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Research Article

Improvement of quality control of water for pharmaceutical purposes obtained in the field

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An important component of military healthcare activities is the development of new models of complete scheduled medical supplies, including those intended for the production and quality control of medicines in military pharmacies and in military field hospitals. The article presents data on the creation of a self-sufficient set that allows to monitor the quality of purified water and water for injection in the field during a specified period. Now the available complete scheduled medical supplies do not contain materials and items for water quality control.

The goal of the article was to substantiate the approaches to the creation of a set of "Complete scheduled medical supplies for monitoring the quality of purified water and water for injection" (CQW), the selection of the nomenclature and the determination of the number of materials and items necessary for its completion, also the assessment of patentability. The CQW is a set with regulated property in terms of composition and quantity, which are statically fixed in a plastic container and ready for use. There are advantages indicated (self-sufficiency, portability, protection from the effects of external environmental conditions, etc.).

The authors of the article make a conclusion about the patentability of the product (application for invention N 2023101440). At the end of the article, the conclusion is formulated that the inclusion of the CQW in the composition of the complete scheduled medical supplies will improve the production activities of military pharmacies in the field, which will greatly contribute to improving the efficiency of medical care for the wounded and injured in military conflicts and extreme situations.

Keywords: field conditions; injection water; in-pharmacy control; military pharmacies; purified water; stacking kit; sterilization and distillation unit; water for pharmaceutical purposes.

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Научная статья

Совершенствование контроля качества воды для фармацевтических целей, получаемой в полевых условиях

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Разработка новых образцов комплектно-табельного оснащения, в том числе предназначенного для изготовления и контроля качества лекарственных средств в аптеках этапов медицинской эвакуации и военных полевых госпиталей, является важным компонентом деятельности военного здравоохранения. В статье представлены данные по формированию самодостаточного набора, позволяющего в течение установленного периода контролировать показатели качества воды очищенной и воды для инъекций в полевых условиях. На сегодняшний день имеющиеся комплекты медицинского имущества не содержат материалов и предметов для проведения внутриаптечного контроля качества воды.

Целью исследования явились обоснование подходов к формированию «Укладки-комплекта для контроля качества воды очищенной и воды для инъекций», подбору номенклатуры и установление количества материалов и предметов, необходимых для ее укомплектования, а также проведение оценки патентоспособности. «Укладка-комплект для контроля качества воды очищенной и воды для инъекций» представляет собой совокупность регламентированного по составу и количеству имущества, которое статично закреплено в пластиковом контейнере и готово к применению. Указывается на преимущества комплекта (самодостаточность, портативность, защищенность от воздействий внешних условий среды и т. п.).

Авторы статьи делают заключение о патентоспособности изделия (заявка на изобретение № 2023101440). Сформулирован вывод о том, что включение «Укладки-комплекта для контроля качества воды очищенной и воды для инъекций» в состав комплектно-табельного оснащения позволит улучшить производственную деятельность военных аптек в полевых условиях, что в немалой степени будет способствовать повышению эффективности оказания медицинской помощи раненым и пострадавшим в военных конфликтах и экстремальных ситуациях.

Ключевые слова: внутриаптечный контроль; вода для инъекций; вода для фармацевтических целей; вода очищенная; военные аптеки; полевые условия, стерилизационно-дистилляционная установка, укладка-комплект.

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BACKGROUND

Providing the Armed Forces of the Russian Federation with weapons, military and special machinery, and material and technical means created based on breakthrough research is considered an unconditional priority in achieving the goals of national security [1]. In this regard, the development of new types of complete and standard equipment, including those intended for the manufacture and quality control of medicinal products (MPs) in pharmacies of medical evacuation chains, and military field hospitals, is an important component of the activities of military healthcare [1]. However, the sets of medical equipment used for this purpose, namely, military pharmacy kit, assistant pharmacy kit, and injection pharmacy kit, do not contain a sufficient range of materials and items for intra pharmaceutical quality control of MPs, including water for injection (WFI) and purified water (PW), which are the most important components of liquid sterile and nonsterile MPs [2, 3]. The quality indicators and methods for testing these types of water for pharmaceutical purposes are regulated by pharmacopoeial articles FS.2.2.0019.18 "Water for Injections" [2] and FS.2.2.0020.18 "Purified Water" [3] [4]. Moreover, the requirements of these pharmacopoeial articles fully apply to water for pharmaceutical purposes in the field. Accordingly, research on the development of a "Stacking kit for the quality control of PW and WFI" (hereinafter referred to as the WQC stacking kit [WQK]) is extremely relevant [5].

This study aimed to substantiate approaches to the formation of a WQK and the range and quantity of materials and items necessary for its completion and evaluate the patentability of the WQK.

MATERIALS AND METHODS

The research materials were legislative and regulatory legal acts of the Russian Federation, regulatory legal acts of federal executive authorities (including the State Pharmacopoeia of the Russian Federation, XIV edition), resources of information retrieval systems (including the Federal Institute of Industrial Property and State Public Scientific and Technical Library), and scientific publications in the field of manufacturing and quality control of MPs. During the study, systemic and problematic methodological approaches were used, which were implemented using content analysis, structural–functional methods, logical analysis, comparative and descriptive methods, and patent search techniques. A patent search was performed by subject and nominal algorithms, and by the search for patent analogs (prototypes).

To form the WQK, instruments and tools for laboratories, laboratory grassware, consumables, chemical reagents and indicators, books and forms of accounting and reporting, and a plastic storage container with dividers were used.

RESULTS AND DISCUSSION

Substantiation of approaches to the formation of the WQK

The quality control of pharmaceutical substances and excipients is an obligatory stage in the technological process of drug manufacturing. However, in the field, testing of pharmaceutical substances, excipients and manufactured drugs is associated with many risks. Moreover, the quality indicators and frequency of control of MPs manufactured in medical evacuation chain pharmacies and military field hospitals must comply with the established requirements [4] [6, 7]. Thus, in PW and/or WFI, the absence of chloride ions, sulfate ions, calcium salts, and pH is monitored daily. Additionally, WFI is tested for the absence of reducing agents, ammonium salts, and carbon dioxide. PW and WFI are also quarterly subjected to complete qualitative and quantitative analyses. The results of the tests are recorded in the "Registration log of the results of the control of PW and WFI."

In the field, the control of water quality indicators for pharmaceutical purposes should be performed as soon as possible and close to the technical means of its production (e.g., sterilization–distillation unit [SDP]). Moreover, the use of approaches and material and technical equipment provided for stationary conditions for this purpose is practically impossible [8].

As part of the military scientific support of development activity on the creation of a modern sterilization and distillation unit (SDP-4), designed to obtain PW and WFI in the field, research was performed on the initiative to create a self-sufficient set of laboratory equipment (devices, tools, utensils, etc.) and consumables (reagents, indicators, etc.) that can be used, during the established period, to control the physical and chemical indicators of the quality of PW and/or WFI obtained in the field, provisioned by pharmacopoeial articles FS.2.2.0019.18 (WFI) and FS.2.2.0020.18 (PW) [9].

[1] Order of the President of the Russian Federation of July 2, 2021 No. 400 "On the National Security Strategy of the Russian Federation."

[2] FS.2.2.0019.18. Water for Injections. State Pharmacopoeia of the Russian Federation, XIV, 3rd ed., Moscow (2018).

[3] FS.2.2.0020.18. Purified Water. State Pharmacopoeia of the Russian Federation, XIV, 3rd ed., Moscow (2018).

[4] Order of the Ministry of Health of the Russian Federation No. 751n dated October 26, 2015 "On Approval of the Rules for the Manufacture and Delivery of Medicinal Drugs by Pharmacy Organizations, Individual Entrepreneurs Licensed for Pharmaceutical Activities."

Brief description of the WQK

The WQK represents a set of properly regulated in terms of composition and quantity (medical consumable items, apparatus, laboratory devices and tools, laboratory glassware, consumable materials and accessories, pharmacy consumable items, consumable sanitary and household property, chemical reagents and indicators, books and accounting and reporting forms for material assets, standard equipment, and containers), which ensures the implementation of all procedures to control the quality indicators of PW and WFI in accordance with the established requirements. All components of the WQK are statically fixed in a plastic opaque container for storage and transportation and are ready for use.

The set of analytical reagents included diluted nitric acid 16%, silver nitrate solution 2%, barium chloride solution 6.1%, diluted hydrochloric acid 7.3%, ammonium chloride ammoniac buffer solution pH = 10.0, Eriochrome black T indicator mixture, sodium edetate (Trilon B) 0.05 M, potassium permanganate 0.1 M, diluted sulfuric acid 16%, calcium hydroxide solution, Nessler's reagent, and laboratory tools. In addition, the WQK included a universal reagent paper (pH = 0–14.0), brush for washing test tubes, log for recording the results of the PW and WFI tests (20 sheets), pencil, glass pencil (vitreograph), 100-mL shake flask without a ground joint, graduated centrifuge test tube, chemical test tubes 14 × 120 mm, laboratory glass spirit lamp with a cap, 50-mL chemical beaker with a spout, stand for 10 test tubes, and some other items.

The WQK is self-sufficient and easy to use and can be formed at a relatively low cost. It is designed for a senior pharmacist (pharmacist); according to the consumables, it is intended for 1 month of work (for 30–35 tests). A prototype of the WQK is presented in Fig. 1.

The approbation of the WQK was performed during preliminary and state tests of prototypes of SDP-4 sterilization and distillation unit in the Institute of Pharmacy of the Tyumen State Medical University of the Ministry of Health of Russia. Data convincingly indicate that with the use of WQC, the methods (techniques) provided for by the relevant pharmacopoeial articles, the established quality indicators of PW and/or WFI can be controlled within a month [10].

Providing the chains of medical evacuation, military field hospitals, and other medical units equipped with technical means for obtaining PW and/or WFI (e. g., water distillers or sterilization–distillation installations) with the WQK s is encouraged.

Evaluation of the WQK patentability

The results of a patent search established that the utility model Complete Field Laboratory for Chemical Analysis of Water and Soil Extracts water quality kit is the closest prototype of the WQK[5]. Its fundamental difference from the proposed WQK is its purpose, as the field laboratory does not belong to the field of pharmacy and is not intended to assess the quality of drugs and/or excipients (in this case, PW and WFI). In addition, its disadvantages are the difficulty in conducting the necessary analyses in the field and the relatively high cost of components (e.g., due to the presence of devices for photocolorimetric analysis).

Based on this, the patentability of the WQK was established, which was the basis for the preparation and filing of an application for an invention (accepted under the number 2023101440)[6].

[5] A.G. Muravyov, B.V. Smolev, and A.N. Ustrova, RF patent for utility model No. 123777/ 27.07.2010 Bull. No. 21, Complete Field Laboratory for Chemical Analysis of Water and Soil Extracts WQK (variants).

[6] A positive decision dated February 14, 2023 on application No. 2023101440 dated January 24, 2023 for the invention by Yu.V. Miroshnichenko, R.A. Enikeeva, E.Yu Alekseychuk "Stacking kit for control of the quality of purified water and water for injection in the field."

Fig. 1. Stacking kit "Set for the analysis of purified water and water for injection in the field."

CONCLUSION

In the course of the initiative scientific research, for the first time, a WQC kit was created to control the quality of PW and WFI in the field. The results of the patent search showed its novelty and patentability. The inclusion of the WQK in the composition of standard basic equipment will significantly improve the production activities of military pharmacies in the field, which will greatly contribute to improving the efficiency of providing medical care to the wounded and injured in military conflicts and extreme situations.

ADDITIONAL INFORMATION

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REFERENCES

1. Miroshnichenko YuV, Ivchenko EV, Kononov VN, et al. Perspective directions of innovative development of pharmacy in military healthcare in Russia. *Bulletin of the Russian Military Medical Academy.* 2022;24(1):179–188. (In Russ.) DOI: 10.17816/brmma101106

2. Lopatin SA, Yudin AB, Volodin AS, Bokarev MA. Problematic issues and prospects for improving water quality control in the field. *Military Medical Journal.* 2022;343(4):45–52. (In Russ.) DOI: 10.52424/00269050_2022_343_4_45

3. Rodionov EO. Approaches to equipping military pharmacies in the field. *Modern organization of drug supply.* 2015;(2):66. (In Russ.)

4. Ozderbieva DA, Mal'ceva EM. The comparative analysis of pharmacopoeia requirements to the purified water and water for injections. *Actualscience.* 2016;2(12):201–204. (In Russ.)

5. Sobolenko AK, Prigorelov OG, Zlenko VE, et al. Mobile pharmaceutical complexes: realities and development prospects. In: *Prikladnyye voprosy voyennoy meditsiny*. Materials of the All-Russian interdepartmental scientific-practical conference. Saint Petersburg. 2021. P. 196–199. (In Russ.)

6. Klimkina EA, Enikeeva RA, Zhidkova UU, Vatanskaya OA. Approaches to the production of medicines in the field. *Modern organization of drug supply.* 2021;8(1):61–62. (In Russ.)

7. Rodionov EO, Saushkina AS, Klimkina EA. Production and quality control of medicines in the field. *Russian Military Medical Academy Reports.* 2020;39(S3–4):238–240. (In Russ.)

8. Miroshnichenko YuV, Bunin SA, Kononov VN, Popov AA, Rodionov EO. Justification of modern approaches to classification of medical equipment sets. *Military Medical Journal.* 2016;337(3):22–29. (In Russ.) DOI: 10.17816/RMMJ73551

9. Miroshnichenko YuV, Enikeeva RA, Alekseychuk EYu. Comparative analysis of the tactical and technical characteristics of military equipment designed to obtain water for pharmaceutical purposes in the field. In: Kononov V.N., Golubenko R.A., eds. *Aktual'nye voprosy razvitiya rossiyskoy farmatsii — Il'inskie chteniya.* Materials of the XI annual interuniversity interregional scientific conference, St. Petersburg, December 09–10, 2021. Saint Petersburg: Voenno-medicinskaya akademiya imeni S.M. Kirova, Publishing House; 2022. P. 179–189. (In Russ.)

10. Miroshnichenko YuV, Yakovlev SV, Kononov VN, et al. Implementation of modern approaches to testing organic equipment of the medical service of the armed forces. *Military Medical Journal.* 2018;339(4):49–54.

СПИСОК ЛИТЕРАТУРЫ

1. Мирошниченко Ю.В., Ивченко Е.В., Кононов В.Н., и др. Перспективные направления инновационного развития фармации в военном здравоохранении России // Вестник Российской Военно-Медицинской Академии. 2022. Т. 24, № 1. С. 179–188. DOI: 10.17816/brmma101106

2. Лопатин С.А., Юдин А.Б., Володин А.С., Бокарев М.А. Проблемные вопросы и перспективы улучшения контроля качества воды в полевых условиях // Военно-медицинский журнал. 2022. Т. 343, № 4. С. 45–52. DOI: 10.52424/00269050_2022_343_4_45

3. Родионов Е.О. Подходы к оснащению военных аптек в полевых условиях // Современная организация лекарственного обеспечения. 2015. № 2. С. 66.

4. Оздербиева Д.А., Мальцева Е.М. Сравнительный анализ фармакопейных требований к воде очищенной и воде для инъекций // Actualscience. 2016. Т. 2, № 12. С. 201–204.

5. Соболенко А.К., Пригорелов О.Г., Зленко В.Е., и др. Подвижные фармацевтические комплексы: реалии и перспективы развития. В сб.: Прикладные вопросы военной медицины. Материалы Всероссийской межведомственной научно-практической конференции. Санкт-Петербург, 2021. 2021. С. 196–199.

6. Климкина Е.А., Еникеева Р.А., Жидкова Ю.Ю., Ватанская О.А. Подходы к изготовлению лекарственных средств в полевых условиях // Современная организация лекарственного обеспечения. 2021. Т. 8, № 1. С. 61–62.

7. Родионов Е.О., Саушкина А.С., Климкина Е.А. Изготовление и контроль качества лекарственных средств в полевых условиях // Известия Российской Военно-медицинской академии. 2020. Т. 39, № S3–4. С. 238–240.

8. Мирошниченко Ю.В., Бунин С.А., Кононов В.Н., Попов А.А., Родионов Е.О. Обоснование современных подходов к классификации комплектов медицинского имущества // Военно-медицинский журнал. 2016. Т. 337, № 3. С. 22–29. DOI: 10.17816/RMMJ73551

9. Мирошниченко Ю.В., Еникеева Р.А., Алексейчук Е.Ю. Сравнительный анализ тактико-технических характеристик во-

енной техники предназначенной для получения воды для фармацевтических целей в полевых условиях. В сб.: Актуальные вопросы развития российской фармации — Ильинские чтения. Материалы XI ежегодной межвузовской межрегиональной научной конференции, Санкт-Петербург, 09–10 декабря 2021 года / Под редакцией В.Н. Кононова, Р.А. Голубенко. СПб.: Военно-медицинская академия имени С.М. Кирова, 2022. С. 179–189.

10. Мирошниченко Ю.В., Яковлев С.В., Кононов В.Н., и др. Реализация современных подходов к проведению испытаний комплектно-табельного оснащения медицинской службы вооруженных сил российской федерации // Военно-медицинский журнал. 2018. Т. 339, № 4. С. 49–54.

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