Administration of Drugs for Pharmacotherapy of Tuberculosis According to GSP Requirements

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Abstract. This research paper outlines the findings from a comprehensive investigation focused on the dispensation and management of antituberculosis medications in pharmaceutical practices. The examination of antituberculosis medications was conducted using various classification systems, including ATC codes, clinical and pharmacological, classification and legal, nomenclature and legal groups. The study provides a detailed analysis of the harmonization process for GxP standards within Ukraine, offering a thorough understanding of the current practices. Additionally, the research looks into the supply chain dynamics of antituberculosis medication distribution. Developed within the study are strategic guidelines for the proper storage of these medications, essential for maintaining their efficacy and safety. A systematic proposal for the spatial organization of storage facilities in the wholesale sector is presented, ensuring compliance with GSP. The study's goal was to refine the methodologies involved in the storage and management of antituberculosis drugs, with the ultimate aim of enhancing the efficiency of tuberculosis treatment protocols. This, in turn, is expected to elevate the caliber of healthcare delivery and pharmaceutical care available to patients afflicted with tuberculosis. Expanding on the study's contributions, the paper highlights the implications of these findings for public health policy and the potential to streamline pharmaceutical organization. By drawing attention to the criticality of adherence to rigorous storage protocols, the research underscores the necessity of meticulous oversight in the pharmaceutical supply chain. The insights gained from the study are not only pivotal for healthcare providers but also for policymakers tasked with the mandate of curbing the tuberculosis epidemic. The proposed recommendations provide a scaffold for future enhancements in drug management practices.

Keywords: administration, tuberculosis, antituberculosis drugs, pharmacotherapy, GSP.

Introduction. The administration of drugs for the pharmacotherapy of tuberculosis requires proper medical care, pharmaceutical support, and compliance with the requirements of GxP practices [1]. Compliance with administration standards when storing drugs for tuberculosis pharmacotherapy in the wholesale network is relevant and necessary [2].

The World Health Organization has said that the number of deaths from tuberculosis in Europe is rising again after falling for almost 20 years. Specialists of the WHO European region told AFP that this figure continues to decrease compared to previous years. The increase in deaths from tuberculosis in 2021 is most likely the result of delayed or non-diagnosis of tuberculosis due to disruptions in tuberculosis services during the COVID-19 pandemic, resulting in increased disease severity and associated deaths. The most affected country is called Ukraine, where about 3,600 people died from tuberculosis. In addition, the prevalence of drug-resistant tuberculosis also increased in 2021: one in three cases of the disease was resistant to rifampicin, the main drug used to treat the disease [3-9].

The issue of modeling the main material flows of the control and authorization system for regulating the circulation of anti-tuberculosis drugs is relevant today.

A structured analysis of legal relations between various participants in drug supply chains began to be conducted in Ukraine in 2004. The analysis included manufacturers, hospitals, pharmacies, doctors, and patients [10-12].

Today it is important to use effective, quality, safe and available medicines for pharmacotherapy of tuberculosis. It is also important to use innovative technologies on the principles

of evidence-based medicine, forensic pharmacy, evidence-based pharmacy, medical and pharmaceutical law.

Continuation of the research on the structure of zones, sectors, and areas of storage of drugs of clinical-pharmacological, classification-legal, nomenclature-legal groups in the wholesale network in accordance with the requirements of GSP (Good Storage Practices) is aimed at administration to improve the efficiency, quality, safety, and availability of drugs [13].

The purpose of the study was to systematize and analyze aspects of the administration of drugs for the pharmacotherapy of tuberculosis, taking into account different classification systems and legal norms.

Main research's tasks:

1. Administration of anti-tuberculosis drugs. Research of anti-tuberculosis drugs by ATC codes, clinical and pharmacological, classification and legal, nomenclature and legal groups to obtain a more complete understanding of their characteristics and features of use.

2. Features of the harmonization of national GxP standards in Ukraine. Analysis of the main material flows of the administration of anti-tuberculosis drugs in the context of interaction between different participants of the supply chain.

3. Development of recommendations for the storage of anti-tuberculosis drugs. Analysis of storage of anti-tuberculosis drugs. To propose the structure of zones, sectors, and districts for the storage of anti-tuberculosis drugs in the wholesale network in accordance with the requirements of the GSP in order to improve the efficiency, quality, safety, and availability of anti-tuberculosis drugs.

The article is aimed at improving the practice of storage and administration of anti-tuberculosis drugs to optimize the treatment process of tuberculosis, increase the quality of medical care, and pharmaceutical support for patients.

Materials and methods. The methodology for researching was based on the theoretical principles of pharmaceutical and medical law in the areas of: administration of prescriptions, risk management and safety of pharmacotherapy.

The term of the study was 2021-2024. The object of the study were anti-tuberculosis medicines, which are in circulation on the pharmaceutical market of Ukraine, approved for medical use, registered in the State Register of Drugs of Ukraine as of March 2024, and also included in the clinical instruction, standards of medical care "Tuberculosis".

Methods of the research – administration, management, organizational and legal, normative, documentary, clinical and pharmacological, comparative, graphic analysis.

The research of the article is a fragment of research works of Lviv Medical Institute LLC on the topic of "Improving the system of circulation of drugs during pharmacotherapy on the basis of evidentiary and forensic pharmacy, organization, technology, biopharmacy and pharmaceutical law" (state registration number 0120U105348, implementation period 2021-2026); Kharkiv Medical Academy of Postgraduate Education on "Improving the organizational and legal procedure for providing patients with drugs from the standpoint of forensic pharmacy, organization and management of pharmacy" (state registration number 0116U003137, terms 2016-2020) and "Pharmaceutical and medical law: integrated approaches to the system of drug circulation from the standpoint of forensic pharmacy and organization of pharmaceutical business" (state registration number 0121U000031, terms 2021-2026); Luhansk State Medical University "Conceptual interdisciplinary approaches to pharmaceutical provision and availability of drugs, taking into account organizational and legal, technological, analytical, pharmacognostic, forensic and pharmaceutical, clinical and pharmacological, pharmacoeconomic, marketing, social and economic competencies" (state registration number 0123U101632, terms 2023-2027); Petro Mohyla Black Sea National University on the topic "Conceptual interdisciplinary approaches to the drug circulation system, taking into account organizational and legal, technological, biopharmaceutical, analytical, pharmacognostic, forensic and pharmaceutical, clinical and pharmacological, pharmacoeconomic, pharmacotherapeutic aspects" (state registration number 0123U100468, implementation period 2023-2028); Private Scientific Institution "Scientific and Research University of Medical and Pharmaceutical Law" on the topic "Multidisciplinary research of post-traumatic stress disorders

during war among patients (primarily combatants)" (state registration number 0124U002540, implementation period 2024-2028).

Results and discussion.

The first stage of the research. Administration of anti-tuberculosis drugs.

At this stage of the research, the author conducted an analysis of classification systems for drugs used in the pharmacotherapy of tuberculosis. ATC codes of anti-tuberculosis drugs were studied. Antituberculosis drugs according to ATC codes (Anatomical Therapeutic Chemical Classification System) were studied. The ATC system is an internationally recognized system for classifying drugs according to the main clinical-pharmacological and anatomical-therapeutic groups [24].

Clinical and pharmacological groups were analyzed from the point of view of their clinical and pharmacological properties. Efficiency, side effects and other characteristics affecting the use of drugs in the pharmacotherapy of tuberculosis have been systematized [25-27].

Classification and legal groups were analyzed according to their legal status and classification according to the current legislation regulating the circulation of drugs [28-31].

The nomenclature and legal groups of anti-tuberculosis drugs were studied according to the features of appointment, release, availability for patients [32].

During the study, first- and second-line antituberculosis pharmacotherapy drugs, as well as combined drugs, were systematized (Tables 1, 2, 3). International non-proprietary names, clinical and pharmacological properties and use were studied. A more complete understanding of the characteristics and features of the use of drugs in the pharmacotherapy of tuberculosis was obtained based on the principles of evidence-based medicine and evidence-based pharmacy [14-24].

Table 1. International non-proprietary name and the clinical and pharmacological groups of the first-line antituberculosis medicines.

No.	International non-proprietary name	ATC code – Clinical and pharmacological group	Classification and legal group	Nomenclature and legal group
1.	Isoniazide	J04AC01 – anti-tuberculosis agents	General	According to the doctor's prescription
2.	Rifampicin	J04AB02 – anti-tuberculosis drugs. Antibiotics	General	According to the doctor's prescription
3.	Rifabutin	J04AB04 – anti-tuberculosis drugs. Antibiotics	General	According to the doctor's prescription
4.	Pyrazinamide	J04AK01 – agents for system use. Antitubercular drugs	General	According to the doctor's prescription
5.	Ethambutol	J04AK02 – antimicrobial agents for systemic use, agents acting on mycobacteria, antituberculosis agents	General	According to the doctor's prescription
6.	Streptomycin	J01GA01 – antimicrobial agents for systemic use	General	According to the doctor's prescription

Source: own development

Table 2. International non-proprietary name and the clinical and pharmacological groups of the second-line antituberculosis medicines.

No.	International non-proprietary name	ATC code – Clinical and pharmacological group	Classification and legal group	Nomenclature and legal group
1.	Kanamycin	J01GB04 – antimicrobial drugs for systemic use; aminoglycosides	General	According to the doctor's prescription
2.	Amikacin	J01GB06 – agents for system use; aminoglycosides	General	According to the doctor's prescription
3.	Ethionamide	J04AD03 – agents affecting mycobacteria. Antitubercular drugs.	General	According to the doctor's prescription
4.	Protionamide	J04AD01 – agents affecting mycobacteria. Antitubercular drugs. Derivatives of thiourea.	General	According to the doctor's prescription
5.	Sodium aminosalicylate	J04AA02 – anti-tuberculosis drugs	General	According to the doctor's prescription
6.	Capreomycin	J04AB30 – anti-tuberculosis drugs. A/B Capreomycin.	General	According to the doctor's prescription
7.	Cycloserine	J04AB01 – agents acting on mycobacteria. Antibiotics.	General	According to the doctor's prescription
8.	Terizidone	J04AK03 – anti-tuberculosis drugs. Other antituberculosis drugs.	General	According to the doctor's prescription

Source: own development

Table 3. International non-proprietary name and the clinical and pharmacological groups of the combined antituberculosis drugs.

No.	International non-proprietary name	ATC code – Clinical and pharmacological group	Classification and legal group	Nomenclature and legal group
1.	Rifampicin + Ethambutol + Isoniazide	J04AM02 – anti-tuberculosis drugs	General	According to the doctor's prescription
2.	Rifampicin + Isoniazide + Pyrazinamide + Ethambutol	J04AM06 – combined anti-tuberculosis drugs	General	According to the doctor's prescription
3.	Sodium aminosalicylate+ Isoniazide	J04AM – combined anti-tuberculosis drugs	General	According to the doctor's prescription
4.	Rifampicin + Isoniazide	J04AM02 – combined anti-tuberculosis drugs	General	According to the doctor's prescription

Source: own development

First-line antituberculosis drugs have 6 International non-proprietary names with ATC code – Clinical and pharmacological group J04 (83.3%) and J01 (16.7%). All drugs belong to the general classification-legal group. Dispensed with a doctor's prescription (Table 1).

Antituberculosis drugs of the second line for pharmacotherapy include 8 International non-proprietary names with ATC code – clinical and pharmacological group J04 (75.0%) and J01 (25.0%). All drugs of general classification and legal group. Dispensed with a doctor's prescription (Table 2).

Combined drugs for anti-tuberculosis pharmacotherapy have four International non-proprietary names with ATC code – clinical and pharmacological group J04 (100.0%). All drugs of general classification and legal group. Dispensed with a doctor's prescription (Table 3).

The study showed the following results according to the first task of the work on drugs of anti-tuberculosis therapy of the first, second line and combined drugs:

- International non-proprietary names of first- and second-line antituberculosis drugs, as well as combined drugs, were analyzed. The clinical and pharmacological groups and characteristics of the drugs were studied.
- The classification and legal, nomenclature and legal groups of drugs were analyzed. The distribution of antituberculosis drugs by classification and legal group, nomenclature and legal group made it possible to understand the regulatory context and conditions of their use and circulation.
- The research phase focused on the structured analysis of antituberculosis drugs and their classification characteristics. This paves the way for further research on optimizing and improving the treatment process of tuberculosis, in particular through the selection of optimal drugs and increasing the efficiency of their pharmaceutical supply and use.

The second stage of the research: Modeling of material flows.

At the second stage of the research, modeling of the main material flows in the circulation system of anti-tuberculosis drugs was carried out. The interaction between various participants of the supply and consumption chain (manufacturers-warehouses-hospitals-pharmacies; doctors-patients-pharmacists) was studied.

Prospects for cooperation with the countries of the European Union have been determined. There are views on the lowering of standards. The components of adaptive management of the appropriate range of drugs for tuberculosis pharmacotherapy have been established.

An important aspect of interaction with the countries of the European Union is the harmonization of pharmaceutical legislation in Ukraine. The lowering of the level of European integration standards occurs as a result of the involvement of private structures (pharmaceutical companies, enterprises, etc.) in the creation of national standards in the control and authorization system for regulating the circulation of drugs. It applies to the system of first-level legal relations between legal entities in the "manufacturer-warehouse-hospital-pharmacy" chain and to the system of second-level legal relations between natural persons in the "doctor-patient-pharmacist" chain. Practice shows that WHO recommendations have been implemented in many countries of the European Union [33]. Wholesale and retail pharmaceutical manufacturers, warehouses, firms, institutions take an active part in the development of technical specifications (rules) based on European requirements (Table 4).

Table 4. Interaction of the countries of the European Union and Ukraine with pharmaceutical organizations: reasons and prospects.

	The main reasons	**Perspective**
Firstly	Standards are no longer a national political issue	The government is less interested in participating in their implementation
Secondly	Pharmaceutical organizations have the technical knowledge and experience necessary to create specifications (for example, rules for storage, transportation, drug accounting, etc.), because they employ	The state can use this knowledge and experience and allow them to perform a significant share of the work, while saving public funds

	pharmacists, chemists, biologists, and lawyers who are engaged in the field of drug circulation	

Source: own development

Noted that the private pharmaceutical business is closely involved in the creation of national GxP standards. The pharmaceutical industry can make great efforts to ensure that the established GxP standards are appropriate for production, distribution, wholesale, retail, prescribing, and use in medical practice. It is believed that in the period before harmonization (for example, in a country that is a candidate for joining the European Union), national governments have complete control over all national standards [34, 35]. Arguments and views on the harmonization of national GxP standards are given below (Table 5).

Table 5. Features of the harmonization of GxP national standards.

Argument		***Point of view***
The first	Countries fulfill the requirements with different degrees of responsibility	This can lead to the presence in circulation of drugs of a low level of standards and quality. Countries that apply high levels of standards will also become freer to use them, so as not to find themselves in an uncompetitive environment. There must be mutual trust between countries implementing GxP standards. Some countries are less effective than others
The second	Countries fulfill requirements for harmonization, liberalization and deregulation of their legislative framework taking into account national conditions	At the same time, citizens (patients) believe that the state cares for them. They do not take responsibility for well-being when purchasing and using drugs. For example, patients do not always read the instructions for the medical use of drugs. They do not pay attention to the rules of storage, dosage regime and course, temperature regime, side effects, interaction with other drugs, food, contraindications to use, precautionary measures, etc. Therefore, it is important that GxP standards are of the same appropriate level both in the countries of the European Union and in the candidate countries for joining the European Union

Source: own development

Harmonization of national GxP standards is relevant for the pharmaceutical provision of tuberculosis pharmacotherapy at the wholesale network level on the basis of pharmaceutical law. The author investigated the harmonization of GxP standards using the example of "Good Distribution Practice" (GDP) [2].

One of the provisions of the GxP requirements is the conditions for proper storage of drugs at the GSP level. GSP requirements guarantee the preservation of the quality of antituberculosis drugs in the system of legal relations "manufacturer-distributor-pharmacy-hospital" [36].

Domestic and foreign drug manufacturers and distributors are a real barrier to the penetration of low-quality, unregistered, ineffective, falsified drugs into the pharmaceutical market. The specified actions have signs of crimes provided for in Art. 202, 203, 227, 321 of the Criminal Code of Ukraine [37, 38]. A small number of large wholesalers working with a retail network affects the reduction of non-production costs, improves the quality of transport service, and guarantees the necessary quality control of drugs. GSP requirements provide high-quality, effective, safe antituberculosis pharmacotherapy for patients with musculoskeletal disorders, post-traumatic stress disorder, nervous

system disorders, depressive disorders, addictions (alcoholic hepatitis), infections (monkeypox virus), etc. [39-45].

Proper storage of antituberculosis drugs, Good Storage Practice (GSP), includes all storage measures at the wholesale level (wholesale pharmacy base, pharmacy warehouse) (Fig. 1).

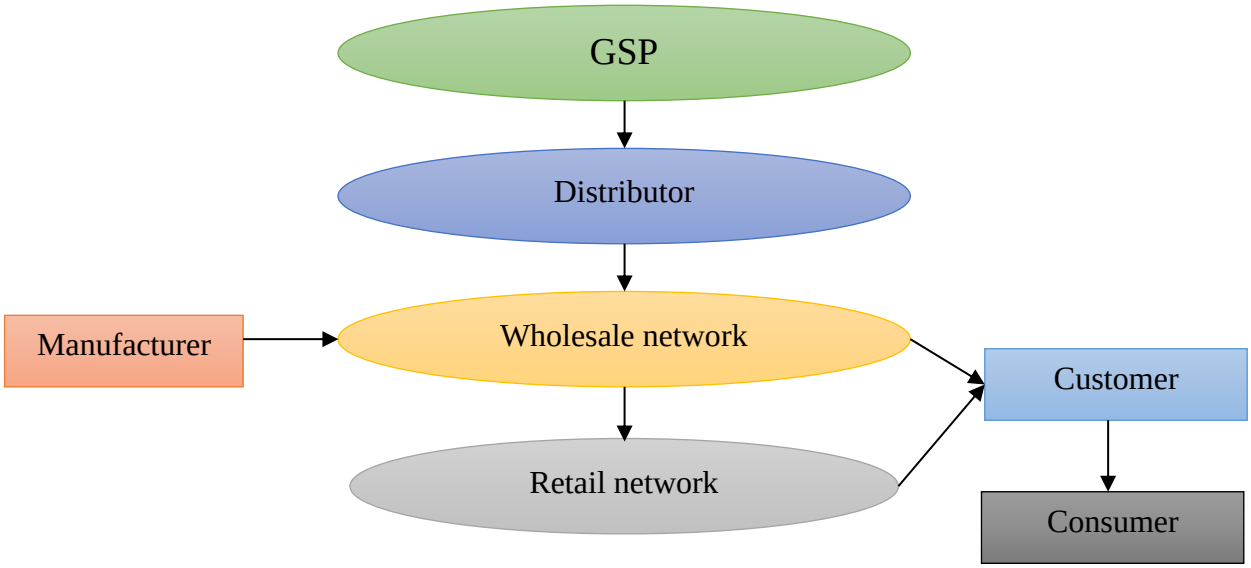

Fig. 1. Components of Good Storage Practice (GSP) for pharmaceutical support of tuberculosis pharmacotherapy.
Source: own development

The main material flows of the GSP administration of anti-tuberculosis drugs between individual zones, sectors and storage sections in the wholesale network are shown in Fig. 2.

Fig. 2. The structure of the GSP wholesale network of anti-tuberculosis drugs.
Source: own development

The study showed the following results according to the second task of the work on the development of national GxP standards in Ukraine and the analysis of the main material flows of the administration of anti-tuberculosis drugs:

❖ WHO recommendations have been implemented in many countries of the European Union. The main reasons and prospects for cooperation between the countries of the European Union and Ukraine have been proven. Features of harmonization of GxP national standards were given.

❖ Manufacturers of anti-tuberculosis drugs and their distributors are key figures who ensure quality control at every stage of their circulation. Their responsibility is to prevent low-quality or counterfeit products from entering the market.

❖ GSP components for pharmaceutical support of tuberculosis pharmacotherapy were proposed.

❖ The main material flows of the GSP administration of anti-tuberculosis drugs between individual zones, sectors and storage sections in the wholesale network have been developed.

The third stage of the study: Development of recommendations for the storage of drugs

At this stage of the research, the author focused on the development of recommendations for the storage of anti-tuberculosis drugs in the wholesale network in order to comply with GSP requirements. Various aspects of storage, the structure of zones, sectors, and districts in the wholesale network of anti-tuberculosis drugs are considered. For this:

- the structure of the storage area for drugs of different classification and legal groups is defined (Fig. 3);
- the structure of the storage sector of drugs that require a special control regime is shown (Fig. 4);
- the structure of the storage sector for drugs that require the appropriate temperature regime is established (Fig. 5);
- the structure of the sector for storing drugs that require the appropriate temperature regime is outlined (Fig. 6);
- the structure of the hazardous substances storage sector is defined (Fig. 7);
- the structure of the storage sector of drugs of the general group is proposed (Fig. 8);
- the module of the site of drug delivery is determined (Fig. 9);
- the module of the section of prohibited drugs was developed (Fig. 10);
- the author presents the module of the commission area (Fig. 11);
- systematized the module of the drug delivery area (Fig. 12);
- the structure of the quality control area was studied (Fig. 13);
- the responsibility of specialists for the relevant stages of circulation of anti-tuberculosis drugs in the wholesale network has been established (Table 6).

The development of recommendations for the storage of anti-tuberculosis drugs will allow to optimize the storage process and ensure compliance with GSP requirements. A carefully designed and effectively implemented storage system can help prevent losses, improve the efficiency of the supply chain, distribution, and ensure the quality, availability, and availability of anti-tuberculosis drugs.

All drug movements, status changes due to quality control checks must be documented. Only due to this, it is possible to ensure the necessary and continuous monitoring of the movement of drugs of various classification and legal groups, based on the rules of the GSP (Fig. 3).

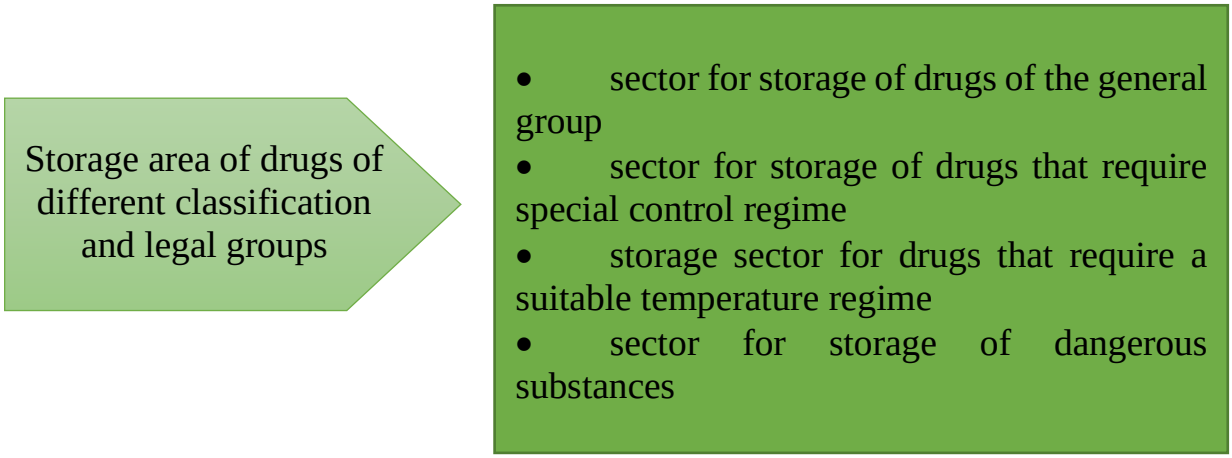

Fig. 3. The structure of the storage area of drugs of different classification and legal groups.
Source: own development

The sector for storage of drugs that require a special control regime. It includes three sections, where drugs of the following classification and legal groups must be stored under appropriate conditions: 1) section of narcotic, psychotropic drugs, and precursor drugs; 2) section of poisonous drugs; 3) section of potent drugs (Fig. 4).

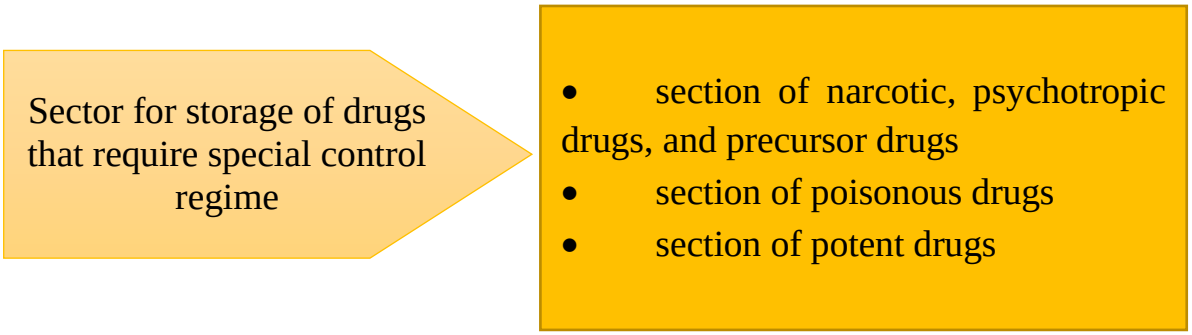

Fig. 4. The structure of the storage sector of drugs that require a special control regime.
Source: own development

The sector for storage of drugs that require an appropriate temperature regime. It consists of eight sections, where drugs should be stored in appropriate conditions, taking into account the physical and chemical properties of the ingredients. Depending on the production features of distribution, this sector may have the following sections:
1) section for storing drugs that require protection from light;
2) section for storing of thermolabile drugs;
3) section for storing drugs that absorb air moisture;
4) section for storing drugs that have volatile properties;
5) section for storing drugs that lose crystallization water;
6) section for storing drugs that require a special temperature regime;
7) section for storing drugs that react with carbon dioxide in the air;
8) section for storing of scented preparations;
9) section for storing of dye preparations (Fig. 5).

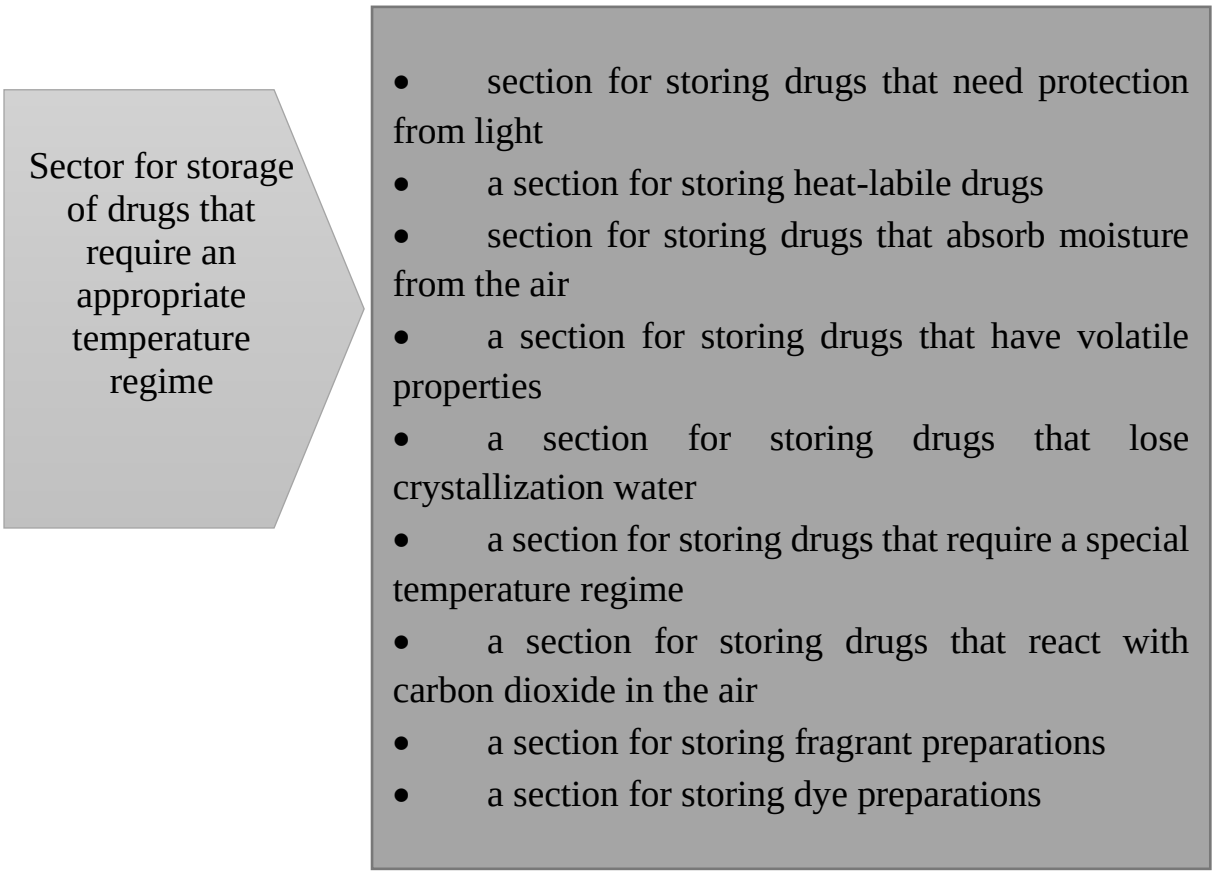

Fig. 5. The structure of the storage sector of drugs that require a suitable temperature regime
Source: own development

In the sector for storage of drugs that require an appropriate temperature regime, the following sections can be separately allocated for the storage of medicinal plant raw materials that require appropriate storage conditions: 1) a section for the storage of medicinal plant raw materials that contains nutrients; 2) a section for storing medicinal plant raw materials, which contains essential oils; 3) a section for storing medicinal plant material that has an irritating effect (Fig. 6).

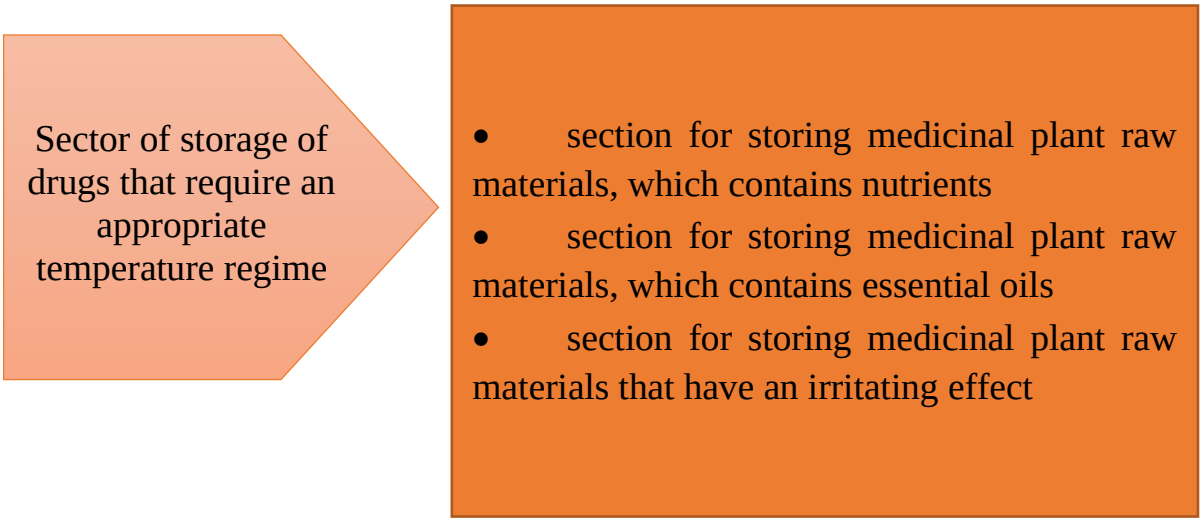

Fig. 6. The structure of the sector for the storage of drugs that require a suitable temperature regime.
Source: own development

The hazardous substances storage sector is organized for the storage of drugs that have flammable and explosive properties. Improper storage and handling of these drugs can cause a fire. In addition to large material losses, it is possible to cause serious damage to the health of employees. Depending on the physical and technical properties of the named groups of drugs, the following sections can be organized:
1) section of flammable substances for storage of flammable and combustible drugs;
2) section of explosive substances for storage of explosive substances and substances capable of forming explosive mixtures or compressed gases (Fig. 7).

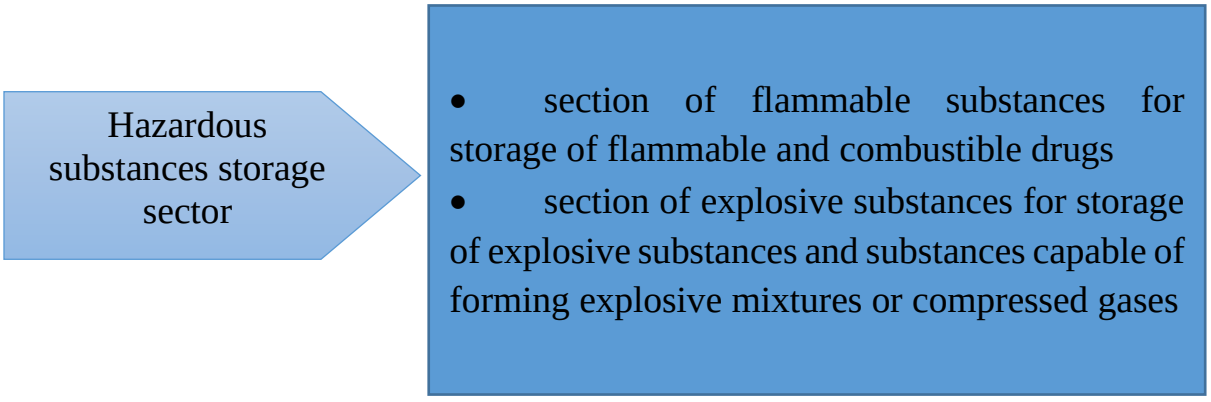

Fig. 7. Structure of the hazardous substances storage sector.
Source: own development

The drug storage area of different classification and legal groups (Fig. 2), which consists of the corresponding drug storage sectors (Fig. 3), in turn, has the necessary drug storage areas in each sector. The structure of the storage sector on the example of drugs of the general group is shown in Fig. 8.

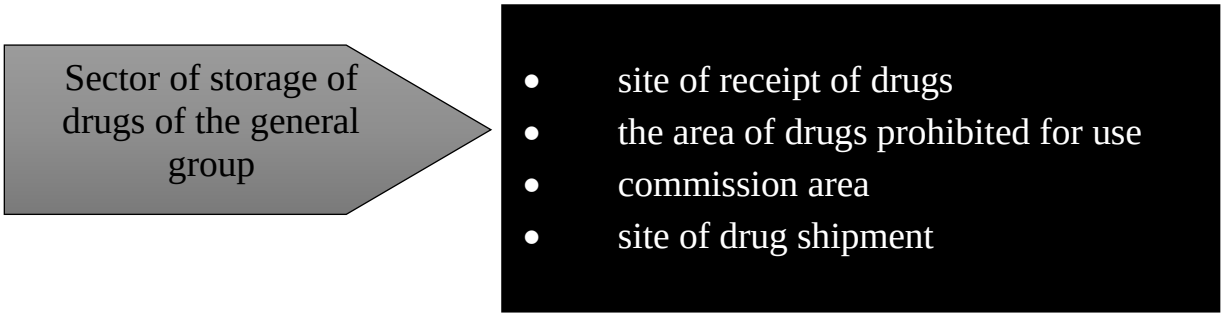

Fig. 8. Structure of the storage sector of drugs of the general group.
Source: own development

The same structure (Fig. 8) has the storage sectors of drugs of other classification and legal groups. Let's consider the tasks performed by the corresponding areas of drug storage in accordance with GSP requirements.

- Area of entry of drugs (Fig. 9):
- coverage of all quantitative data of one incoming batch;
- production of labels for packages (package means the smallest, fully packed unit on a pallet) and drawing up a sampling plan;
- if necessary, removal from pallets;
- provision of warehouses and storage areas;
- is always potentially quarantined.

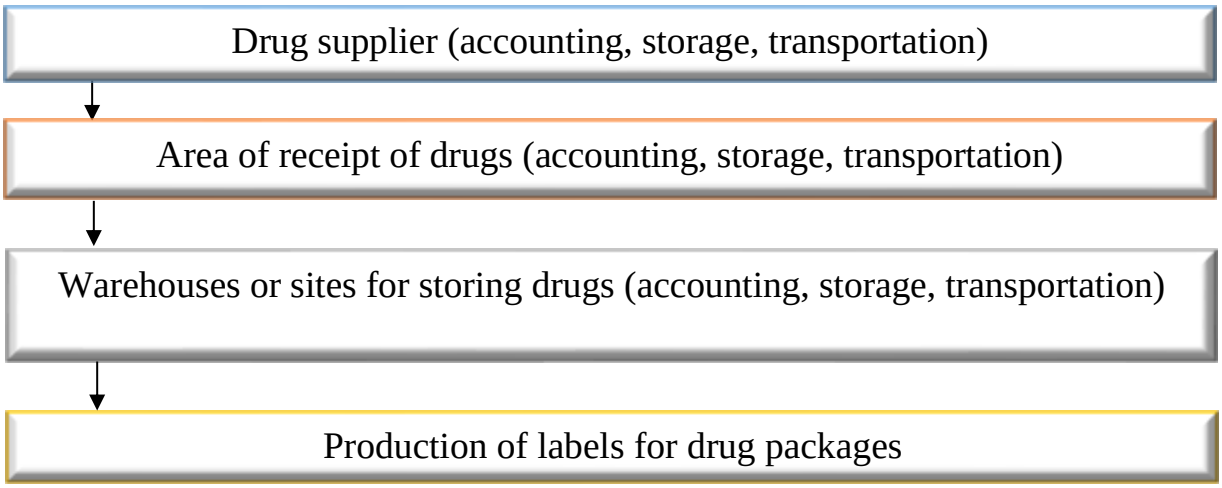

Fig. 9. The module of the site of receipt of drugs.
Source: own development

- The area of drugs prohibited for use (Fig. 10):
- intermediate place of storage of rejected drugs;
- quarantine sector – a separate room with warning instructions and limited access;
- storage of drugs that do not meet the specifications (advertised products or those that are returned, products with an expired shelf life, etc.).

- Commission area (Fig. 11):
- selection of drugs according to the order control regime for delivery to the applicant;
- cooking only if there is a written order;
- clear, unmistakable labeling of all packages;

➢ in case of need – special packaging for drugs with the appropriate control regime and storage conditions;
➢ documentation of order processing.

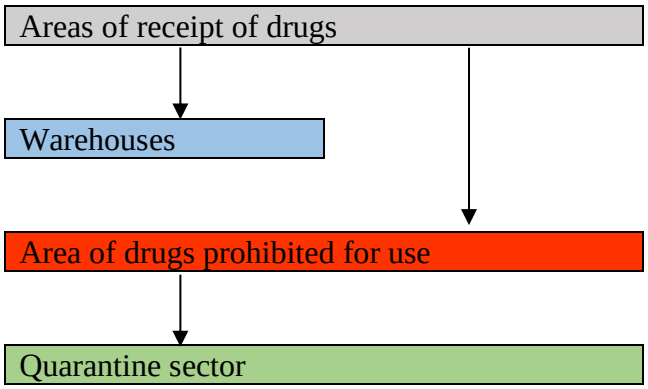

Fig. 10. Module of the area of prohibited drugs.
Source: own development

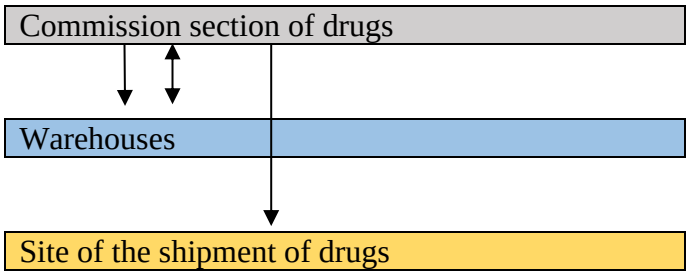

Fig. 11. Commission site module.
Source: own development

➢ Drug delivery area (Fig. 12):
➢ only approved for use "free" drugs can enter this area.

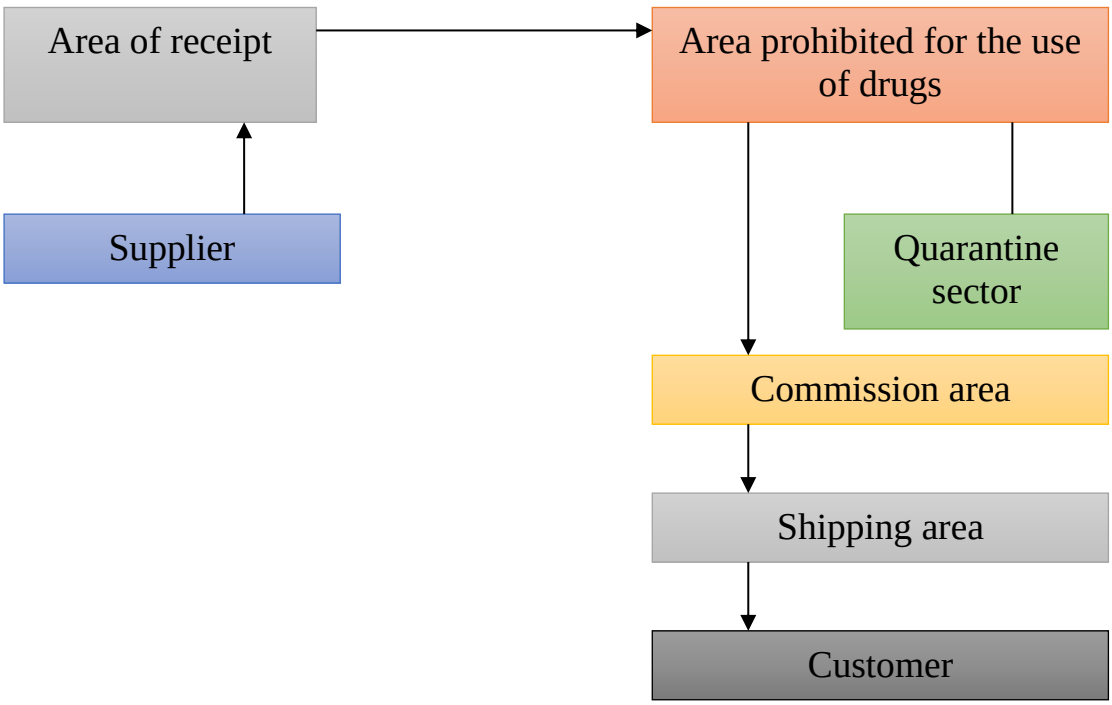

Fig. 12. The module of the drug delivery site.
Source: own development

The first quality control of drugs begins with the performance of incoming control and sampling. The incoming control of drugs begins with a check for compliance with the specifications and other enclosed documents with which the drugs entered the wholesale network. At the same time, all drugs receive a specific designation and the status of "quarantine".

Quarantine is the status of drugs isolated physically or in another effective way, until a decision is made to resume their circulation or remove them from circulation with further utilization or destruction. In case of doubt about the quality of the drugs during the input control, the authorized person takes samples of the drugs and sends them for laboratory tests. At the time of conducting such studies, until the final resolution of the question of their quality, a series of drugs is in quarantine, isolated from other drugs, with the designation "Release prohibited until separate order." Sampling should be carried out in suitable premises, with appropriate equipment and suitable equipment. After sampling, they are sent to the quarantine area of the storage. After, in accordance with the quality control, a permit for use in the retail network will be issued, drugs from the quarantine sector are transferred to the drug transfer sector. If there is a validated warehouse management system with the help of a computer, then you can abandon the quarantine zone in the middle of the warehouse. In this case, only the data record of the corresponding cargo unit will change to "free". Commissioning of drugs occurs only if there is a commission list. For this, an appropriate number of samples are selected for research and, in case of a positive conclusion, sent to the transmission sector.

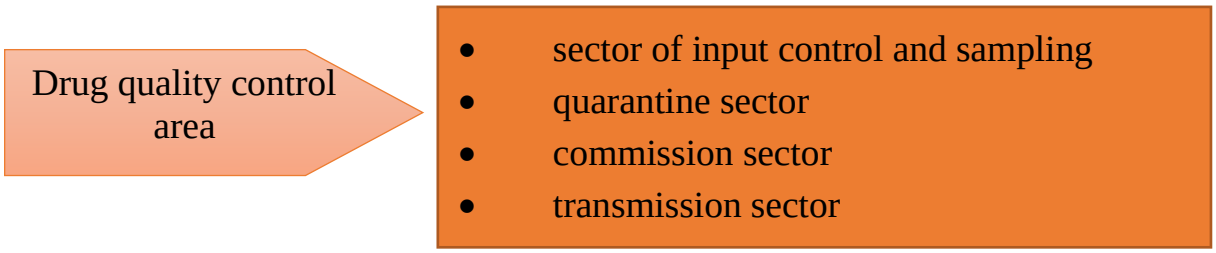

Fig. 13. Structure of the drug quality control zone.
Source: own development

As soon as the drugs have received permission to leave, they are transported to the shipping warehouse (shipping area, Fig. 2).

According to the degree of automation of the wholesale network (full automation or manual) and its management system (using a computer or manually), quarantined or ready-to-ship drugs can be stored in their own premises, in the areas of one large warehouse or in open areas.

In the commission area, according to the written order, preparations are being prepared for shipment. Medicines must have protective packaging, clear and unambiguous labeling.

The same principles apply to transportation conditions as to storage conditions, which means that drugs that must be stored refrigerated must also be transported refrigerated. In this case, the conditions during transportation are documented continuously in the same way as the conditions during storage.

Special responsibility for compliance with GSP regulations rests on the qualification of personnel employed at the stage of storage and at the stage of transportation, who must have appropriate qualifications in the specialty and practical work experience. All employees must occupy jobs only in accordance with the level of their education and qualifications, regularly undergo appropriate training, advanced training courses on the fulfillment of GSP requirements on the basis of pharmaceutical law (Table 6).

Table 6. The responsibility of specialists for the relevant stages of circulation of anti-tuberculosis drugs in the wholesale network.

Management personnel	**Responsibility for:**

Head of the production area	Material locks and intermediate warehouse in production, designation, assigned leaflets
Head of the warehouse	Entry and exit of goods, designation, storage process
Head of the quality assurance department	Sampling, issuing status, marking
Head of the sales department	Movement of goods, compliance with advertising slogans and conditions of transportation

Source: own development

The study showed the following results according to the third task of work on the development of recommendations for the storage of anti-tuberculosis drugs and the analysis of the storage of anti-tuberculosis drugs:

- Storage structure for antituberculosis drugs has been developed, which takes into account different classification and legal groups of drugs and GSP requirements. This contributes to increasing the effectiveness, quality, safety, and availability of these drugs.
- Separate storage sectors are defined, such as sectors for drugs that require a special control regime, appropriate temperature regime and dangerous substances. This contributes to the optimal organization of storage and ensures compliance with regulations.
- Modules have been developed for each section of drug circulation, including receipts, prohibited drugs, commission section and dispatch. This helps to optimize the process of drug management and ensures their quality and safety.
- The responsibility of specialists for each stage of circulation of anti-tuberculosis drugs in the wholesale network has been determined. It helps systematize the management process and ensures compliance with regulations and quality standards.

Conclusions. The general conclusions of the article indicate a significant contribution of each stage of research to the systematization and analysis of aspects of the administration of drugs for the pharmacotherapy of tuberculosis, taking into account various classification systems and legal norms. Three stages of research into the administration of anti-tuberculosis drugs were conducted. During the first stage of the research, an analysis of international and national standards related to anti-tuberculosis drugs was carried out. This analysis made it possible to obtain an objective view of the requirements and the regulatory context of their use and circulation. At the second stage of the study, the peculiarities of the harmonization of national GxP standards were studied. The main material flows of the administration of anti-tuberculosis drugs are analyzed. This made it possible to determine the key issues of ensuring the quality and safety of drugs in the process of their circulation. At the third stage of the study, recommendations for storage and quality control of anti-tuberculosis drugs were developed. These recommendations take into account different classification and legal groups of drugs comply with GSP requirements. Contribute to improving the effectiveness, quality, safety, availability of anti-tuberculosis drugs in pharmacotherapy.

Conflict of interest. The author confirms the authorship of this work and have approved it for publication. The author also certify that the obtained data and research were conducted in compliance with the requirements of moral and ethical principles based on the medical and pharmaceutical law, and in the absence of any commercial or financial relationships that could be interpreted as a conflict or potential conflict of interest.

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