SCIENTIFIC JUSTIFICATION OF THE ORGANIZATION OF COMBINED AND SEPARATE PHARMACEUTICAL MANUFACTURES OF PARENTERAL MEDICINAL FORMS

In the process of creation and industrial production of innovative or generic drugs, business needs or state requests are transformed into specific technical and organizational solutions.

Volumes and target sales markets with their rules of the game will determine not only the production capacity, the level of technical execution, but also the mode of organization of pharmaceutical production based on permissible combinations of products. The suitability of pharmaceutical products for the production site, and the site for products of parenteral dosage forms, is a vital scientific and practical problem for conducting pharmaceutical business, which requires scientific justification.

Ensuring the quality of the technological process of pharmaceutical product production in the conditions of compatible and separated productions is subject to the requirements defined by the international regulatory and normative documents of the FDA, EMA, EMEA/PIC-S. The regulatory requirements regulated by ICH Q9 regarding the concept of risk assessment and the GMP Guideline on Good Manufacturing Practice necessitate the identification of pharmacotoxicological characteristics, determination of physico-chemical and technological properties of active pharmaceutical ingredients. For the practical adaptation of the regulatory requirements of ICH Q9 with the cooperation of representatives of the pharmaceutical industry, consultants and regulators in the ISPE RiskMaPP Baseline® Guide – Risk-Based Manufacturing of Pharmaceutical Product, a holistic approach to the management of risks caused by the properties of active pharmaceutical ingredients (API) for the patient is proposed, producers and the environment.

The modern level of technology development allows to reliably prevent cross-contamination even with combined production, however, to ensure the quality of the pharmaceutical product, the problem of monitoring the cleaning of technological equipment also requires scientific justification.

Mass serial pharmaceutical production developed in the second half of the 20th century; the history of research on pharmaceutical cross-contamination takes its cue from the first American
regulatory documents of GMP, from 1963, in which the very concept of cross-contamination was not defined. In those days, for drugs produced by the pharmaceutical industry, there was a need to establish strict limits and measures to prevent the undesirable impact of cross-contamination on the quality of pharmaceutical products (for example, the production of penicillin) as a result of inadequate cleaning of shared equipment from residues of APIs when switching to another product or air migration of particles of different APIs in the production of different products at the same site were just discussed by regulators and experts of the pharmaceutical industry [3].

With the development of industrial pharmacy, the phenomenon of cross-contamination became an objective scientific and practical problem in the conditions of the application of compatible productions, which required scientific justification and solution.

Over the past decades, cross-contamination, i.e. contamination of raw materials or products with other raw materials or API of another pharmaceutical product, has become the most important subject of inspection and the key reason for established non-conformities.

EU standards, GMP and PIC-S GMP harmonized with it, provide the wording of clause 3.6: "Manufacturing of some other products, such as specified antibiotics, specified hormones, cytotoxins, specified highly active medicinal products and products for non-medical purposes, should not be carried out using the same and the same technical means, for such products, in exceptional cases, the principle of production based on the implementation of processes can be applied with the help of the same technical means, if special measures are taken and the necessary validation is carried out" [3].

Therefore, the implementation of a systematic analysis of regulatory requirements and best practices of industrial pharmaceutical enterprises is a primary task when designing new productions of ready-to-use dosage forms (MSF), or preparing them for successful GMP audit.

Solving the problem of improving the organization of combined and separate pharmaceutical production of parenteral medicinal forms, in the conditions of innovative development of the enterprise, requires new methodological and organizational approaches [4; 5; 6].

Among scientists and industry experts, the vast majority are supporters of a clear list and concept of risk assessment based on ICH Q9. Since the EMEA / PIC-S area is home to almost half of the world's pharmaceutical production, the impact of the final wording of p. 3.6, 5.18, 5.19 on the further development of industrial pharmacy is difficult to overestimate [7; 8].

Regulatory bodies do not provide an unambiguous judgment on the topic of coexistence in separate production of heterogeneous highly active substances. The business of transnational giants may be interested in stricter requirements for the segregation of pharmaceutical productions in order to increase entry barriers for generic companies.

The balance between risks and benefits is the key idea behind best practices, the choice of research design for pharmaceutical development and implementation in production, ensuring the quality of the technological process.

Based on the study of the physico-chemical and toxicological properties of API and its mechanism of action, a holistic approach to risk management of pharmaceutical production of highly active drugs allows choosing a scientifically based strategy for their control, saving time and investment for the benefit of the patient and society as a whole.

References:


