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EUROPEAN PHARMACOPOEIA OF 8-TH EDITION: MAJOR CHANGES IN THE CHAPTER «VACCINES FOR VETERINARY USE» (review)

The basic changes and improvements that have occurred in the chapter "Vaccines for veterinary use" of the last, 8-th edition of European Pharmacopoeia has been shown. Developed the general criteria of acceptability which are not repeated in the articles for each vaccine and are applied to all vaccines, even if for there is no certain vaccines separate article. Significantly reduced the number of animals used for testing. In connection with the entry Ukraine's membership in the European Pharmacopoeia Commission, this document is intended to play an important role in improving the normative and legislative base for the production and quality control of domestic veterinary immunobiological products.

***Keywords**: European Pharmacopoeia, vaccines for veterinary use, harmonization, quality.*

Introduction. European Pharmacopoeia (EP) is the governing document used in most European countries in the manufacture of pharmaceutical products. EP consistent with the provisions of the International Pharmacopoeia and specifies their characteristics in relation to European countries. Pharmacopoeia includes a description of active and supplementary, as well as methods of analysis of pharmaceutical products [1–4].

European Pharmacopoeia set up by the Convention and developed by the European Directorate for the Quality of Medicines Health Care (EDQM), which is part of the Council of Europe (Strasbourg, France) [5]. EP first edition published in 1967.

Since the 5th edition, which came into force on 1 January 2005, the EP published in two volumes. Volume 1 contains general sections and pharmacopoeia monograph (for example with dosage forms, methods of analysis, reagents, etc.) Volume 2 contains articles about pharmacopoeia substances.

The eighth edition published EP 1 July 2013 and entered into force on 1 January 2014. Both volumes contain a total of 2,224 monographs and 345 general chapters, illustrated with diagrams or chromatograms and 2500 descriptions reagents. The Commission to develop a European Pharmacopoeia includes 38 countries, namely 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, Slovakia, Slovenia, Spain, Sweden, Switzerland, Macedonia, Turkey, Ukraine, United Kingdom and European Union. EP is the official pharmacopoeia listed countries and the European Union. There may be additional Pharmacopoeia (for example, in the UK and Germany).The Convention is open for signature by all European countries. Other countries have been granted observer.

EP issued in English and France, in addition, there are official translations of the German and Spanish. At present the translation ER Ukrainian. Note that came into force on 11.20.2012, the Law of Ukraine of 16.10.2012, № 5441-VI «On Ukraine's accession to the Convention on the Elaboration of a European Pharmacopoeia as amended by the Protocol to it", according to which Ukraine received the status of member of the European Pharmacopoeia Commission vote. EP requirements are legally binding in the member states of the European Pharmacopoeia Convention.

The goal of the work. Standards of production and quality control, including vaccine preparations should be harmonized with the international requirements, which will promote animal health and the free movement of goods between countries. An important element is the use of total harmonization of control methods provided by EP that should be governing for domestic developers and manufacturers of vaccine preparations. As such we consider it necessary to draw attention to the major innovations that have occurred in the last, 8th edition of EP.

Materials and Methods. Carried out the analysis of the information concerning the changes, those have occurred in the European Pharmacopoeia of 8th edition in the chapter "Vaccines for veterinary use" [1–4].

Results of research and discussion. Last years in Ukraine considerably enlarged the list of registered veterinary means of prevention purposes. This situation requires increased state control over the quality, efficiency and the safety of vaccines for veterinary use.

EP is a document regulating the general methods of control preparations which in turn works in favor of quality assurance. Last EP, the 8th editions in the "Vaccines for veterinary use" gained of certain changes and improvements.

All articles relating to vaccines of veterinary appointments have been revised taking into account the Directive 2001/82 / EC of the European Parliament and the EU Council "On normative legal regulation turnover of veterinary medicinal products in the EU", which refers to all medicines and describes those research that must include in the registration submission dossier to obtain a registration certificate.

Thus, the prompted the new format of order to avoid unnecessary repetition. For that purpose been developed the general criteria of acceptability that do not repeated in monographs for each vaccine and apply to all vaccines, even if is no separate of the monograph for certain vaccine.

Directive 2010/63 / EU on the protection of animals used for scientific purposes raised the issue of replacement, reduction and optimization of use of animals. Improving the of the technological process for the production of veterinary vaccines of what is happening in recent years the introduction of new requirements for the active control during production, control of raw materials, close attention to the preservation and use of the main seed (Master seed lot), and careful calculation of the ratio between risk and benefit – has allowed to remove the requirement to test the safety of each batch of vaccine using sensitive animal species. As a result, significantly reduced the number of animals used for quality control of veterinary vaccines.

But there are three exceptions to this general rule: the vaccine inactivated against actinobacillosis of pigs, vaccine inactivated against atrophic rhinitis of pigs and veterinary appointments vaccines against tetanus, for which saved tests on sensitive types of animals by using 2 doses of vaccine, since these vaccines is inherent risk to safety, that depends on a batch of vaccine. In order to avoid confusion, the name of the test has been replaced by "The determination of the residual toxicity."

At the same time were added provisions that under certain circumstances are allowed to check each batch of vaccines using the sensitive animals. For example, in the case of significant change in the manufacturing process, receiving an unexpected message regarding unwanted reaction or that the final series do not meet the data that were provided at the beginning of the licensing process.

In the general monograph "Vaccines for veterinary use" somewhat weakened the requirements for sterility of vaccines intended for poultry administered orally or via spraying. However, this is only possible on the condition that the vaccine

manufactured by using of fertilized chicken eggs, and if method of storage of the vaccine (in the lyophilized or the frozen) does not allow bacteria to multiply. This the weakening does not apply to the vaccines manufactured by using cell cultures.

Investigation of indicators of impact on the system of reproduction should be described in future cases where the vaccine is intended for breeding animals or if there are significant differences from the data set out in the general monograph.

As explained in the "Technical instructions for the development and use of monographs for immunological veterinary medicinal products", any vaccine of veterinary appointments must conform to requirements the general monograph "Vaccines for veterinary use".

Conclusions and prospects for further research. Thus, EP 8th edition has become an important tool in the hands of domestic developers and manufacturers of vaccine preparations for veterinary purposes. In connection with the entry Ukraine's membership in the European Pharmacopoeia Commission, this document is intended to play an important role in improving the normative and legislative base for the production and quality control of domestic veterinary immunobiological products.

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ЕВРОПЕЙСКАЯ ФАРМАКОПЕЯ 8-ГО ИЗДАНИЯ: ОСНОВНЫЕ ИЗМЕНЕНИЯ В РАЗДЕЛЕ «ВАКЦИНЫ ДЛЯ ВЕТЕРИНАРНОГО ИСПОЛЬЗОВАНИЯ» (обзорная статья) / Блоцкая О.Ф.

Приведены основные изменения и усовершенствования, которые произошли в Европейской фармакопее последнего, 8-го издания в разделе «Вакцины для ветеринарного использования». Разработаны общие критерии приемлемости, которые не повторяются в статьях для каждой вакцины, а применяются для всех вакцин, даже если для определенной вакцины нет отдельной статьи. Значительно уменьшено количество животных, которых используют для тестирования. В связи с входом Украины в члены Европейской фармакопейной комиссии, данный документ предназначен играть важную роль в совершенствовании нормативно-законодательной базы для производства и контроля качества отечественных ветеринарных иммунобиологических препаратов.

Ключевые слова: *Европейская фармакопея, вакцины ветеринарного использования, гармонизация, качество.*

ЄВРОПЕЙСЬКА ФАРМАКОПЕЯ 8-ГО ВИДАННЯ: ОСНОВІ ЗМІНИ В РОЗДІЛІ «ВАКЦИНИ ДЛЯ ВЕТЕРИНАРНОГО ВИКОРИСТАННЯ» (оглядова стаття) / Блоцька О.Ф.

Наведено основні зміни та вдосконалення, що відбулися в Європейській фармакопеї (ЄФ) останнього, 8-го видання в розділі «Вакцини для ветеринарного використання». Розроблено загальні критерії прийнятності, які не повторюються у статтях для кожної вакцини, а застосовуються для всіх вакцин, навіть якщо для певної вакцини немає окремої статті. Значно зменшено кількість тварин, яких використовують для тестування. Разом з тим, було додано положення, що за певних обставин дозволено проводити випробування кожної серії вакцини на чутливих видах тварин. Наприклад, у випадку внесення значних змін в процес виробництва, одержання повідомлень про неочікувані (небажані) реакції, або повідомлень в тому, що кінцеві серії не відповідають даним, що надавались на початку процесу ліцензування.

Стандарти виробництва та контролю якості, в тому числі вакцинних препаратів, повинні бути гармонізовані з міжнародними вимогами, що сприятиме забезпеченню здоров'я тварин та вільному руху продукції між країнами. Важливим елементом гармонізації є використання загальних методів контролю передбачених ЄФ, які мають стати регулюючими для вітчизняних розробників і виробників вакцинних препаратів.

У зв'язку з набранням Україною членства в Європейській фармакопейній комісії, даний документ призначений відігравати важливу роль в удосконаленні нормативно-законодавчної бази щодо виробництва та контролю якості вітчизняних ветеринарних імунобіологічних препаратів.

Ключові слова: *Європейська фармакопея, вакцини ветеринарного використання, гармонізація, якість.*

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