Drug Chemistry and Technology Basics,
Cleaner Production and Mega-Trends in Pharmaceutical Industry

# Quality Assurance in Medicines

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# Questions

1. Are there any differences between counterfeit drugs and substandard drugs? Which type is more dangerous in your opinion?
2. Define counterfeit medicine and discuss how it can be identified
3. How can the production and marketing of counterfeit medicines be stopped?
4. *Drug abuse is considered a major social problem. What types of drugs are normally abused? Give a couple of examples from each type

# LECTURES

1. Introduction
2. Terminology of Drugs
3. Drug Design and Quality standards
4. Falsification of Medicines
5. Quality Assurance in Medicines
6. Control by Pharmacopeias
7. Trends in Pharmaceutical Industry

# Quality Assurance in Medicines

The development, production and use of drugs **is controlled by the state**

**Authorized agencies of the state** implement the state policy in the field of circulation of drugs by means of:

- ✓ state registration of medicinal products
- ✓ licencing of pharmaceutical activity
- ✓ medicinal product quality control system
- ✓ pharmacovigilance system
- ✓ supervision over conditions of commercial production, pharmacy manufacture, sale, storage, transportation and medical use in health care organisations of medicinal products
- ✓ withdrawal from circulation of low-grade and counterfeit medicinal products
- ✓ exercise of other functions provided for by the legislation of the state

# Authorized Agencies

**The European Medicines Agency (EMA)** is a European Union agency for the evaluation of MP

*Prior to 2004, it was known as the European Agency for the Evaluation of MP (**EMEA**)*

**The Food and Drug Administration (FDA or USFDA)** is a federal agency of the United States Department of Health and Human Services.

*The FDA is responsible for protecting and promoting public health through the regulation and supervision of food safety, tobacco products, dietary supplements, drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, cosmetics etc.*

# Quality Assurance in Medicines

**Fundamental principles of the state policy in the field of medicinal product (MP) circulation:**

- ✓ **state regulation of the medicinal product circulation;**
- ✓ **availability of medicinal products;**
- ✓ **support to and development of international cooperation**

# Availability of Medicinal Products

… an essential condition for provision of the population with timely medical assistance

The state shall ensure availability of MP by means of:

- ✓ the most complete saturation of **the internal market with safe, effective** and **quality MP**, in the first place those included in the list of main medicinal products

- ✓ improvement of the MP distribution system

# State Registration of Medicinal Products

MP may be produced, sold and used
in the territory of the state after their
**state registration (confirmation of state registration)**

… the procedure for recognition of the MP compliance with the requirements to its safety, efficiency and quality conducted for the purpose of permission of the **commercial production**, **sale** and **medical use** of the MP manufactured **in the state**, as well as **sale** and **medical use** of the MP **supplied from abroad**

# State Registration of Medicinal Products

State registration **IS NOT REQUIRED** for:

- ✓ MP manufactured in **pharmacies**
- ✓ MP intended for use as **exhibition samples**
- ✓ MP intended for conduct of **non-clinical studies** and **clinical trials**
- ✓ MP brought to the territory of the state by a natural person **for personal needs**
- ✓ MP intended for commercial production **for export only**
- ✓ pharmaceutical substances, if the master files for MP that have such pharmaceutical substances in their formulation contain documents issued by manufacturers of these pharmaceutical substances complying with the requirements set for the documents being a part of the master file

# State Registration of Medicinal Products

**Medicinal plant raw materials** are subject to state registration as a medicinal product after passing the stage of production process of creation of a certain dosage form

**State registration (confirmation of state registration)** of medicinal products is carried out by **authorized agencies of the state**

For state registration (confirmation of state registration) of a medicinal product the applicant submits **the master file** (registration dossier)

# The Master File

… documents submitted by the applicant for state registration (confirmation of state registration) of the MP and constraining information about safety, efficiency and quality of the MP, as well as about the posted price of the MP, other documents defined by authorized agencies of the state

# The Marketing Authorisation

A registered MP is entered into **the State Register of MP**

**Marketing authorisation** with a 3–5 year validity period is issued for the MP registered in the state for the first time

**Marketing authorisation** – a document issued for the MP based on the results of the conducted state registration (confirmation of state registration)

**Registration number** – a coded identification assigned to the MP based on the results of the state registration

# The Marketing Authorisation

Upon expiration of the marketing authorisation validity the MP must pass the procedure of **confirmation of state registration**

**Validity of the marketing authorisation IS CANCELLED** in the following cases:

- ✓ expiration of validity of the marketing authorisation issued for the term of 3–5 years
- ✓ non-elimination, by the applicant, of circumstances that entailed suspension of the marketing authorisation
- ✓ the applicant's refusal to conduct clinical trials of the MP prescribed by the authorized agency
- ✓ the applicant's submission of application for termination of the marketing authorisation

In case of any changes in the information contained in the documents included in the master file the master file is amended accordingly

# The medicinal product quality control system

The quality of the MP of **domestic manufacture** is determined by its compliance with:

- ✓ the requirements of the manufacturer's pharmacopoeial monograph
- ✓ pharmacopoeial monographs of the State Pharmacopeia

The quality of the MP of **foreign manufacture** is determined by the compliance with:

- ✓ the requirements of the regulatory document of its manufacturer containing the indicators and methods used for quality control of the MP (the manufacturer's regulatory document)

The quality of MP manufactured **in pharmacies** is determined by their compliance with:

- ✓ the requirements of the State Pharmacopeia

# The medicinal product quality control system

**The MP of domestic manufacture** **non-complying** with the requirements of the manufacturer's pharmacopoeial monograph, pharmacopoeial monographs of the State Pharmacopeia, as well as **the MP of foreign manufacture** **non-complying** with the requirements of the manufacturer's regulatory documents are recognized as **LOW-GRADE**

# Quality of a Medicine

… is compliance of a medicine with the requirements of the pharmacopoeia monograph or, in case of non-availability of the latter, of the normative documentation or normative document

**Normative documentation** is a document containing a list of quality characteristics and quality control methods for a medicine for medical use as determined under the relevant expert examination results, established by the manufacturer

**Drug quality standard** – a normative document containing a list of **regulated indicators** (quality characteristics, critical indexes, quality indexes, Q-factors) and methods of quality control of drugs

# Drug quality standards

## Drug quality standards:

1. State Pharmacopeia
2. pharmacopoeial monograph
3. the manufacturer’s pharmacopoeial monograph
4. state standard

# Drug quality standards

Each batch of the registered MP before being placed into sale, as well as medicinal products available in circulation are subject to quality control in **testing laboratories accredited in the accreditation system of the state** for the purpose of MP tests

In Belarus:

**The Center for Examinations and Tests in Health Service State Enterprise** http://www.rceth.by/en

# The pharmacovigilance system

… a set of measures aimed at timely detection of all changes in **the risk and benefit ratio** of the MP, as well as at **minimisation of negative consequences** of their use

… supervision during a fourth step of clinical trials (connected with GPP)

MP **manufacturers**, as well as **medical and pharmaceutical officers** must **provide information** about detected adverse reactions, including side reactions, of the MP in accordance with the procedure defined by the authorized agencies

# The pharmacovigilance system

**Main tasks of supervision** over conditions of *commercial production, pharmacy manufacture, sale, storage, transportation and medical use* in health care organisations of MP are **prevention** of coming into circulation and **timely withdrawal** from circulation of **LOW-GRADE** and **COUNTERFEIT** MP, their destruction or return to the manufacturer or the supplier in order to provide the population and public health organisations with **safe, efficient and quality MP**

# Thank You !

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