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CRIMINAL THREAT OF OCCURRENCE OF LOW-QUALITY AND COUNTERFEIT MEDICAL PRODUCTS

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Abstract: *The world is changing fast. Advances in technology, radical changes in communication and access to information, cheap transportation and the growth of global transnational corporations are influencing the shaping of the relief of our daily lives. The quality of medicines and medical products is one of the many areas that are exposed to the pressure of the stated determinants of world socio-economic trends. Poor quality and counterfeit medical products, such as vaccines and drugs, pose a serious and growing global health challenge. Other medical devices, such as diagnostic kits and means of preventing infection, including, but not limited to, masks and hand sanitizers, are also on the market in low-quality and counterfeit versions. In this paper, the author considers all these medical devices as possible low - quality and falsified health products. Following the existing normative framework at the national and international level, the author presents various aspects of the criminal threat caused by the presence of low-quality and falsified medical devices. By considering the strategy of combating the gravitational problem, the author finalizes his view of the importance of low-quality and counterfeit medical products for the vital values of today's society.*

Key words: *medical products, drugs, low-quality medical products, counterfeit medical products, medical devices, harmful products.*

INTRODUCTION

Non-standard and counterfeit medical products are the backbone of problems that affect the sustainability of public health and the degree of trust in health systems leading to economic losses around the world (Rahman M. S. et al., 2018: 1294; Ozawa S. et al., 2018: 2). The leading cause of non-standard drugs is the lack of good manufacturing practice and poor quality control, while the essential reason for counterfeiting drugs should be sought in economic benefits (Bakker-'t H.I. et al., 2021: 2). Especially countries with low and medium living standards have a large presence of such medical products, most likely due to less availability of basic medicines and fragile supply chain control. The World Health Organization has launched a "three-step" strategy to combat the problem of substandard and counterfeit drugs, which are prevention, detection and response (World Health Organization, 2017: 46-59). The focus of this review is on the current situation and possible improvements in the detection and analysis of the criminal threat to health and life, which is represented by the appearance of irregular medical products. Better assessment of the problem requires cooperation at the international and national levels between stakeholders such as governments, regulators, customs and drug manufacturers (Bakker-'t H.I. et al., 2021: 2). As a guarantor of the success of this cooperation, clear definitions of low-quality and counterfeit medicines are necessary.

NATIONAL AND INTERNATIONAL NORMATIVE DETERMINANTS

The domestic legislator pays attention to low-quality and counterfeit medical devices, considering them in the Law on Medicines and Medical Devices ("Official Gazette of RS", No. 30/2010, 107/2012, 113/2017 - other law and 105/2017 - other law) and the Criminal Code ("Official Gazette of the RS", No. 85/2005, 88/2005 - amended, 107/2005 - amended,

72/2009, 111/2009, 121/2012, 104/2013, 108/2014 , 94/2016 and 35/2019). First of all, a medicine is normatively defined as "a product which is placed on the market in a certain strength, pharmaceutical form and packaging and which contains a substance or combination of substances which has been shown to treat or prevent diseases in humans or animals, as well as the substance or a combination of substances that can be used or administered to humans or animals, either with the intention of restoring, improving or altering physiological function through pharmacological, immunological or metabolic action or making a medical diagnosis."[1] The types of drugs are listed exhaustively and in the formal legal sense can be of "human origin (blood and blood products); of animal origin (microorganisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products); of plant origin (microorganisms, whole plants, parts of plants, plant secretions, extracts) ", as well as of "chemical origin (chemical elements, chemical substances found in nature in a given form, as well as chemical products obtained by chemical change or synthesis)", where, in the sense of this law, "blood and blood components intended for transfusion are not considered a medicine"[2]. Then follows a group of protective norms which, under precisely prescribed conditions, prohibit the production of medicines[3], trade in medicines[4], advertising of medicines[5], advertising of medicines to the general public[6], but also the prohibition of the production of medical devices[7].

By analyzing the mentioned provisions, the attitudes of the legislators of common meaning, which are an integral part of these protective norms, can be abstracted. We single out the following prohibitions: "prohibition of the production of a drug that does not have a drug license[8]", and thus "trade in a drug for which no drug license has been issued[9]", which is why it is prohibited "that the manufacturer of the medicinal product trades the medicinal product from its production program to other legal entities, except for those who have a manufacturing license.[10]" This drug cannot be advertised[11]. We will also single out the following explicit prohibitions of the legislator, which are directly related to the topic of our paper. In that sense, the production of a medicine "that does not have the appropriate quality documentation" and a "fake medicine" is prohibited[12]. Consequently, the sale of such a drug[13] or medical device is prohibited[14]. It is clear that the national legislation has regulated a group of norms with the problem of low-quality and fake, ie counterfeit medicines and medical devices. In support of that, we emphasize the criminal offenses provided by the Criminal Code of the Republic of Serbia, which do not allow and punish quackery and non-pharmacy[15], negligent conduct in the preparation and dispensing of drugs[16], as well as the production and marketing of harmful products[17]. Long-term imprisonment in connection with serious offenses against human health is the best indicator of the attitude of the domestic legislator who foresaw serious bodily injuries and death as a special criminal offense, as special qualifying circumstances due to which the above illegal activities, and the issuance of drugs and the production and placing on the market of harmful products, may impose prison sentences of a possible duration of one to eight years[18].

1 According to Article 14 paragraph 1 of the Law on Medicines and Medical Devices.

2 According to Article 14, paragraph 2 of the Law on Medicines and Medical Devices.

3 According to Article 109 of the Law on Medicines and Medical Devices.

4 According to Articles 134 and 140 of the Law on Medicines and Medical Devices.

5 According to Article 167 of the Law on Medicines and Medical Devices.

6 According to Article 168 of the Law on Medicines and Medical Devices.

7 According to Article 188 of the Law on Medicines and Medical Devices.

8 According to Article 109 of the Law on Medicines and Medical Devices.

9 According to Article 134 of the Law on Medicines and Medical Devices.

10 According to Article 140 of the Law on Medicines and Medical Devices.

11 According to Article 167 of the Law on Medicines and Medical Devices.

12 According to Article 109 paragraph 4 and paragraph 5 of the Law on Medicines and Medical Devices.

13 According to Article 134 paragraph 4 and paragraph 6 of the Law on Medicines and Medical Devices.

14 According to Article 188 paragraph 3 and paragraph 5 of the Law on Medicines and Medical Devices.

15 According to Article 254 of the Criminal Code of the Republic of Serbia.

16 According to Article 255 of the Criminal Code of the Republic of Serbia.

17 According to Article 256 of the Criminal Code of the Republic of Serbia.

18 According to Article 259 of the Criminal Code of the Republic of Serbia.

The World Health Organization has, first of all, determined illicit medical products as substandard, fake, falsely marked, falsified ie altered[19]. The said international organization then revised the terms it uses in this field, which is why, according to the existing classification, such medical products are marked as low-quality, unregistered, unlicensed and counterfeit (Bakker-'t H.I. et al., 2021: 2). In this regard, low-quality products are defined as those that do not meet their standards or quality specifications, counterfeit drugs as well as those in which their chemical identity, composition or source is intentionally, fraudulently or falsely presented, while unregistered or unlicensed products are those that are not subject to assessment ie approval by a national or regional regulatory body (World Health Organization, 2017: 1). However, in practice there is no consensus according to which these terms are exclusively applied and there are often different interpretations of the same or similar manifestations of the presence of low-quality and counterfeit medical devices in legal and illegal markets of health products in the world (Grech J. et al., 2018: 612 ; Koczwara A. et al., 2017: 2921; Bakker-'t HI et al., 2021: 2).

POSSIBLE FORMS OF CRIMINAL THREAT

The most commonly counterfeited types of drugs, globally present, from the aspect of pharmacology, belong to antantimalarials, antibiotics and drugs that accompany a certain way of life - for example antidepressants, drugs against stress and pain ... (Assemat G., et al. 2019: 163). Many factors determine which type of drug will be counterfeited, such as: region, requirements, shortages, price of drugs and how easy they are to counterfeit.

Regional variations in the types of counterfeit drugs can have different causes. Due to fragile regulatory systems, countries with a lower and middle standard of living make the environment more attractive to counterfeiters compared to economically rich countries. Some diseases, such as malaria, are more common in certain areas of the world. This fact is the cause of the increase in the demand for antimalarials, which often causes a shortage of this type of medicine. Demand in countries with a high standard of living is more focused on medical products that are part of the lifestyle, such as stimulants for sexual activities or weight loss drugs (Koenraadt R. et al., 2018: 348).

The media can also influence the demands for certain drugs: the assumption of the possibility that the anti-malarial drug hydrochloroquine would be effective against SARS-CoV-2 immediately increased the demand for this medical product (Gnegel G. et al., 2020:73; Mackey T. K. et al., 2021: e72).

Expensive drugs are an attractive target for counterfeiters. Protein- and polypeptide-based drugs have come into the focus of both illegal manufacturers and smugglers because they are expensive and counterfeiting is more difficult to detect (Venhuis BJ et al., 2018: e209; Degardin K. et al., 2019: 487). Detection is more difficult because these drugs are mostly colorless liquids and require complex detection methods. Because these proteins and polypeptides are mainly targeted at diseases such as cancer, viral infections, and diabetes, their falsification can lead to serious health risks (Janvier S. et al., 2018:175).

Medicinal products that are difficult to analyze, but are not necessarily expensive, are produced on a plant basis, as is the case with traditional Chinese medicines. The quality of these drugs is difficult to determine and confirm due to their complex composition (Chen D. D. et al., 2017: 292). Although these herbal remedies do not appear to pose the greatest health risk due to synthetic active pharmaceutical ingredients, their overuse can cause serious harm. (Rahman M. S et al.. 2018:1300).

The most important medical products for investigation due to counterfeiting are those whose use carries the greatest risk to public health. This risk may increase in cases where illegal medications:

- do not have appropriate active pharmaceutical ingredients;
- contain an incorrect dose of active pharmaceutical ingredients;
- contain harmful ingredients or
- are issued to patients due to misdiagnosis of the disease (Bakker-'t H.I. et al., 2021: 3).

Proper medicines can affect public health due to shortages, but just like counterfeit medicines by containing harmful ingredients they can endanger public health. This is precisely the reason why both legal and illegal drugs should be the subject of research and analysis. In this sense, the exchange of data at the national and international level is important for monitoring criminal

19 The above refers to the period before May 2017

trends regarding the presence and manifestations of low-quality and counterfeit medical devices. In this way, attention can be proactively focused on drugs whose illicit production and distribution contribute to the disruption of public health intensively and on a wider scale.

In addition to medicines, organized criminal groups also target the following medical devices: face masks, disinfectants, medical tests, surgical equipment and instruments, thermometers, a wider range of medical devices (eg headphones, syringes, gauze, saline, accessories for first aid), and bottles with medical oxygen content (United Nations Office of Drugs and Crime, 2020:8).

In the production itself, the content of the medicine is an indicator of its illegal handling. Already in this first step in the development of a medical product, criminal activities affect the deviation from the prescribed composition and the use of the necessary ingredients. In that sense, the medicine is made as non-standard, and thus of poor quality, and its content is inappropriate and harmful to the health of the users. The variation of this illegal procedure can be reflected in the inappropriate composition of the alloy for artificial limbs or parts of the skeleton (eg for hips, femurs, bones of the hand and forearms). In the second case, a low-quality alloy of an artificial part of the skeleton or limb can endanger the organism with the chemical elements of which it is made. Thus, in terms of the harmfulness of low-quality and counterfeit medical products, the sign of equality can be posted, as well as in comparing the health hazards of medicines and other medical products. The only difference can exist in relation to the time of occurrence of harmful consequences and their intensity.

The distribution of low-quality and counterfeit medical products is carried out by well-organized and widespread networks of organized criminal groups. This phase of placing fake medical products implies storage, loading, transport and delivery (direct or with previous storage) to intermediaries, who will make them available to users through illegal engagement of direct suppliers or through illegal activity of a certain pharmacy institution.

The totality of the described criminal procedure is additionally accelerated by the use of online possibilities, ie by influencing the supply and demand of medical products via the Internet, and especially its invisible and hidden parts in the darknet. Illegal production, criminal distribution and illegal sale of low-quality and counterfeit medical products can be possible only with a lack of legal regulations, inefficient actions of law enforcement agencies, passive and disinterested relationship between public media and the health system, as well as corrupt influence of organized criminal groups on legislative, executive and judicial power (United Nations Office of Drugs and Crime, 2020:13).

PROBLEM-SOLVING STRATEGY

Counterfeit products appear on the world market in various stages of production and domestic and international distribution. Each of these phases is accessible to illegal activities.

In the distribution phase, drugs can be easily tracked and controlled using bar codes, holograms, quick response codes, radio frequency identification marks, watermarks or other markings on packaging. However, counterfeiters could avoid this detection by reusing the packaging. Another challenge in detecting counterfeit drugs in the distribution phase is online sales, in which combinations of some readily available and inexpensive products (eg lactose and vitamin C) are used to display the supply of drugs that are in short supply or in high demand (eg certain antiviral drug). Prescription drugs such as antibiotics, painkillers, sleeping pills, anti-inflammatory drugs and cytostatics can be purchased at online stores on the web (Tamsma F. et al., 2019:12).

In the case of imported drugs, the place to verify the authenticity of medical devices is at customs. The control of this type requires good, fast and easy handling of analytical devices for detecting counterfeiting of drugs in order to reduce the workload of customs personnel. Even if small quantities of low-quality and counterfeit medical devices are identified, which are distributed regionally, these data may be important for spotting trends related to certain types of drugs, ie medical devices and other health care products, which are imported as non-standard or counterfeit, and on the basis of which a better assessment of this problem can be reported.

Effective pharmacovigilance may serve at a later stage of detection of counterfeit drugs[20]. It is essential that the harmful effects of poor quality and counterfeit medical products are properly

20 According to the Rulebook on the manner of reporting, collection and monitoring of adverse drug reactions ("Official Gazette of RS", No. 64/2011, 75/2017 and 82/2017 - corr.), pharmacovigilance is "a set of activities related to the collection, detection , assessment, understanding and prevention of adverse drug reactions, as well as other drug-related problems".

documented and that these data are stored in a central record so that they can be exchanged between healthcare professionals around the world.

There is also a special question as to which drugs or medical products need to be controlled? While verification of all drugs is not possible due to limited control time and associated costs, random sampling would be the most scientifically justified method for obtaining a proper estimate of the prevalence of this problem. The second option is a targeted approach, in which the difficulty is the selection of criteria for the selection of medical devices to be tested. Possible criteria could refer to the types of drugs that are most frequently falsified or include those medical products that are of the greatest importance for public health, ie combine such criteria in order to perform control as effectively as possible.

In certain cases, there is a clear suspicion of falsification of a medical device, such as altered packaging or incorrectly or falsely labeled drugs. Other deviations, such as lower concentrations of active pharmaceutical ingredients or additional impurities in the composition of the drug or alloy of the medical device, may be the result of counterfeiting or poor production. Low-quality medical products, as well as those that have been counterfeited, must be systematically checked in order to detect and distinguish counterfeit from substandard and authentic drugs. With this strategy, suspicious drugs can be classified as real, low-quality, degraded or fake. The strategy begins with the division of the sample into subsets, one part of which is visually inspected for quantification by high pressure liquid chromatography, and the other is used for spectroscopic screening or colorimetric testing (Bakker-'t H.I. et al., 2021:3).

The second strategy for testing drugs for falsification and deviation from the prescribed standard consists of different protocols, depending on whether the sample is presented as a drug or not. These protocols are designated as: screening protocol, medical protocol and falsification protocol. Non-destructive analysis has been proposed for all protocols, such as microscopy of spectral fingerprints, which would be the first step after visual inspection because there may be a limited amount of sample. Further, the product is generally analyzed by liquid or gas chromatography combined with various detection systems, such as mass spectrometry. However, the most systematic methods require different, often expensive, analytical techniques, which is why there is still no generally accepted methodological approach at the global level. (Roth L. et al., 2018:44-45).

The advantage of using combined analytical techniques must be determined before testing in order to limit the number of instruments or devices and the time required to detect a counterfeit medical device, primarily a drug. Despite the lack of a general strategy, it is still important to choose the most appropriate analytical technique for each specific case of a potentially counterfeit drug. The desired result, e.g. detecting the presence of the active substance or the difference between counterfeit and authentic drugs, determines which techniques can be used. The general approach in the analysis of suspected falsified drug, in most cases, involves visual inspection followed by relatively simple and fast techniques for analysis such as thin layer chromatography, colorimetry or disintegration of the substance (Bakker-'t H.I. et al., 2021:4).

Analytical testing of all drugs to detect counterfeits is an impossible task. In practice, the detection of counterfeit drugs is based on the recognition of the drug as suspicious, based on appearance or clinical effect, which is why the disputed drug is sent to the laboratory for analysis . Other indications that the drug is of dubious quality are reports of adverse effects or internationally observed trends related to counterfeit drugs or their classes.

Clear and open communication at the national and international level is needed to effectively provide information on existing trends regarding the presence of types of medical products of dubious quality.

The next challenge is to choose the appropriate screening strategy. A wide range of tools is available for the analysis of counterfeit drugs. However, each case requires careful consideration of the critical attributes that may be present in a particular medical product or even a project related to a new drug.

In the control of medicines and other medical products, different results often occur after the application of the same analytical techniques in different laboratories. The conclusion is that proper staff training is key to the success of the analysis of counterfeit drugs and that it is necessary to expand the material, technical and methodological space for personal development of entities responsible for quality control, correctness and authenticity of medical products.

CONCLUSION

Barcodes and stamps should be incorporated into medical products of all countries of production, because a simple procedure of scanning the packaging would significantly make it difficult to counterfeit, ie it would be easier to detect unlabeled or incorrectly labeled medicines. A visual inspection of the primary and secondary packaging of a medical device can provide relevant information on the suspicion of its authenticity, which is why it represents a logical first step in performing control. However, subsequent chemical analysis is needed, which may be conditioned on budgetary constraints in low- and middle-income countries.

Combining different low-cost analytical techniques can improve the ability to distinguish genuine from counterfeit medicines and other medical products and devices. Certain drugs, such as those that contain protein or represent the dosage content of the injection, require expensive analytical techniques to rule out the possibility of falsification. This is accompanied by the development and improvement of sensitive portable devices for performing the analysis of the authenticity of medicines, where the main problem is exactly the maintenance of instruments such as portable spectroscopes.

Nevertheless, in the last half decade, significant progress has been made in chemometry and the origin of active substances, as well as in the development and application of pharmacological methodologies and tools useful in detecting and analyzing low-quality and counterfeit medicinal products (Bakker-'t HI et al., 2021: 9). This progress is needed in order to enable the conditions for strengthening the capacity of public health around the world and to give hope that the scope of the problem of illicit and counterfeit medical products will be reduced, and thus the criminal threat that sustains and encourages it will be suppresed.

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