FM, which has now become large-scale and poses a serious threat to public health. False data on the presence of FM in circulation, both overestimated and underestimated, interfere control and regulatory and law enforcement agencies from adequately counteracting this shameful phenomenon. Thus, along with the dynamic development of the pharmaceutical industry, there is a functioning of the shadow economy in the field of drug circulation and a steady tendency to increase the quantity of FM in the pharmaceutical market of Ukraine (https://www.apteka.ua/article/430840).

According to the Law of Ukraine № 5065-VI dated 05.07.2012 (https://zakon.rada.gov.ua/laws/show/5065-17), introduced criminal liability for falsification into the Criminal Code of Ukraine, namely Article 305 "Smuggling of narcotic drugs, psychotropic substances, their analogues or precursors or falsified medicines" and Article 321-1 "Falsification of medicinal products or circulation of falsified medicinal products", which for the manufacture, purchase, transportation, shipment, storage for the purpose of selling or selling scienter FM for imprisonment for a term from 3 years to life imprisonment with confiscation of FM, raw materials and equipment for their manufacture. We analized the statistics data on registered criminal offenses and the results of their pre-trial investigation that are published on the official website of General Prosecutor's Office of Ukraine. Was summarized the data about the quantity of criminal offences for the spread of FM according the Article 321-1 during 2017–2019 (Table 4).

Table 4. Criminal offences for the spread of FM, the Article 321-1 during 2017–2019.

Year	Registered	Notified about the suspicion	Filed to the Court whit indictment	Terminated proceedings	No decision taken
2017	23	3	3	9	20
2018	40	2	1	7	39
2019	29	2	2	6	27

The analysis of the dynamics of criminal offenses, for which at the end of the reporting period the decision to complete or stop was not made, shows a their fairly high share of the total number of criminal offenses, namely 87% (2017), 97.5% (2018), 93.1% (2019), indicating the low efficiency of consideration of criminal cases. According the statistical data of the Unified State Register of Court Decisions during 2017–2019 were passed only 7 sentences under the Article 321-1 of the Criminal Code of Ukraine (Table 5).

Table 5. Sentences under Article 321-1 of the Criminal Code of Ukraine.

Year	2017	2018	2019
Number	3	2	2

Analisis of data showed the high latency of this crime and the difficulties in establishing the factual circumstances of this crime, the need to clarify the methods for identifying, preventing and investigating this crime, the actual lack of studying the experience of low enforcement organizations from another countries.

After analyzing the information of scientific sources on the circulation of drugs in the pharmaceutical market of Ukraine we can identified the main factors that stimulate the circulation of falsified drugs, the most significant factors are: unstable economic situation in Ukraine, developed system of online sales of medicines, which does not allow authorized drug control authorities to check their quality, the lack of medicines in an epidemic situation create shortage and the possibility of the distribution of FM, high drug prices in line with the average solvency of the population, as well as a large difference in market prices, which stimulates the sale of cheaper FM, as well as access to high-performance equipment and modern pharmaceutical technologies, which causes a high level of falsification of drugs. Also non-compliance with international norms of the existing legal framework governing the import, production, sale of drugs, insufficients human, financial and information resources to combat drug trafficking of improper quality, ineffective activity of the authorized drug control authorities implementing state policy in the field of prevention and counteracting of FM, insufficient or no sanctions for illegal actions in the field of drug quality, bad interaction between spesialists of the SMDC, the customs and law enforcement authorities to track the distribution channels of FM, a significant number of intermediaries in the pharmaceutical market, which contributes to interference in the chain of illegal sales channels, insufficient level of implementation of good practices (GxP) (Demchenko and Soloviov 2014; Gutorova N et al. 2019).

In connection with the complication of the socio-economic situation in Ukraine according to the Law of Ukraine "On temporary features of state control measures in the sphere of economic activity" was introduced the moratorium on inspections during 2014–2018, which prohibited state regulatory authorities to conduct scheduled inspections, including inspections of pharmacies and wholesale warehouses. The establishment of a moratorium on the implementation of measures of state control over the quality of medicines made it impossible to use effective measures to prevent the circulation of FM in the national pharmaceutical market. This was an additional factor that contributed to the increase in cases of drug falsification.

It is established, that the main ways of entering into the market of FM are: illegal supply of medicines abroad under the guise of other goods, repackaging of expired medicines in Ukraine for further sale and release of FM at unlicensed domestic enterprises using high-technology equipment and attracting qualified specialists.

Thus, the variety of reasons that contribute to the falsification of drugs requires the application of comprehensive measures to prevent, detect and prompt withdrawal from circulation of drugs. But, today, measures to counter the spread of FM in the domestic pharmaceutical market are not effective enough and need to be improved the or-

ganization of quality control of medicines in Ukraine. According to the WHO recommendations, the nature, extent and causes of counterfeiting vary from country to country, which is why there is no single strategy to address the problem (https://www.who.int/medicines/services/counterfeit/faqs). Therefore, each country must independently develop its own strategy to combat against falsified drugs, the appropriate regulatory framework, taking into account its capabilities.

Regulatory legal acts to combat the falsification of medicines

Today in Ukraine there is a gradual harmonization of current legislation on quality assurance of medicines in accordance with regulatory-legal acts adopted in the EU. As part of this process, effective mechanisms for ensuring the quality of medicines are being implemented in manufacturers and wholesale warehouses in accordance with the requirements of good practices harmonized with EU legislation, including in the field of prevention of falsification of medicines. In recent years, Ukraine has taken the following steps to implement EU legislation to domestic:

- Ukraine has been a full member of The International Pharmaceutical Inspection Cooperation Scheme (PIC / S) since 2011 and implements a regulatory policy in the field of pharmaceutical market control in accordance with legislation similar to that in force in European countries;
- implemented the requirements of GMP and GDP rules;

According to the Law of Ukraine № 5038 dated 04.07.2012 (https://zakon.rada.gov.ua/laws/show/5038-17), economic activity on import of medicinal products subject to licensing from 01.03.2013. Therefore, this law obliges all importers of foreign drugs in Ukraine to obtain an additional license to sell their drugs in Ukraine. In addition, the government has introduced a mandatory inspection of manufacturers for compliance with GMP requirements. Those manufacturers who already have GMP certificates only need to confirm it. Import of drugs into the territory of Ukraine, the production of which does not meet these requirements, is prohibited from 15.02.2013.

To increase the effectiveness of preventing drug falsification the Council of Europe Convention on the counterfeiting medical products and similar crimes involving threats to public health (the MEDICRIME Convention) was signed in December 2010 and entered into force in Ukraine in January 2016. Due to the harmonization of Ukrainian legislation with the requirements of the MEDICRIME Convention, the legal regulation of FM circulation in Ukraine has been improved, as well as international cooperation in this field has been established. The Convention obliges the member states to introduce civil, criminal and administrative responsibility for the falsification of medical products. The introduction of criminal liability for crimes related to the counterfeiting of medicines in Ukraine indicates an awareness of their big danger, compliance with MEDICRIME Convention requirements should help improve the provision of the population with quality and safe medicines.

Transformation processes in Ukraine related to European integration, dynamic development of the domestic pharmaceutical sector, setting of additional requirements for the quality and safety of medicines determine the need of realization of state policy aimed at implementing modern methods against FM (https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf). The European directives contain a set of special economic regulations aimed at counteracting the trafficking of falsified medicines (https://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:174:0074:0087:EN:PDF). From 09.02.2019 it is mandatory for EU countries application the Commission Delegated Regulation 2016/161 of 2 October 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 (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX-%3A32016R0161). This document establishes the procedure for marking each package of medicine with an individual code to ensure the safety of medicines and prevent their falsification. The development and implementation of modern technology for drug packaging protection 2D barcode system, which allow tracking and obtaining the necessary information at all stages of drug circulation (Kovacs at al. 2014; Mackey and Nayyar 2017). 2D barcode system make it possible to organize effective control of medicines throughout the supply chain from producer to consumer and prevent the emergence of FM in the legal supply system. According to the Resolution of the Cabinet of Ministers of Ukraine № 653 in July 2019 approved the Procedure for the introduction of a pilot project on labeling with identifications signs and monitoring of drug circulation, the necessary changes should be implemented during 2019–2023 (https://zakon.rada.gov.ua/laws/show/653-2019-%D0%BF#Text). Today the use of 2D barcode system is a large-scale and promising tool to prevent drug falsification at all stages of circulation, which is being introduced by more and more pharmaceutical manufacturers around the world.

Thus, Ukraine carried out some positive changes in the field of quality assurance and control of medicines. However, despite a significant number of positive changes, state control in the field of drug circulation still remains difficult, insufficiently effective and needs effective modern measures. To build an effective quality assurance system in Ukraine, an effective system must be created not only to detect and promptly withdraw from the circulation of FM, but also to track the channels of their appearance and distribution in the pharmaceutical market and prosecute those involved and those who facilitate the trafficking of FM. Also, it is necessary to establish active cooperation

with the relevant international organizations dealing with the problem of combating FM.

To counteract the spread of FM on the Ukrainian pharmaceutical market, it is necessary to develop a national strategy of action in 3 areas – "prevent, detect and respond":

- patients should not be allowed access to FM by creating a system for the rapid removal of these products from pharmacies and hospitals. It is also important to conduct a broad information campaign to increase the level of knowledge and understanding of the threats of FM by both patients and medical staff. It is necessary to ensure the integrity of supply channels, closing the possibility of entering the system of such drugs. Finally, a strong regulatory system should be in place so that police and customs officers also have the necessary information and tools to protect the public from FM;
- FM should be detected. This requires investment in strengthening border controls, improving the notification system for such drugs, smarter inspections and increasing access to laboratories and equipment for field screening of drug samples;
- a system for notifying and recalling detected FM should be established, the regulatory system should be strengthened, and legal procedures should become more transparent. To enhance the effectiveness of these actions, there must be a strong political will to counter FM, and all interested partners must work together. The problem FM is not only a problem of the health care system, it requires the involvement of regulators, law enforcement, customs, logisticians and other interested partners.

The fight against FM requires the active participation of political leaders who would translate policy into concrete action by attracting the necessary human and financial resources. Such involvement is not a cost, it should be seen as an investment to protect business and the market, as well as the integrity of health systems.

Conclusion

The studies showed that the Ukrainian pharmaceutical sector is in the process of creating an effective system of drug quality assurance, which is based on international principles, regulatory support and application of regulatory functions. But today there are still problems in the field of drug quality, which hinder the country's transition to international standards. The generalization of the results of the study allowed to formulate the following conclusions:

- the dynamics of changes in the domestic pharmaceutical market and a wide range of factors influencing the development of the criminal pharmaceutical business cause problems of quality assurance and falsification of medicines;
- state regulation and quality control of drugs at the current stage of development of the pharmaceutical market requires the latest approaches, the introduction of modern technologies for detection and rapid withdrawal of FM from circulation;
- the problem of drug falsification was assessed and the causes of drugs in circulation and ways of their distribution were studied. Analysis of the annual official statistics of the State Service of Ukraine on Medicines and Drug Control for the period of 2008–2019 on the number of detected FM in circulation and the data of General Prosecutor's Office of Ukraine on criminal offenses for the period of 2017–2019 showed a steady trend of increasing FM and insufficient implementation of effective measures to combat them;
- to increase the effectiveness of drug quality control and reliable resistance to the spread of FM in Ukraine should be comprehensive measures to combine information and human resources, to establish active cooperation with the relevant international organizations dealing with the problem of combating FM.

Justified that the most important priorities of state policy, which allow to raise the quality and safety of medicines, are to improve the system of state regulation and quality control of medicines, strengthening criminal liability for falsification of drugs and harmonization of pharmaceutical legislation of Ukraine with European legislation, optimization of the system of detection and operative withdrawal from circulation of FM and also tracking of channels of their receipt and distribution by means of implementation of the mechanism of introduction in practice of effective system of obligatory 2D barcode system of drug packaging and carrying out constant monitoring at all stages of drug circulation.

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