RESOLUTION
of the Ministry of Health of the Republic of Belarus
No. 72 dated May 14, 2015
On approval of instruction on cases and procedure of inspection of industrial production of medicinal products (recognized defective medicinal products) for compliance with the requirements of Good Manufacturing Practice

*(Registered in the National Register of Legal Acts of the Republic of Belarus on June 23, 2015, 8/*30005*)*

On the grounds of sixth part of Article 10 of the Law of the Republic of Belarus “On medicinal products” dated July 20, 2006, third Paragraph of the third part of the first and second parts of Article 4 of the Provision on the order and conditions of the state registration (confirmation of the state registration) of medicinal products and pharmaceutical substances, introduction of changes into the registration dossier approved by Regulation of the Council of Ministers of the Republic of Belarus No. 254 dated April 1, 2015 “On state registration (confirmation of the state registration) of medicinal products and pharmaceutical substances and introduction of changes and additions in Regulation of the Council of Ministers of the Republic of Belarus” No. 1269 dated September 2, 2008”, seventh Paragraph of Sub Article 8.17 of Article 8 and of Sub Article 9.1 of Article 9 of the Provision of the Ministry of Health of the Republic of Belarus approved by Regulation of the Council of Ministers of the Republic of Belarus dated October 28, 2011 No. 1446 “On certain issues of the Ministry of Health and measures on realization of Decree of the President of the Republic of Belarus No. 360 dated August 11, 2011”, the Ministry of Health of the Republic of Belarus RESOLVES:

1. To approve the annexed Instruction on cases and order of inspection of industrial production of medicinal products (recognized defective medicinal products) for compliance with the requirements of Good Manufacturing Practice.

2. This Resolution enters into force following its official publication.

Minister Vasily I. Zharko

APPROVED
Resolution
of the Ministry of Health of the Republic of Belarus
No. 72 dated May 14, 2015

INSTRUCTION
on cases and procedure of inspection of industrial production of medicinal products (recognized defective medicinal products) for compliance with the requirements of Good Manufacturing Practice

CHAPTER 1
GENERAL PROVISIONS

1. This Instruction defines the cases and order of inspection of industrial production of medicinal products and pharmaceutical substances (hereinafter, unless stated otherwise, — medicinal products) for compliance with the requirements of Good Manufacturing Practice (hereinafter, unless stated otherwise, — inspection) during:

carrying out the complex of preliminary technical works related to carrying out examinations, inspections, tests and other investigations preliminary to the state registration (the confirmation of the state registration) of medicinal products, introduction of changes into the registration dossier for a medicinal product previously registered in the Republic of Belarus (hereinafter, unless stated otherwise, — the complex of preliminary technical works);

recognition of defectiveness of a medicinal product registered in the Republic of Belarus (hereinafter — recognition of a defective medicinal product).

2. For the purposes of this Instruction the terms and their definitions are used in the meaning determined by the Law of the Republic of Belarus dated July, 20 2006 “On medicinal products” (the National Register of Legal Acts of the Republic of Belarus, 2006 No. 122, 2/1258) as well as the following terms and their definitions :

Site master file — a document that is compiled by the manufacturer of medicinal products (hereinafter — manufacturer) and contains information on activity of a site and related sites (including the surrounding buildings), stages of industrial production and (or) quality control of medicinal products on every stage of industrial production as well as on politics of the manufacturer in the field of quality of medicinal products;

Discrepancy — a criterion used for the assessment of compliance of industrial production of a medicinal product with Good Manufacturing Practice in case of partial or full revelation of the requirements of Good Manufacturing Practice.

3. The inspection during carrying out the complex of preliminary technical works preceding the state registration (confirmation of the state registration) of medicinal products is conducted in cases when industrial production of a medicinal product (a particular stage of industrial production of a medicinal product in a definite dosage form) is conducted on the site that was not inspected within last 5 years.

The inspection during carrying out the complex of preliminary technical works before the introduction of changes into the registration dossier for a medicinal product previously registered in the Republic of Belarus, due to changes during the production of a medicinal product, is conducted in case of carrying out the production on a new site.

4. The inspection in case of the recognition of a defective medicinal product is conducted in cases, when:

a medicinal product for the first time registered in the Republic of Belarus is recognized defective, the first batch (lot) delivered to the local market;

a medicinal product in two or more batches (lots) is recognized defective during twelve month as of the date of the recognition of a defective medicinal product of the previous batch (lot);

a medicinal product of foreign production is recognized defective in the presence of a similar medicinal product of domestic production, containing the same pharmaceutical substance or a combination of pharmaceutical substances in the same dosage form and dosage;

a recognized defective medicinal product resulted or may result in risk occurrence of industrial production of a medicinal product posing a risk to human life and health.

5. In the presence of two and more remote sites of the manufacturer, the inspection is conducted on all sites, on which different stages of industrial production of the medicinal product in a certain dosage form are conducted.

6. The industrial production of medicinal products is considered compliant with the requirements of Good Manufacturing Practice on condition that during inspection the discrepancies that resulted or may result in a production of a medicinal product posing a hazard to a human, or a defective medicinal product, were not determined. The determination of discrepancies is carried out by methods enabling to document the compliance of industrial production of a medicinal product with the requirements of Good Manufacturing Practice.

7. In a case of rejection or the failure of the possibility to conduct the inspection by the manufacturer in the order and terms determined by this Instruction, the industrial production of a defective medicinal product is considered non-compliant with the requirements of Good Manufacturing Practice.

CHAPTER 2
THE PROCEDURE OF ORGANIZATION AND CARRYING OUT INSPECTION

8. The decision on carrying out inspection in cases determined in Article 4 of this Instruction is accepted by the Ministry of Health of the Republic of Belarus (hereinafter — the MOH) on the basis of the test reports of medicinal products issued by test laboratories accredited in the System of Accreditation of the Republic of Belarus for the tests of medicinal products, taking into account suggestions of the Center for Examinations and Tests in Health Service Republican Unitary Enterprise (hereinafter — Center for Examinations and Tests in Health Service RUE (RUP)) submitted to the MOH within three calendar days after the recognition of a defective medicinal product.

The manufacturer of a medicinal product is notified of the decision taken and terms of carrying out inspection in writing.

9. The inspection is carried out by the Center for Examinations and Tests in Health Service RUE (RUP).

10. The term during which the inspection is conducted should not exceed ninety calendar days with the exception of case envisaged by Paragraph two of this Article.

At the request of the manufacturer, the term of the inspection may be prolonged (postponed) by the MOH up to sixth month on condition that during this term the supplies of other batches (lots) or parts of batches (lots) of the recognized defective medicinal product in the Republic of Belarus will not be carried out.

11. For carrying out inspection, the Center for Examinations and Tests in Health Service RUE (RUP), in consultation with the MOH, forms the inspection team of specialists of the MOH system, the Center for Examinations and Tests in Health Service RUE (RUP) and, as appropriate, involved inspectors (hereinafter — inspectors), appoints the leading inspector, heading the inspection team, as well as confirms the inspection programme.

12. The inspection programme is submitted to the manufacturer of medicinal products preceding the inspection.

13. The inspection includes:

examination of a site master file, documents of the registration dossier and other documents relating to the purposes of this inspection;

visiting the site of carrying out activity on industrial production of a medicinal product;

informing the representatives of the manufacturer by the leading inspector on the beginning of inspection, its purposes and order of conduct;

examination of premises (stock areas) and production, engineering systems, equipment of the site, monitoring of the process of industrial production of medicinal products and control of their quality, monitoring of the activity of workers on working places, responsible person survey, audit of documents and records in compliance with the inspection programme;

acquaintance of the representatives of the manufacturer with preliminary inspection results;

registration of inspection results;

consideration and assessment of inspection results.

As appropriate, inspectors may apply technical facilities, including equipment with sound and videotape recording, filming and photographing, after the written approval of the manufacturer.

CHAPTER 3
DOCUMENTING OF INSPECTION RESULTS, THEIR REVIEW AND ASSESSMENT

14. The inspection results are registered with the help of a report on inspection of industrial production of medicinal products for compliance with the requirements of Good Manufacturing Practice, using the form in accordance with the Annex of the following Instruction (hereinafter — inspection report) that is signed by all inspectors, including the leading inspector.

15. The industrial production of a medicinal product is considered non-compliant with the requirements of Good Manufacturing Practice if it does not meet the condition defined in Article 6 of this Instruction.

In the case referred to in the first paragraph of this Article, based on the results of the inspection within 20 calendar days, the inspection report is submitted to the applicant and (or) to the manufacturer, in which

points 1–6, containing conclusions on inspection results and recommendations for eliminating the determined discrepancies that led to the recognition of industrial production of a medicinal product non-compliant with the requirements of Good Manufacturing Practice, are filled out by the inspectors.

16. In submitting to the leading inspector the data representing the elimination of the determined discrepancies resulted in the recognition of industrial production of a medicinal product non-compliant with the requirements of Good Manufacturing Practice, and (or) data on measures undertaken (planned measures to be taken) aimed at elimination of discrepancies (hereinafter — data on elimination of discrepancies) after one month from the moment of sending inspection report to the applicant and (or) to the manufacturer, during 10 calendar days the leading inspector carries out their review and assessment, by results of which points 7 and 8 of the inspection report are filled out.

17. In the absence, after one month, the data on elimination of discrepancies, and in case of their invalidation, the industrial production of a medicinal product is considered non-compliant with the requirements of Good Manufacturing Practice.

18. Based on the review and assessment of inspection results, taking into account the available data on elimination of discrepancies, the Center for Examinations and Tests in Health Service RUE (RUP) directs:

inspection report within thirty calendar days after carrying out inspection to the applicant and (or) to the manufacturer;

documents related to carrying out inspection of industrial production of a recognized defective medicinal product, including inspection report and data on elimination of discrepancies in the MOH (if available).

19. On the basis of the inspection report and other documents submitted by the Center for Examinations and Tests in Health Service RUE (RUP), the MOH makes a decision on a recognition of industrial production of a defective medicinal product compliant (non-compliant) with the requirements of Good Manufacturing Practice, concerning which, it informs the manufacturer in writing during five calendar days after the date of its adoption.

20. The results of the inspection, conducted within the complex of preliminary technical works, are taken into consideration when registering the conclusion on compliance of a medicinal product, pharmaceutical substance with the requirements of safety, efficacy and quality issued by the Center for Examinations and Tests in Health Service RUE (RUP) in the order established by legislation.