Pursuant to the article 79 of the Law on Medicines ("Official Gazzette of the Republic of Montenegro", No 80/04 and "Official Gazzette of Montenegro", No 18/08), Ministry of Health passes

Rulebook on Content and Manner of Conducting Pharmaceutical Testing of Medicines with the Aim of Quality Control

Rulebook is published in the “Official Gazzette of Montenegro No 4/2010” from 22 January 2010

I GENERAL PROVISION

Article 1

This Rulebook determines in more detail content and manner of conducting pharmaceutical testing of a medicine with the aim of quality control.

II CONTENT AND MANNER OF CONDUCTING PHARMACEUTICAL TESTING

Article 2

Pharmaceutical testing of a medicine with the aim of quality control includes assessment of documentation on quality, laboratory control of a medicine and quality control process performed by the Agency for Medicines and Medical devices (hereinafter: Agency).

Article 3

Documentation on quality of a medicine includes pharmaceutical-chemical-biological documentation, cefrificate of quality control, labelling of a medicine and documentation on eiquipment associated to the medicine..
Documentation from paragraph 1 of this article is assessed by the Agency.
Assessment of documentation from paragraph 2 of this article includes assessment of compliaance of required parameters with specification limits.

Article 4

Laboratory testing of a medicine with the aim of quality control is conducted in accordance with principles of good laboratory practice and applicable testing methods stated and described in parts of documentation for obtaining marketing authorization.
In terms of laboratory tested parameters, a medicine is adequate if testing results remain within specification limits which are valid untill expiration date of a medicine.

Article 5

Specification limits from articles 3 and 4 of this Rulebook must be in compliance with the criteria set out in the European pharmacopoeia, national pharmacopoeia or other recognized pharmacopoeia or proven methods of analysis.

Article 6

Data contained in the certificate of quality control are listed as follows:
1. number, i.e. certificate mark;
2. name of a medicine, (INN) international non-proprietary name of active substance(s);
3. pharmaceutical form, strength, packaging, packaging contents;
4. marketing authorisation holder;
5. number and date of issuance of marketing authorisation;
6. batch number;
7. date of manufacturing;
8. expiration date (in years);
9. sampling date and the date of receipt of the samples at the site of analysis;
10. type of immediate and outer packaging;
11. terms of storage (temperature, humidity, exposure to light);
12. manufacturer, manufacturing site;
13. warnings;
14. quality analysis that includes:
- stated specifications that include general requirements for given pharmaceutical form and which were approved in the process of obtaining marketing authorization and which are in compliance with European pharmacopoeia, national pharmacopoeia or other recognized pharmacopoeia or proven methods of analysis submitted by a manufacturer;
- submitted certificate of laboratory testing with individual required parameters, signed by responsible person of a manufacturer or verified laboratory;
- note that the batch of a medicine complies with all stated specifications; and
15. name, address, phone, fax, e-mail and signature of the responsible person.
The Agency may assess the certificate of quality control of a medicine even when it does not contain all the information specified in paragraph 1 of this article, if it does not affect the assessment of the quality of medicine and provided that that piece of information may be found in submitted documentation for obtaining marketing authorization

Article 7

Documentation on quality control of sensitive medicines conducted in accordance with EU guidelines in EU Member States, EEA Signing States or in Switzerland includes:
- OCABR certificate (certificate of release on to the market in accordance with EU guidelines) issued by competent authority on the territory of EU, EEA or Switzerland or OBPR certificate (certificate of release on to market in accordance with EU guidelines on the basis of expert-administrative assessment of manufacturer's protocol of manufacture and testing) issued by competent authority on the territory of EU, EEA or Switzerland for less sensitive medicines for veterinary use from EDQM list (European Directorate for Quality);
- copy of immediate and outer packaging of a medicine;
- explanation in case that data in the certificate and packaging differ due to repackaging.

Article 8

Documentation on quality control of sensitive medicines conducted in EU Member State, but OCABR or OBPR certificate from article 7 paragraph 1 indent 1 of this Rulebook has not been issued, or quality control was conducted outside of EU in the state with the same requirements as EU member states, contains:
- certificate issued by competent authority of release on to the market of the state concerned;
- manufacturer's protocol of manufacturing and testing of a medicine;
- copy of immediate and outer packaging of a medicine;
- explanation in case that data in the certificate and packaging differ due to repackaging.

Article 9

Pharmaceutical testing of a medicine with the aim of quality control before release on to the market (in the process of issuance of marketing authorisation, its amendment, complement, and renewal) is performed by:
- assessment of the certificate of quality control and/or;
- laboratory testing of routine, non-routine and, if needed, special analysis conducted in cases where manufacturer has not (fully) implemented guidelines of good manufacturing practice and∨
- laboratory testing of routine, non-routine and, if needed, special analyses conducted in cases where there are professionally justified reasons for it and when manufacturer meets the requirements of good manufacturing practice.

Parameters of laboratory testing of a medicine, raw material and, when needed, intermediates or other excipients of a medicine are approved by the Agency on the basis of latest scientific and technological guidelines.

Article 10

Pharmaceutical testing of a medicine with the aim of quality control of every batch of sensitive medicines (immunological medicines, radiopharmaceuticals and medicines derived from blood or plasma) is performed by:
- assesment of the certificate of manufacturer which must be in compliance with European pharmacopoeia, national pharmacopoeia or other recognized pharmacopoeia or proven methods of analysis submitted by the manufacturer;
- assessment of the certificate issued by indipendent laboratory of EU member state or other state with the same requirements for release of a medicine to to the market;
- analytical testing of routine, non-routine and, if needed, special analysis conducted in cases where manufacturer has not (fully) implemented guidelines of good manufacturing practice;
- analytical testing of routine, non-routine and, if needed, special analyses conducted in cases where there are professionally justified reasons for it and when manufacturer meets the requirements of good manufacturing practice.

Article 11

If the certificate of release of a medicine on to the market was not issued by competent authority in the EU member state or in the state with the same requirements regarding release of sensitive medicine on to the market, i.e. the certificate is not in line with EU guidelines, then it must be acoompanied by:
- laboratory certificate of the manufacturer;
- protocol of medicine manufacturing and protocol of analytical testing of a medicine, in accordance with requirements for release of batch of medicine on to the market;
- certificate by national competent authority of release of batch of medicine on to the market in the state of the manufacturer.

Article 12

When medicines derived from blood and plasma are concerned, beside certificate of release of batch of a medicine on to the market, shall also submit:
- certificate of testing of plasma pools issued by competent authority of the EU member state or of states with the same requirements regarding release of sensitive medicine on to the market ;
- protocol of medicine manufacturing in accordance with requirements for release on to the market in EU member states or in states with the same requirements regarding release of sensitive medicine on to the market;
- analytical certificate by manufacturer of finished medicine which must be in compliance with European pharmacopoeia, national pharmacopoeia or other recognized pharmacopoeia or proven methods of analysis submitted by a manufacturer.

Article 13

Control of random sampling at least once during the validity of marketing authorisation, is conducted by laboratory testing of routine and, if needed and if there are professionally justified reasons for it, non-routine analyses described in the documentation for that medicine.
Control of random sampling includes:
- assessment of the certificate of laboratory testing of a medicine from article 6 of this Rulebook and/or
- qualitative and quantitative analysis of active substances and analysis of excipients;
- assessment of packaging and patient information leaflet.

Article 14

Control of random sampling during the validity of marketing authorisation is conducted on the basis of following criteria:
- suspicion concerning possible defect in quality a medicine;
- professionally justified opinion on medicines with high risk to a user;
- amendments in documentation submitted in the procedure of obtaining marketing authorisation;
- high consumption of a medicine (large batches or great number of batches);
- deviations from specifications in previously conducted controls;
- of medicines whose manufacturer has not (fully) implemented guidelines of good manufacturing practice.

Article 15

Identified problems are solved by laboratory testing of parameters which tested negative in previous testings, as well as by solving other identified problems (eg. impurities) .

Article 16

Sampling is done on principle of random samples, in such manner that represent sample is provided.
Number of units of samples is determined on the basis of documentation for obtaining marketing authorisation.
When planning quality control it is necessary to take into account all market segments and respect geographical and demographic criteria.

Article 17

Control laboratory or laboratory whose results are accepted by the Agency, after conducted analytical testing of a medicine, i.e. assessment of the certificate of quality control of batch of a medicine, issues certificate of quality control, which, beside data from article 6 of this Rulebook, also includes data on:

- legal/natural person that sent samples to the control, i.e. which smaples were taken from;
- date of fulfillment of all the conditions for the commencement of the quality control;
- assessment of outer and immediate packaging, patient information leaflet and equipment associated to a medicine.

Article 18

Quality control of magistral and galenic medicines as well as of starting materials for their manufacturing is conducted in accordance with criteria set out European pharmacopoeia, national pharmacopoeia or other recognized pharmacopoeia or proven methods of analysis.

III FINAL PROVISION

Article 19

This Rulebook shall come into force on the 8th after being published the "Official Gazzette of Montenegro."
No 03-83
Podgorica, 12 January 2010

Minister
Doc. dr Miodrag Radunovic