Pursuant to Article 85 paragraph 5 and Article 88 paragraph 6 of the Law on Medicines („Official Gazette of Montenegro“ No 56/11 and 6/13), the Ministry of Health hereby issues

RULEBOOK ON MORE DETAILED CONDITIONS AND MANNER OF DETERMINING FULFILLMENT OF CONDITIONS FOR MANUFACTURE OF MEDICINES

(„Official Gazette of Montenegro” No 72/15 from 21 December 2015)

I GENERAL PROVISIONS

Article 1

This Rulebook prescribes in more details conditions to be fulfilled by a legal person manufacturing medicinal products, the manner of determining the fulfillment of those conditions and contents of the manufacturing authorization for medicinal products.

Article 2

Terms used in this Rulebook for natural persons in masculine gender include the same terms in feminine gender.

II CONDITIONS TO BE FULFILLED BY LEGAL PERSONS MANUFACTURING MEDICINAL PRODUCTS

Article 3

Legal person performing manufacturing of medicinal products (hereinafter: manufacturer) shall act in accordance with Guidelines of Good Manufacturing Practice and Guidelines of Good Distribution Practice in terms of introducing and maintaining the pharmaceutical quality system, personnel, premises, equipment, documentation managing, work processes, manufacture, quality control, complaints, products recall, counterfeit medicinal products suspicion, internal monitoring and transport.

Article 4

Manufacturer shall establish and maintain an effective pharmaceutical quality system with clearly defined and documented responsibilities, procedures and risk management measures for activities performed.

In accordance with paragraph 1 of this Article, a manufacturer may conclude a contract with other legal and natural persons to perform certain activities.

Manufacturer shall perform manufacturing activities in a manner assuring that medicinal products, in terms of quality, safety and efficacy, pose no risk to patients’ health.

Article 5

In addition to the person responsible for manufacture with experience and training in the implementation of Good Manufacturing Practice and persons responsible for quality control and for batch release with experience and training in quality control and placing each batch onto the market, a manufacturer shall, depending on the scope and type of an activity, have personnel with experience, knowledge and training in the implementation of Guidelines of Good Manufacturing Practice and Good Distribution Practice.

In performing activities referred to in paragraph 1 of this Article, responsible persons for manufacture, quality control and batch release shall sign a statement on independence in decision-making.
For employees referred to in paragraph 1 of this Article, a manufacturer shall provide initial and ongoing training in the implementation of Guidelines of Good Manufacturing Practice and Good Distribution Practice.

Article 6

Manufacturer shall ensure continuous availability of responsible persons referred to in Article 5, paragraph 1 of this Rulebook.
Manufacturer should have an organizational chart of functional units including units for management, monitoring of the manufacturing process and units for tasks that persons referred to in paragraph 1 of this Article are responsible for.

Article 7

In accordance with Guidelines of Good Manufacturing Practice and Good Distribution Practice, a manufacturer shall, depending on the scope and type of activity, have appropriate premises and equipment for manufacturing of medicinal products in accordance with defined conditions for manufacturing and storage of medicinal products.
In order to prevent cross contamination in manufacturing of the medicinal products, all necessary technical and organizational measures must be taken.
Premises must be clean, dry and maintained within acceptable environmental conditions prescribed for the manufacture and storage of medicinal products.
Premises and manufacturing equipment shall be laid out, designed and operated in a such way as to minimize the risk of error and to permit effective cleaning and maintenance in order to avoid contamination, cross contamination and, in general, any adverse effect on the quality of the medicinal product.

Article 8

In accordance with Guidelines of Good Manufacturing Practice, a manufacturer should have the equipment which is subjected to calibration, appropriate qualification and validation at appropriate time intervals, for which adequate documentation and evidence should be provided.
Manufacturer shall establish and follow appropriate hygiene-health programs including wearing protective and work clothing.

Article 9

All manufacturing operations shall be done according to written procedures and instructions that are in line with principles of Good Manufacturing Practice.
All standard operating procedures, instructions, contracts, records and data shall be documented in paper or electronic form in a legible, clear and unambiguous manner.
All data is recorded at the time of performing each operation and in a manner to ensure traceability of all significant activities or events with a clearly defined time and so to insure monitoring of each batch of a medicinal product.
All activities shall be fully described in the documentation on pharmaceutical quality system and implemented in a manner to keep the identity and quality of the medicinal product.
Selection, qualification and approval of suppliers of starting materials should be documented as part of the pharmaceutical quality system.

Article 10

Repacking of imported medicines into their own packaging and putting Patient Information Leaflet shall be done in accordance with manufacturing authorisation.

Providing additional sticker and enclosing package leaflet shall be done according to regulations on labeling of inner and outer packaging.

Article 11

All deviations from the procedures and manufacturing processes should be appropriately documented and approved.

Each new manufacturing process, or major variation to the existing manufacturing process should be validated.

Article 12

Manufacturer of medicinal products should have a separate department for quality control of medicinal products, headed by a person responsible for quality control of medicinal products.

Manufacturer of medicinal products shall have quality control laboratory appropriately staffed and equipped to carry out the necessary examination and testing of starting materials, intermediates and finished products and packaging materials.

If a manufacturer does not have its own quality control laboratory, it may conclude a contract with one or more quality control laboratories meeting requirements referred to in paragraph 2 of this Article.

Article 13

The manufacturer shall implement a system for recording and reviewing all received complaints together with a system for immediate recalling of medicinal products from the market.

Any complaint concerning a quality defect shall be recorded and investigated by the manufacturer.

Article 14

In accordance with the established program, a manufacturer shall conduct internal controls in order to verify compliance with principles and guidelines of Good Manufacturing Practice, as well as to propose necessary corrective measures.

All internal controls and preventive and corrective measures shall be recorded.

Article 15

Manufacturer of medicinal products derived from blood, radiopharmaceuticals and biotechnology medicinal products should also fulfill specific conditions aimed at reducing risks during the manufacturing process for these medicinal products and in accordance with Good Manufacturing Practice.

III MANUFACTURING AUTHORISATION

Article 16

In addition to conditions defined by the Law, the following data shall be submitted to the Agency for Medicines and Medical Devices (hereinafter: Agency), along with the application for the issuing of manufacturing authorization:

1) evidence on having appropriate premises (proprietary certificate, or lease agreement);
2) lay-out of the space with premises legend, verified by licensed architect;
3) study on meeting minimum technical and construction conditions in the space envisaged for carrying out the activity in question;
4) sanitary approval for carrying out the activity in question;
5) list of equipment and technical data on it;
6) documentation on personnel;
7) plan of the procedure of destruction of medicinal products and a written statement of the applicant on handling of medicinal products which are pharmaceutical waste, in accordance with regulations;
The application referred to in paragraph 1 of this Article shall be submitted on a form published on the Agency's portal.
Manufacturer shall, along with the request for amendments to the manufacturing authorization for medicinal products, submit a description of the amendment with the justification and necessary documentation, and, in case of the request for termination of the authorization, reasons for termination of activities should be stated.
Evidence on payment of the prescribed fees shall be submitted along with the request referred to in paragraphs 1 and 3 of this Article.

Article 17

The Agency shall, based on the application and evidence from Article 16 of this Rulebook, issue a manufacturing authorization.
Evidence on fulfilling conditions for issuing the authorization referred to in paragraph 1 of this Article shall be assessed by the Commission, established by the General Manager of the Agency.

Article 18

Manufacturing authorisation shall contain:

- Logo, name and address of the Agency
- Data on manufacturing authorisation holder
- Description of the manufacturing process or part of the process which the authorisation is issued for
- Name and pharmaceutical form of the medicinal product which the authorisation is issued for
- Headquarters of the manufacturer, manufacturing site, quality control site, and site responsible for batch release
- Data on the person responsible for the manufacture
- Data on the persons responsible for quality control and batch release
- Number and date of the authorisation
- Validity period of the authorisation
- Signature of the responsible person in the Agency; and
- Legal precept.

Article 19

The Agency shall, after the check of conditions fulfillment and at the request of the manufacturer, issue a certificate on the implementation of Guidelines on Good Manufacturing Practice.

The form of certificate of the implementation of Good Manufacturing Practice is published on the Agency's portal.

Article 20

If the Agency finds failure to fulfill principles and guidelines on Good Manufacturing Practice, the Agency shall not issue the certificate and shall inform the competent inspection on it.

IV FINAL PROVISION

Article 21

This Rulebook shall enter into force on the eighth day of its publication in the "Official Gazette of Montenegro".

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Podgorica, 17 December 2015

Minister,
Prof. dr Budimir Šegrt, m.p.