Chapter I: Concept of state system structure in drug quality control.

Objectives

- Exploring the state system structure in drug quality control
- Examining quality management systems in the pharmaceutical industry
- Understanding the role of pharmacopoeias
- Developing knowledge of quality documentation and standards

1. Introduction

Every medicine is characterized by special requirements of efficiency and safety, which determine its quality. High-grade medicines and their active substances always comply with all regulatory requirements. Medicine quality control is carried out during the whole manufacturing process (at every stage), also when releasing the drug on the market and during its circulation there.

2. Concept of state system structure in drug quality control

The concept of state system structure in drug quality control refers to the organization and management of quality control processes for drugs. This includes the establishment of protocols and procedures for testing, analysis, and evaluation of drug products to ensure that they meet the required standards for safety, efficacy, and quality. The state system structure may involve the use of various analytical techniques and technologies, such as chromatography, spectroscopy, and microbiological methods, as well as the implementation of quality management systems and regulatory frameworks to monitor and control drug quality throughout the entire supply chain. The ultimate goal of the state system structure in drug quality control is to safeguard public health by ensuring that drugs are safe, effective, and of high quality.

3. Quality management systems

The process of standardization and quality control is implemented in three main areas: identification of medicines, purity assessment (absence of impurities) and assay. Drugs quality indicators together with the methods of their analysis are stated in special regulatory

documents (RD). The main one is Pharmacopoeia. There are other several quality management systems used in drug quality control. Here are a few examples:

3.1. **Good Manufacturing Practice (GMP):** GMP is a set of guidelines that ensure that pharmaceutical products are consistently manufactured and controlled according to quality standards. GMP covers all aspects of the manufacturing process, including the facilities, equipment, personnel, documentation, and procedures.

3.2. **International Organization for Standardization ISO 9001**: ISO 9001 is a quality management system standard that can be applied to any industry, including the pharmaceutical industry. ISO 9001 provides a framework for implementing a quality management system that focuses on customer satisfaction, continuous improvement, and the prevention of defects.

3.3. **Pharmacopeial standards:** Pharmacopeial standards are a set of standards for the identity, strength, quality, and purity of drugs and drug ingredients. These standards are developed by organizations such as the United States Pharmacopeia (USP) and the European Pharmacopoeia (Ph. Eur.) and are used by regulatory authorities and pharmaceutical companies to ensure the quality of drugs.

3.4. **The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines**. The ICH is a global organization that brings together regulatory authorities and the pharmaceutical industry to develop and harmonize guidelines for the development, registration, and post-approval of pharmaceutical products. The ICH guidelines provide a framework for ensuring the quality, safety, and efficacy of drugs by establishing standards for the design, conduct, and reporting of clinical trials, as well as for the manufacturing and quality control of drug products. The guidelines cover various aspects of drug development and quality control, including stability testing, impurity testing, analytical methods validation, and risk management. By implementing the ICH guidelines, pharmaceutical companies can ensure that their products meet the required standards for quality and safety, and regulatory authorities can rely on a common set of standards for evaluating drug products.

4. Common approaches for quality control of drugs : Pharmacopoeia

Pharmacopoeia, or pharmacopoea1 (literally,"drug-making"), in its modern technical sense, is a book containing directions for the identification of samples and the preparation of

compound medicines It is published by the authority of a government or a medical or pharmaceutical society. Descriptions of preparations are called ***monographs***.

Pharmacopoeia is a collection of official documents (standards and regulations) that sets quality standards for pharmaceutical substances (active pharmaceutical ingredients – API), excipients, diagnostic and medicinal products in different pharmaceutical forms. The provisions of Pharmacopoeia are based on the achievements of pharmaceutical chemistry and pharmaceutical analysis, its criteria, methods and techniques.

Pharmacopeia has two main sections: **general chapters and specific monographs**.

Monographs: A detailed written study of a single specialized subject or an aspect of it.

Specific monographs. Specific monographs are devoted to individual substances or finished dosage forms of medicines (USP, JP).

Pharmacopoeia monograph is the standard of quality for specific (individual) drug.

The general chapters contain information about the methods of analysis, reagents, etc. For example, there are a lot of general chapters in Ph.Eur: Methods of Analysis (Apparatus. Physical and physicochemical methods. Identification. Limit tests. Assays. Biological tests. Biological assays) – Methods in pharmacognosy – Pharmaceutical technical procedures – Materials for Containers–Allergen products – Dosage Forms – Essential oils – Extract – Herbal drugs – Products of fermentation – Radiopharmaceutical preparations – Recombinant DNA technology – Substances for pharmaceutical use – Vaccines for human – Vaccines for veterinary use – Vegetable fatty oils.

4.1.The State Pharmacopeia

The State Pharmacopeia is the official document, which is under state supervision and its requirements are mandatory for all institutions in the state, engaged in the manufacture, storage and use of medicines, including herbal (medicinal plant materials).

In the world pharmaceutical practice, the recognized leaders among the pharmacopoeias are the **Pharmacopoeia of Europe, the United States pharmacopoeia and Japan pharmacopoeia**.

The Convention developed and the circle of members Pharmacopoeia expanded. Today its membership includes 36 countries and 22 observers. Russia has observer status. Members of *the European Pharmacopoeia Commission are:*

Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, the former Yugoslav Republic of Macedonia, Turkey, United Kingdom and the European Union.

The observers to the European Pharmacopoeia Commission are:

Albania, Algeria, Australia, Belarus, Brazil, Canada, China, Georgia, Israel, Madagascar, Malaysia, Morocco, Republic of Kazakhstan, Russian Federation, Senegal, Syria, Tunisia, Ukraine, United States of America and WHO (World Health Organization).

Pharmacopoeia of Europe: Now a new Ph. Eur. edition is published every three years and additional Updates – every few months. The 7th edition of Ph. Eur. has come into force since 2011. The European Pharmacopoeia has a classic structure. But its peculiarity is that, unlike the USP and BP, it does not contain monographs for dosage forms. It presents the monographs only for substances. The European Pharmacopoeia is published by the Directorate for ***the Quality of Medicines & HealthCare of the Council of Europe*** (EDQM). Commission of European Pharmacopoeia, which includes all members and observers, also regulates work on Ph. Eur. Its functions include the work program adoption, definition of expert groups as well as pharmacopoeia texts approval.

After each monograph has been approved, special group of experts regulates it. The proposals from national delegations, expert groups, and pharmaceutical industry representatives replenish Ph. Eur. The decision on new monograph inclusion depends on the therapeutic effect of drug, widespread of it use, on the number of countries that have approved it and on its proven quality.

United States pharmacopoeia: The first edition of the United States Pharmacopoeia – National Formulary (USP – NF) was published in 1820. Current edition is USP 42-NF 37 (2019). It came into force on May 1, 2011. This is the most dynamically developing Pharmacopoeial standard. This document, as its name implies, is really a collection that

includes two different standards: Pharmacopeia and National Formulary. The latter pertains to some excipients and other substances that are not drugs.

Japanese Pharmacopoeia (JP): JP is another leading international pharmacopoeia. The new edition is published every five years. Current edition (JP 17) came in 2016. JP is published not only in Japanese but also in English.

British Pharmacopoeia (BP): BP has been published since 1864, the current edition – BP 2019. BP operates in the United Kingdom simultaneously with the European Pharmacopoeia. BP monographs for substances are practically the same as the corresponding Ph. Eur. monographs. BP also contains monographs for finished dosage forms of medicines.

4.2.Harmonization of pharmacopoeias

Increased facilities for travel have brought into greater prominence the importance of an approach to uniformity in the formulae of the more powerful remedies, in order to avoid danger to patients when a prescription is dispensed in a different country from that in which it was written. The first attempts were made by international pharmaceutical and medical conferences to settle a basis on which an international pharmacopoeia could be prepared, but due to national jealousies and the attempt to include too many preparations nothing has yet been achieved.

Globalization processes indicated the need for harmonization of medicines quality requirements. Harmonisation of various countries pharmacopoeia requirements is determined by ICH (www.ich.org) – the International Conference on Harmonization of Medicines Quality and the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. The World Health Organization and three leading Pharmacopeias (Ph. Eur, USP, and JP) are directly involved in ICH activity. The purpose of ICH is to develop common requirements for standardization, quality control, efficiency, safety, production and registration of medicines. Representatives from three leading Pharmacopoeias meet twice a year since 1990 in the Pharmacopoeial Discussion Group to try to work towards «compendial harmonisation»'. Specific monographs are proposed, and if accepted, proceed through the stages of review and consultation. Adoption of a common monograph provides a common set of tests and specifications for a specific material. Not surprisingly, this is a slow process

5. Order of development of technical documentation of standards in pharmacy

The order of development of technical documentation of standards in pharmacy generally follows the same steps as described earlier. Here are the general steps:

5.1. Identification of the need: The first step is to identify the need for a standard in a specific area of pharmacy, such as manufacturing, quality control, distribution, use, or disposal of drugs.

5.2. Development of the draft standard: Based on the identified need, a draft standard is developed. This draft describes the objectives, scope, definitions, requirements, and recommendations for the specific area of pharmacy concerned.

5.3. Consultation: The draft standard is then subjected to consultation with relevant stakeholders, such as manufacturers, regulators, pharmacists, healthcare professionals, patient associations, and consumers. Comments and suggestions are gathered and taken into account to improve the draft standard.

5.4. Revision: Based on the received comments, the draft standard is revised and modified if necessary to reflect the concerns and comments of the stakeholders.

5.5. Adoption: Once the draft standard is finalized, it is submitted to a vote by the members of the standardization committee for adoption**.**

5.6. Publication: Once adopted, the standard is published and made available to the public. It can be used as a reference for the pharmaceutical industry, regulators, healthcare professionals, and patients.

5.7. Update: Like all standards, pharmaceutical standards are regularly reviewed and updated to reflect technological advancements and changes in industry requirements. Updates are generally made according to a defined schedule and after consultation with relevant stakeholders.

These steps may vary depending on the specific needs of the pharmaceutical industry and the procedures followed by the standardization body responsible for its development.