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Features Of The Drug Labeling System Implementation In The Russian Federation: Positive And Negative Experience

Ekaterina O. Kuchits[1], Oleg V. Gridnev2, Gelya N. Gildeeva[3], Elena V. Pesennikova[4], Sergey S. Kuchits[5]

[1] I.M. Sechenov First Moscow State Medical University, Assistant of the department
[2] I.M. Sechenov First Moscow State Medical University, Doctor of Medical Sciences, Professor
[3] I.M. Sechenov First Moscow State Medical University, Doctor of Medical Sciences, Head of Department
[4] I.M. Sechenov First Moscow State Medical University, PhD of Medical Sciences, Assistant Professor
[5] Deputy chief physician for the prospective development of the City Clinical Hospital named after M.P. Konchalovsky", Moscow Department of Health, 124489, Russia, Zelenograd, ul. Chestnut Alley, d. 2, p. 1

ABSTRACT

In modern conditions of the free market, the falsification of drugs remains one of the main health problems not only in Russia but throughout the world. According to the World Health Organization, the extent of falsification of drugs can vary from one to several tens of percent of the total market for drugs. For this reason, medicines were among the first to fall under the law on mandatory labeling in the Russian Federation.The article describes the prerequisites, stages and difficulties of the transition of the Russian pharmaceutical market from 2020 to the system of mandatory labeling of drugs with identification tools as an element of the state information system for the drugs movement monitoring (DMM) from manufacturers to end consumers.

Keywords: Labeling, drug movement monitoring

Correspondence:
Ekaterina O. Kuchits
I.M. Sechenov First Moscow State Medical University, Assistant of the department

INTRODUCTION

According to reports, Russia ranks second in the world in the substandard drugs turnover [1]. In order to combat the circulation of substandard and falsified drugs, a labeling system is introduced in the Russian Federation [2].

Russia is far from the first country that has decided to introduce mandatory requirements for labeling drugs with special codes [3]. Since the 2000s, active discussions by the world communities on the need to use various technologies for identifying products have led to various initiatives and the pilot projects launch in some countries for the information systems implementation that monitor the drugs movement.

Thus, the European Federation of Pharmaceutical Industry and Associations (EFPIA), in collaboration with a number of other organizations, in September 2009 launched a pilot project. The purpose of the pilot project was to test the feasibility of using the drug packaging coding system in the European Union using a unique identifier in the form of a two-dimensional bar code. The pilot's results confirmed the effectiveness of using a coding system using media in the form of a two-dimensional bar code Data Matrix.

In addition, in several other countries from 2009 to 2011 with the state authorities support, draft laws and regulations were initiated defining methodological recommendations for labeling various levels of drug packages and the concept of introducing drug identification and monitoring systems:

- In 2009, the first version of guidelines for drug labeling was released in South Korea;
- In 2010, the mandatory requirements for drug labeling and serialization were applied in Turkey (aggregation introduced in 2012);
- In 2010, a regulatory document was published in China on the introduction of a drug movement monitoring system;
- In 2011, India published requirements for labeling tertiary (factory) packages of drugs intended for export;
- In 2011, an experiment was conducted in France on the drugs labeling with a two-dimensional code (but without serialization).

FOUNDATION OF A LABELING SYSTEM IN RUSSIA

In Russia, a pilot project on voluntary drug labeling was developed in 2017. More than 3,569 organizations, including 250 pharmacies, 30 hospitals, 23 manufacturers and 4 distributors, took part in the project voluntarily. A unique identification code has been applied to 314 vital medicines [4,5].

The issue of project implementing in Russia at that time was rather acute: in some segments more than 60% of drugs were faked, according to WHO, the Russian Federation is one of the leaders in the sale of counterfeit drugs.

According to the Center for the Advanced Technologies Development (CATD), which is responsible for the labeling system implementation, as of 01.01.2020, more than 23 thousand participants registered in the experiment. In order to protect the population from counterfeiting and taking counterfeit medicines out of circulation, from July 1, 2019, the law on mandatory labeling of high-cost medical products (7 nosologies) entered into force, and already on October 1, 2019, a ban on the production of drugs from the high-cost medical nosologies list was introduced without labeling code [6].

For other drugs, labeling will become mandatory on July 1, 2020. Both in Russia and in other countries, the base is the Data Matrix code (ISO ECC-200), which is a two-dimensional matrix symbolism and consists of two parts:

- product identification code - stored in the information system;
- verification code (crypto-tail) - is present only in the graphic image Data Matrix.

Labeling of drug packages is the application of identification means (DataMatrix code) on the secondary

(consumer) package of the drug (and in its absence, on the primary packaging of the drug), as well as group codes on the tertiary (transport) package of drugs by the group code issuer.

The issuer of identification means in the manufacture of a medicinal product in the territory of the Russian Federation is a manufacturer of medicinal products that prepares (packs) the medicinal product with the application of identification means on the secondary packaging of the medicinal product (and in their absence - on the primary packaging of the medicinal product). When manufacturing a medicinal product outside the territory of the Russian Federation, the issuer is the holder or owner of the registration certificate of the drug or representative office of a foreign organization in the territory of the Russian Federation that is the holder or owner of the registration certificate.

IMPLEMENTING THE LABELING SYSTEM IN THE EAEU COUNTRIES

The Eurasian Economic Union (EAEU) is an international organization for regional economic integration, which currently includes five countries - Russia, Kazakhstan, Belarus, Armenia and Kyrgyzstan. The EAEU provides freedom of goods movement, as well as a unified policy in all sectors of the economy. In 2019, the Resolution of the Board of the Eurasian Economic Commission (EEC) No. 55 on the introduction of the common process for all EAEU member states "Formation, Maintenance and Use of the Unified Register of Registered Medicines of the Eurasian Economic Union" [7] came into force. According to the Order, from January 1, 2021, all medicines are subject to registration according to the uniform rules of the Union. In addition to new registrations, drugs previously registered in accordance with the national laws of the EAEU Member States must be brought into compliance with the EAEU registration requirements by December 31, 2025. The new rules also provide for the creation of a unified system for labeling drugs.

Among the acts of the Eurasian Economic Commission, the most significant is Decision of the Council of the Eurasian Economic Commission dated 03.11.2016 No. 86 "On the Procedure for Interaction of the Member States of the Eurasian Economic Union to identify counterfeit, counterfeit and (or) substandard medicines", which provides for the exchange of data to prevent distribution to the market of drugs with falsified, substandard and counterfeit signs [8].

Also, Decision of the Council of the Eurasian Economic Commission dated November 3, 2016 No. 76 approved the requirements for labeling drugs when used by citizens, as well as in medical and veterinary institutions on the territory of the EAEU countries [9]. Labeling standards, methods for its application, the content of information on various types of packaging of drugs are established. However, this document does not highlight the rules on the use of digital identification in labeling.

In civilian circulation on the market of the EAEU countries, medicines are sold and bought if they have passed state control and supervision in the relevant state body, if the manufacturer has a document confirming the quality standards of the drug. A foreign company that has a certificate of a medicinal product manufacturer must have a document on the compliance of the medicinal product with the pharmacopeia article requirements of the regulatory documentation of the EAEU member states.

The digitalization of the process of monitoring the drugs circulation for medical purposes covers the registration of the drugs circulation system users (their input and output), the results of public sanitary and medical control [10]. If the drugs are falsified, counterfeit, substandard, then their withdrawal from circulation is performed automatically.

The execution of all legally significant documents for introducing the characteristics of the drug into the monitoring information system is confirmed by an electronic signature sent to the federal state information system for monitoring drug circulation, which indicates the manufacturer's obligation to label the product standardly in order to ensure drug traceability. In the EAEU countries, there are harmonized rules for the information monitoring of drugs at the level of national law.

In order to deliver and store identification and professional information regarding subjects participating in the turnover of the pharmaceutical market, measures are being applied to system-digital comparative information monitoring performed using other information systems. There is a comparison of information on subjects of the pharmaceutical market with information on entities included in the unified register of licenses for the production of medicines; unified state register of legal entities; unified state register of individual entrepreneurs; state register of accredited branches, representative offices of foreign legal entities, etc. The system for monitoring the turnover of drugs is connected to a single portal of interdepartmental electronic communication.

DIFFICULTIES IN IMPLEMENTING THE LABELING SYSTEM

The implementation of such a large project as the labeling system introduction is associated with certain objective problems [11].

The first is the cost. The greatest burden fell on the manufacturers. According to various estimates, the total costs of the manufacturing sector for the labeling system implementation will be from 8 to 15 billion rubles. There are two points of view in the professional community on how such significant costs will affect the non-final price of drugs for consumers. On the one hand, there are fears that the price of drugs will increase significantly; according to another point of view, after the introduction of labeling, the cost of legal manufacturers' goods may decrease due to the optimization of business processes and lower costs. Digital labeling will allow businesses to increase productivity, improve logistics schemes, increase market share and ultimately increase revenue. In the most conservative scenario, after the introduction of the labeling system, the prices of legal manufacturers' goods can decrease by 10%. The second problem is the short deadlines for the project implementation. After the approval in December 2018 of part of the regulatory documents establishing specific requirements for certain aspects of the program, the pharmaceutical industry had about a year to launch the labeling system.

And thirdly, the big question for experts is the length of the cryptocode - the verification code, which is centrally generated by the CATD and eliminates the appearance of "doubles" of goods and the possibility of re-launching goods to the market.

In the summer of 2018, five large pharmaceutical companies that participated in the pilot project sent an

appeal to the Russian Parliament, urging not to introduce crypto protection. In their opinion, this measure can lead to a significant increase in the prices of drugs due to additional costs, moreover, it is fraught with international isolation of the entire pharmaceutical industry of the Russian Federation. The initiative of pharmaceutical manufacturers was supported by the CATD Labeling Operator. However, according to the regulatory documents approved in the fall of 2018, the crypto code will remain and, in addition, will be paid - the Ministry of Industry and Trade has developed a resolution on the approval of the fee for the provision of labeling codes necessary for the System identification formation and providing of goods movement monitoring in the DMM system. According to the document, the fee for the labeling codes provision will be 50 kopecks for 1 labeling code, except for drugs included in the List of Essential and Most Important Drugs, the maximum selling price of which does not exceed 20 rubles. There is no charge for such products. These conditions are valid from July 1, 2019.

SUMMARY

Despite all the difficulties and fears associated with the transition to the new system, the system for goods labeling and traceability proposed for the foundation and implementation, is beneficial for all participants in the drug market [4].

For consumers, the DMM system is:

-confidence in the purchase of legal and quality goods;

-protection of life and health;

-a tool for public control and consumer protection.

For business, the DMM system is:

-protection against counterfeit products, respectively, company's name on the market will be protected from reputation losses associated with low-quality products sold under his brand;

-optimization of business processes and cost reduction;

-access to data on the goods promotion along the logistics chain.

For the state, the DMM system is:

-shrink the shadow market and increase labor productivity;

-increase in tax and customs duties;

-saving the budget to ensure control of product markets.

In the next few years, various difficulties will have to be overcome in order to fulfill the requirements of state authorities to ensure the drugs traceability. Only those organizations that can approach the project implementation not as costs but as investments in development, will be able to create potential business growth opportunities through the modern information technologies introduction.

REFERENCES

1. Healthcare [Zdravooxranenie]-2007[Electronicsource]–URL: https://www.newsru.com/russia/14feb2007/lekarstva.html
2. Labeling of drugs: what market participants need to know [2.Markirovka lekarstvenny`x preparatov: chto nuzhno znat` uchastnikam ry`nka] - 2019 [Electronic source] – URL: https://www.ekam.ru/blogs/pos/markirovka-lekarstvennykh-preparatov
3. Nalivayko Yu.A., Denisova N.A. Analysis of the implementation of the project on the launch of mandatory labeling of medicines. Bulletin of the International Scientific Surgical Association. 2019 Vol. 8 № 1: 30-33/
4. Postanovlenie Pravitel'stva RF ot 24 janvarja 2017 g. N 62 "O provedenii jeksperimenta po markirovke kontrol'nymi (identifikacionnymi) znakami i monitoringu za oborotom otdel'nyh vidov lekarstvennyh preparatov dlja medicinskogo primenenija".
5. Federal'nyj zakon ot 28.12.2017 N 425-FZ "O vnesenii izmenenij v Federal'nyj zakon "Ob obrashhenii lekarstvennyh sredstv".
6. Information on the results of state control (supervision) in the field of circulation of medicines for 9 months of 2019: information letter dated 10/17/2019 11-23891/19BH - URL: https://roszdravnadzor.ru/i/upload/images/2019/10/17/1571314772.739-1-8933.pdf (accessed February 13, 2020) - Text: electronic.
7. ECE Regulation No. 55 On the Implementation of the General Process "Formation, Maintenance and Use of the Unified Register of Registered Medicines of the Eurasian Economic Union" of April 2, 2019
8. Decision of the Council of the Eurasian Economic Commission dated 03.11.2016 No. 86 "On the Procedure for the Interaction of the Member States of the Eurasian Economic Union to identify counterfeit, counterfeit and (or) substandard medicines".
9. Decision of the Council of the Eurasian Economic Commission of November 3, 2016 No. 76 on the approval of the "Requirements for the Labeling of Medicinal Products for Medical Use and Veterinary Medicines".
10. Decree of the Government of the Russian Federation dated December 14, 2018 No. 1558 "On approval of the Rules for posting publicly available information contained in the monitoring system for the drugs movement for medical use in the information and telecommunications network" Internet "(including in the form of open data)".
11. Khoroshavina E.S., M.A., A.A., Dadus N.N. Status and prospects of introducing the state information system for the drugs movement monitoring. Education and science in Russia and abroad. 2019, 4 (52): 487-492
12. Gildeeva GN, Belostotsky AV, Gridnev OV. Nitisinone drugs bioequivalence in healthy volunteers in fasting state.Eurasia J Biosci. 2020;14(1), 817-821.
13. Nikitina, A., Gildeeva, G., Grigoriev, A., & Sidorova, A. (2020). 4-Methylamino antipyrine determination in human plasma by high-performance liquid chromatography tandem mass spectrometry. Biomedical Chromatography, e4913. doi:10.1002/bmc.4913
14. Kuchits, S., Gridnev, O., Pesennikova, E., Gildeeva, G., & Andreeva, D. (2019). Comparative research of job satisfaction among the doctor personnel in the Russian federation, under conditions of "performance-based contract of employment." Journal of Human Sport and Exercise, 14(Proc5), S2116–S2126. https://doi.org/10.14198/jhse.2019.14.Proc5.32
15. Gildeeva, G. N., Belostotsky, A. V., Ezhova, E. A., & Yurkov, V. I. (2019). Bioequivalence study of morphine hydrochloride oral solution versus

immediate release tablets. Journal of Global Pharma Technology, 11(6), 220–225.
16. Gildeeva, G. N., & Belostotsky, A. V. (2019). New antihistamine drug in treatment of patients with seasonal allergic rhinitis: Clinical study results. Systematic Reviews in Pharmacy, 10(2), 85–89. https://doi.org/10.5530/srp.2019.2.14
17. Gildeeva, G. N., & Yurkov, V. I. (2018). Microemulsions as Potential Bases for Formulating Modern Transdermal Therapeutics. Pharmaceutical Chemistry Journal, 52(6), 550–552. https://doi.org/10.1007/s11094-018-1858-6
18. Gildeeva, G. N., Belostotsky, A. V., & Sapozhnikova, D. S. (2017). Development and validation of an HPLC method with mass spectrometric detection for quantitative determination of chlormadinone acetate and ethinyl estradiol in human blood plasma. Pharmaceutical Chemistry Journal, 51(2), 142–152. https://doi.org/10.1007/s11094-017-1573-8
19. Gildeeva, G., & Belostotsky, A. (2017, December 2). Pharmacovigilance in Russia: current state of affairs, challenges, and prospects. Current Medical Research and Opinion. Taylor and Francis Ltd. https://doi.org/10.1080/03007995.2017.1336082
20. Gildeeva, G., & Belostotsky, A. (2017, December 2). Pharmacovigilance in Russia: current state of affairs, challenges, and prospects. Current Medical Research and Opinion. Taylor and Francis Ltd. https://doi.org/10.1080/03007995.2017.1336082
21. Smirnova, I. G., Gil'deeva, G. N., & Kukes, V. G. (2012). Optical isomerism and biological activity of pharmaceutical preparations. Moscow University Chemistry Bulletin, 67(3), 95–102. https://doi.org/10.3103/S002713141203008X
22. Guranda, D. T., & Gil'Deeva, G. N. (2010). Preparation of drug polymorphs (a review). Pharmaceutical Chemistry Journal, 44(5), 254–260. https://doi.org/10.1007/s11094-010-0443-4
23. Guranda, D. T., & Gil'Deeva, G. N. (2010). Preparation of drug polymorphs (a review). Pharmaceutical Chemistry Journal, 44(5), 254–260. https://doi.org/10.1007/s11094-010-0443-4
24. Revel'skii, I. A., Kapinus, E. N., Fedoseeva, M. V., Gil'deeva, G. N., Kosenko, V. V., & Revel'Skii, A. I. (2009). Determination of the main component in high-purity organic substances: Current status and prospects. Journal of Analytical Chemistry, 64(9), 926–929. https://doi.org/10.1134/S1061934809090093
25. Gildeeva, G. N., Ejova, E. A., Zakaliukina, E. V., & Ivanova, A. A. (2019). The trans-dermal therapeutic systems as a convenient alternative of traditional medicinal forms. Problemy Sotsial'noi Gigieny, Zdravookhraneniia i Istorii Meditsiny, 27(6), 997–1002. https://doi.org/10.32687/0869-866X-2019-27-6-997-1002
26. Zyryanov, S. K., Butranova, O. I., Ramenskaya, G. V., Gildeeva, G. N., & Shohin, I. E. (2018). In vitro equivalence evaluation of betahistine generic medicinal products as a tool potentially determining the efficacy of pharmacotherapy. Zhurnal Nevrologii i Psihiatrii Imeni S.S. Korsakova, 118(11), 43–48. https://doi.org/10.17116/jnevro201811811143