RESOLUTION No. 52 OF THE MINISTRY OF HEALTH OF THE
REPUBLIC OF BELARUS, DATED MAY 8, 2009

ON REQUIREMENTS TO THE DOCUMENTS FOR MEDICINAL
PREPARATIONS, PHARMACEUTICAL SUBSTANCES APPLIED FOR
STATE REGISTRATION (RENEWAL OF REGISTRATION) AND TO THE
DOCUMENTS SUBMITTED FOR MAKING AMENDMENTS TO THE
REGISTRATION DOSSIER OF A MEDICINAL PREPARATION
(PHARMACEUTICAL SUBSTANCE) PREVIOUSLY REGISTERED IN
THE REPUBLIC OF BELARUS, AND ON ACKNOWLEDGEMENT OF
RESOLUTION N199 OF THE MINISTRY OF HEALTH OF THE
REPUBLIC OF BELARUS DATED NOVEMBER 21, 2008 AS CEASED TO
BE IN FORCE

(in the wording of the Ministry of Health Resolutions No. 129 dated November
20, 2009, No. 124 dated September 13, 2010)

On the grounds of Sub-clause 4.1 of Clause 4, the second paragraph of
Clause 30 of the Regulations on State Registration (Renewal of Registration) of
Medicinal Preparations and Pharmaceutical Substances approved by Resolution
No. 1269 of the Council of Ministers of the Republic of Belarus dated
September 2, 2008, Clause 3 of Resolution No. 171 of the Council of Ministers
of the Republic of Belarus dated February 9, 2009 “On Approval of the List of
Administrative Procedures Performed by the Republican Centre for Health
Improvement and Sanatorium and Health Resort Treatment of Population in
Relation to Legal Entities and Individual Entrepreneurs”, and On Making
Amendments and Addenda to Resolution No. 1430 of the Council of Ministers
254 of the Council of Ministers of the Republic of Belarus “On Making
Amendments and Addenda to Certain Resolutions of the Council of Ministers
of the Republic of Belarus regarding performance of administrative procedures
in the field of public health” dated February 26, 2009, the Ministry of Health of
the Republic of Belarus RESOLVES:

1. To determine that:
   1.1. Documents for domestically-produced medicinal preparations applied
for state registration (renewal of registration) shall comply with the following
requirements:
1.1.1. An application for state registration (renewal of registration) of a domestically-produced medicinal preparation shall be executed on the form according to Appendix 1 to the present Resolution;

1.1.2. A draft instruction on medicinal preparation application shall be submitted in the form of characteristics (brief, general), guidance document with indication that the information contained therein is intended for specialists; and (or) a draft information leaflet shall be submitted in the form of an instruction for patients, guidance document (information leaflet, information for the patient) with indication that the document provided is an information leaflet; package graphic design layout in the Russian or Belarusian language shall contain information to the draft instruction on medicinal preparation application and (or) the information leaflet on the marking of package and label of a medicinal preparation, specified according to Appendixes 2 - 4 hereto. 

(in the wording of Resolution No. 129 of the Ministry of Health dated November 20, 2009)

(see the text in the previous wording)

The sections of a draft instruction on medicinal preparation application and (or) information leaflet may be arranged in a random sequence (in case of absence of any section, written explanation shall be provided).

For medicinal preparations intended for use by public health organizations rendering medical aid in hospital conditions, as well as medicinal preparations available on prescription, only a draft instruction on medicinal preparation application, being the information leaflet, shall be submitted;

1.1.3. The manufacturer’s document containing the description of methods of medicinal preparation producing, a brief scheme of manufacturing, industrial batch size, quality control of intermediate products, data on production process validation or validation plan, when performing registration of a medicinal preparation, for immunobiological medicinal preparations (hereinafter “the IMP”) shall contain detailed description of methods of control over those parameters of a semifinished product which cannot be determined in a finished product, as well as full and detailed descriptions of methods of control and requirements to the quality of produced strains and substrates for the IMP production (cell culture lines, embryos).

In case two or more manufacturers take part in medicinal preparation production, the above mentioned document shall be submitted for each manufacturer participating in the production process, except for manufacturers carrying out packaging of medicinal preparations;

1.1.4. The manufacturer’s document confirming the quality of one batch of a medicinal preparation shall be executed in the Belarusian or Russian language with indication of the manufacturer’s name, its trade mark (if any), name of medicinal preparation, drug dosage form, dose (for single-component medicinal preparations), batch number, batch size, manufacturing date and expiry date,
controlled quality factors according to a draft pharmacopoeial article developed in accordance with the Technical Code of Common Practice TCP 123-2008 (02040) “Pharmacopoeial Articles. The Procedure of Development and Approval”, approved by Resolution No. 37 of the Ministry of Health of the Republic of Belarus dated February 18, 2008, “On Approval of the Technical Code of Common Practice”, test results, marks of quality conformance, and shall be signed by the manufacturer of a medicinal preparation;

1.1.5. The manufacturer’s document containing stability test results of the medicinal preparation (a plan, a report, tables with test results for at least two batches), when performing registration of a medicinal preparation shall be submitted in the form of:

Report on stability test results containing the following data: name of the batches tested (experimental-industrial, industrial or other), batch sizes, justification of conditions under which the investigations were carried out (temperature, relative humidity), justification of choice of suggested primary package (material of the primary package);

Tables with stability test results of a medicinal preparation containing:
- specification parameters which were under control during the whole determined storage life, frequency of control, conditions under which they were carried out, description of primary package, as well as a conclusion on determining the expiration date of the medicinal preparation, signed by the involved staff members and the director and stamped with the seal of the organization which carried out the tests.
- Tables with stability test results for different fillings of a medicinal preparation shall be submitted for all types of primary package declared, with attachment of documents confirming applicability of this package for a medicinal preparation.

For sterile medicinal preparations in multi-dose packages a report on stability study and tables with stability test results of a medicinal preparation after the first unpacking shall be additionally submitted, and for powders intended for preparing solutions and suspensions for internal mode of administration, a report on stability study and tables with stability test results of a prepared drug dosage form shall be additionally submitted;

1.1.6. A report on bioavailability (bioequivalence) study for generic medicinal preparations (if any) when performing registration of medicinal preparations shall be signed by the director and stamped with the seal of the state public health organization which performed these studies. A report on bioavailability (bioequivalence) study for generic medicinal preparations (if any) when performing registration of a medicinal preparation shall be submitted
1.1.6-1. A report on clinical trials of a medicinal preparation conducted in accordance with Good Clinical Practice, when performing registration of a medicinal preparation, signed by the principal investigator, approved by the director and stamped with the seal of a state public health organization, which conducted clinical trials, shall contain information about:

- The results of a clinical trial;
- The contents and scope of a clinical trial protocol approved by the Ministry of Health of the Republic of Belarus and by the competent authority of the country where clinical trial is conducted;
- Results of the inspection of a clinical centre, which conducted the clinical trial, located outside the Republic of Belarus (if any);
- Staff members who conducted the clinical trial (surname and initials, address and place of employment, position, qualifications, responsibilities);
- Each of the trial subjects, confirmed by no less than 5 percent of Case Report Form copies.


(Sub-clause 1.1.6-1 is introduced by Resolution No. 124 of the Ministry of Health, dated September 13, 2010)

1.1.7. A report on nonclinical study of a medicinal preparation when performing medicinal preparation registration shall comply with the requirements of the Technical Code of Common Practice TCP 125-2008 (02040) “Good Laboratory Practice” approved by Resolution No.56 of the Ministry of Health of the Republic of Belarus dated March 28, 3008 “On Approval of the Technical Code of Common Practice”.

A report on nonclinical study of a medicinal preparation when performing medicinal preparation registration shall contain information specified in Appendix 1-1 to the present Resolution.

In case of state registration of medicinal preparations with special characteristics a report on medicinal preparation nonclinical study and a report on medicinal preparation clinical trials conducted in accordance with Good Clinical Practice shall contain:
For a medicinal preparation with an active ingredient that is well studied in medical practice (its efficacy and satisfactory level of safety are recognized and confirmed by materials of clinical and epidemiological trials published in peer-reviewed scientific medical press, and it was used for the first time in the Republic of Belarus more than 12 years ago) - detailed information from peer-reviewed scientific bibliography, which reflects the results of efficacy and safety assessment, experience of medicinal preparation use before and after its state registration, comparative trials, documentary (proven) scientific justification of admissibility of the safety profile and (or) efficacy of this medicinal preparation;

For a medicinal preparation of biotechnological origin (including bioanalogues) – full information about nonclinical studies and clinical trials of a medicinal preparation conducted in accordance with Good Clinical Practice, if the applicant does not prove identity of primary, secondary and tertiary structure of a biomolecule with the original compound, quantitative and qualitative characteristics of all related identifiable impurities and the cell line, from which this biomolecule was produced;

For a medicinal preparation used for treatment of very rare diseases (less than 5 cases per 10,000 population), as well as if the current scientific methods make it impossible to receive full information on efficacy and safety of a medicinal preparation, or obtaining such information conflicts with the accepted principles of medical ethics and deontology – data on postmarketing clinical trials in accordance with a clinical trial protocol approved by the Independent Ethics Committee and by the Ministry of Health of the Republic of Belarus, with reevaluation of the risk-benefit ratio associated with the use of this medicinal product after the completion of the stated trials;

For a homeopathic medicinal preparation of non-injection route of administration – detailed information from bibliography, which reflects the results of efficacy and safety assessment of use based on homeopathic repertory;

For an injection homeopathic medicinal preparation – information containing the experimental evidence of its safety for human body and detailed bibliography, which reflects the results of efficacy assessment of use based on homeopathic repertory;

(Sub-clause 1.1.7 is in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

(see the text in the previous wording)

1.1.8. A report on safety of medicinal preparation application for the last 5 years, when renewing registration of a medicinal preparation, in case of expiration of the registration certificate, shall be executed in accordance with Annex 3 to the Instruction On Procedure of Providing Information on Detected Adverse Reaction to Medicinal Preparations and Control over the Adverse
Reactions to Medicinal Preparations, approved by Resolution No. 52 of the Ministry of Health of the Republic of Belarus dated March 20, 2008 (National Register of Legal Acts of the Republic of Belarus, 2008, No. 92, 8/18478);

1.2. Documents for foreign-produced medicinal preparations applied for state registration (renewal of registration) shall comply with the following requirements:

1.2.1. An application for state registration (renewal of registration) of a foreign-produced medicinal preparation shall be executed on the form according to Appendix 1 to the present Resolution;

1.2.2. A notarized copy of the document on medicinal preparation registration in the country of manufacturing (a registration certificate or a certificate of free sale or a certificate of pharmaceutical product) shall contain data on all participants of the medicinal preparation production. In case of absence of data on the applicant’s status the following documents shall be submitted: a copy of the agreement (contract) with the manufacturer(s) of a medicinal preparation, which covers the issues of the possession rights for the registration documents, liability for the production and quality of a medicinal preparation, and a notarized copy of the document confirming the applicant’s status in the country of its registration;

1.2.3. A draft instruction on medicinal preparation application and (or) a draft information leaflet, package design with marking in the Russian or Belarusian language shall be submitted in accordance with Sub-clause 1.1.2 of Clause 1 of the present Resolution;

(in the wording of Resolution No. 129 of the Ministry of Health dated November 20, 2009)

(see the text in the previous wording)

1.2.4. The manufacturer’s document containing data on medicinal preparation composition with indication of amounts of all ingredients, including excipients, colouring, flavouring, stabilizing agents and other components per dosage form, with reference to the regulatory document on their quality control (monographs or pharmacopoeial articles of the Pharmacopoeia, the manufacturer’s regulatory documents on quality control of a medicinal preparation or an excipient) (hereinafter “the medicinal preparation composition”), shall be executed according to Appendix 5 to the present Resolution.

In medicinal preparation composition it is allowed to use sweeteners and synthetic organic colouring agents included in the list of sweeteners and synthetic organic colouring agents allowed in the medicinal preparation composition according to Appendix 6 to the present Resolution.

In case of use of sweeteners and synthetic organic colouring agents not included in this list, a decision on registration of medicinal preparations
containing such substances shall be taken by the Ministry of Health of the Republic of Belarus after performing expertise of documents submitted;

1.2.5. The manufacturer’s document containing the description of methods of medicinal preparation producing, a brief scheme of manufacturing, industrial batch size, quality control of intermediate products, data on production process validation or validation plan, when performing registration of a medicinal preparation, shall be executed in accordance with Sub-clause 1.1.3 of Clause 1 of the present Resolution;

1.2.6. The manufacturer’s regulatory document containing factors and methods of control over medicinal preparation quality (hereinafter “the manufacturer’s regulatory document”) shall contain a specification indicating quality factors of a medicinal preparation, analysis methods, norms (allowable limits), description of all procedures of quality control for all specification factors, and when using analysis methods included in the State Pharmacopoeia of the Republic of Belarus or in the European Pharmacopoeia, a reference thereto shall be made, as well as copies or digitalized photographs of chromatograms, spectra, microphotographs, drawings and microscopy of herbal raw material.

In case of changing norms (allowable limits) within the shelf life of a medicinal preparation, the norms (allowable limits) at the moment of medicinal preparation production and by the end of its shelf life shall be indicated in the specification, as well as frequency of control of the medicinal preparation quality factors, unless their control for each batch is required;

1.2.7. A regulatory document containing factors and methods of control over the quality of pharmaceutical substances and excipients, when performing registration of a medicinal preparation, shall be presented in the form of an individual pharmacopoeial article (monograph) of the Pharmacopoeia or the manufacturer’s regulatory document.

If a pharmaceutical substance and (or) excipients used in a medicinal preparation production are included in and controlled by the manufacturer under the State Pharmacopoeia of the Republic of Belarus or under the European Pharmacopoeia, then a reference to monographs (individual pharmacopoeial articles) of the correspondent pharmacopoeias shall be made.

The description of methods of pharmaceutical substance producing, a brief scheme of manufacturing (synthesis) shall contain information on the organic solvents used.

(part three of Sub-clause 1.2.7 is introduced by Resolution No. 129 of the Ministry of Health dated November 20, 2009).

For a pharmaceutical substance and (or) excipients of animal origin a veterinary certificate or manufacturer’s declaration of non-use of primary components of animal origin, which potentially can be contaminated with
bovine spongiform encephalopathy, in the manufacturing process, shall be submitted;

1.2.8. Copies of reports on validation of quality control methods of a medicinal preparation, certified in accordance with the procedure established by the legislation, when performing registration of a medicinal preparation, if the methods are not described in the State Pharmacopoeia of the Republic of Belarus or in other pharmacopoeias, shall be submitted in the form of validation reports copies, certified by the applicant;

(see the text in the previous wording)

1.2.9. The manufacturer’s document confirming the quality of one batch of a pharmaceutical substance and medicinal preparation shall be executed in the Belarusian or Russian language with indication of the manufacturer’s name and (or) its trade mark (if any), name of the medicinal preparation, pharmaceutical substance, drug dosage form, dose (for single-component medicinal preparations), batch number, manufacturing date and expiry date, controlled quality factors according to the manufacturer’s regulatory document, test results, marks of quality conformance, and shall be signed by the manufacturer of a medicinal preparation, pharmaceutical substance;

(see the text in the previous wording)

1.2.10. The manufacturer’s documents containing stability test results for at least two batches of a medicinal preparation (a plan, a report, tables with test results), when performing registration of a medicinal preparation, shall be submitted in accordance with Sub-clause 1.1.5 of Clause 1 of the present Resolution;

1.2.11. A copy of a report on nonclinical study of a medicinal preparation, certified by the applicant (manufacturer), when performing registration of a medicinal preparation, shall be executed in accordance with the requirements of the Organization for Economic Cooperation and Development to the principles of Good Laboratory Practice, and shall contain information specified in Appendix 1-1 to the present Resolution;

(Sub-clause 1.2.11 is introduced by Resolution No. 124 of the Ministry of Health, dated September 13, 2010)

1.2.12. A copy of a report on bioavailability (bioequivalence) study for generic medicinal preparations (if any), certified by the applicant (manufacturer), when performing registration of a medicinal preparation, shall be submitted in accordance with the requirements of the World Health Organization concerning registration of multisource (generic) medicinal preparations.
In case a copy of a report on bioavailability (bioequivalence) study for generic medicinal preparations, certified by the applicant (manufacturer), was made before 2006, it shall contain the full text of a normative document regulating implementation of tests during the period specified in the report; (Sub-clause 1.2.12 is introduced by Resolution No. 124 of the Ministry of Health, dated September 13, 2010)

1.2.13. A copy of a report on medicinal preparation clinical trials, conducted in accordance with Good Clinical Practice, certified by the applicant (manufacturer), when performing registration of a medicinal preparation, shall be submitted in accordance with Sub-clauses 1.1.6-1, 1.1.7 of the present Clause; (Sub-clause 1.2.13 is introduced by Resolution No. 124 of the Ministry of Health, dated September 13, 2010)

1.3. Documents for a domestically produced pharmaceutical substance applied for state registration (renewal of registration) shall comply with the following requirements:

1.3.1. Application for state registration (renewal of registration) of a pharmaceutical substance shall be executed on the form according to Appendix 7 to the present Resolution;

1.3.2. Draft pharmacopoeial article shall be executed in accordance with the Technical Code of Common Practice TCP 123-2008 (02040) “Pharmacopoeial Articles. The Procedure of Development and Approval”; (in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010) (see the text in the previous wording)

1.3.3. The manufacturer’s document confirming the quality of one batch of a pharmaceutical substance shall be executed in accordance with Sub-clause 1.1.4 of Clause 1 of the present Resolution;

1.3.4. The manufacturer’s document containing the description of methods of pharmaceutical substance producing, a brief scheme of manufacturing (synthesis), when performing registration of a pharmaceutical substance, shall contain information on organic solvents used in the process of production (synthesis) of the pharmaceutical substance.

In case of treatment of a pharmaceutical substance by excipients in the production process or in case a pharmaceutical substance is a granulated active substance containing excipients (pellets) or several pharmacologically active substances (premixes), then the composition of such pharmaceutical substance and regulatory documents on quality control of all constituent ingredients in accordance with Sub-clause 1.2.7 of Clause 1 of the present Resolution shall be submitted;

1.3.5. The manufacturer’s document containing stability test results for at least two batches of a pharmaceutical substance (a plan, a report, tables with
10

test results), when performing registration of a pharmaceutical substance, shall be submitted in accordance with Sub-clause 1.1.5 of Clause 1 of the present Resolution;

1.4. Documents for a foreign-produced pharmaceutical substance applied for state registration (renewal of registration) shall comply with the following requirements:

1.4.1. An application for state registration (renewal of registration) of a pharmaceutical substance shall be executed on the form according to Appendix 7 to the present Resolution;

1.4.2. The manufacturer’s document containing the description of methods of pharmaceutical substance producing, a brief scheme of manufacturing (synthesis), when performing registration of a pharmaceutical substance, shall contain information on organic solvents used in the process of production (synthesis) of the pharmaceutical substance.

In case of treatment of a pharmaceutical substance by excipients in the production process or in case a pharmaceutical substance is a granulated active substance containing excipients (pellets) or several pharmacologically active substances (premixes), then the composition of such pharmaceutical substance and regulatory documents on quality control of all constituent ingredients in accordance with Sub-clause 1.2.7 of Clause 1 of the present Resolution shall be submitted;

1.4.3. The manufacturer's regulatory document containing factors and methods of control over the pharmaceutical substance quality shall be submitted in accordance with Sub-clause 1.2.6 of Clause 1 of the present Resolution;

1.4.4. The manufacturer’s document confirming the quality of one batch of a pharmaceutical substance shall be executed in accordance with Sub-clause 1.2.9 of Clause 1 of the present Resolution;

1.4.5. The manufacturer’s document containing stability test results for at least two batches of a pharmaceutical substance (a plan, a report, tables with test results), when performing registration of a pharmaceutical substance, shall be submitted in accordance with Sub-clause 1.1.5 of Clause 1 of the present Resolution;

1.5. Documents for a foreign-made pharmaceutical substance applied for state registration (renewal of registration) by a legal entity of the Republic of Belarus, having a special permit (license) to carry out pharmaceutical activities, shall comply with the following requirements:

1.5.1. An application for state registration (renewal of registration) of a pharmaceutical substance shall be executed on the form according to Appendix 7 to the present Resolution;

1.5.2. The manufacturer’s document confirming the quality of one batch of a pharmaceutical substance shall be executed in accordance with Sub-clause 1.1.4 of Clause 1 of the present Resolution;
1.5.3. The manufacturer’s document containing information on organic solvents used in the process of pharmaceutical substance production shall be submitted in the form of a brief scheme of manufacturing (synthesis) of a pharmaceutical substance or in the form of the manufacturer’s written statement of organic solvents used in the process of pharmaceutical substance production.

In case of treatment of a pharmaceutical substance by excipients in the production process or in case a pharmaceutical substance is a granulated active substance containing excipients (pellets) or several pharmacologically active substances (premixes), then the composition of such pharmaceutical substance and the regulatory documents on quality control of all constituent ingredients in accordance with Sub-clause 1.2.7 of Clause 1 of the present Resolution shall be submitted;

1.5.4. A draft regulatory document of the manufacturer containing factors and methods of control over pharmaceutical substance quality shall be submitted in accordance with Sub-clause 1.2.6 of Clause 1 of the present Resolution;

1.6. Documents submitted for making amendments to the registration dossier of a medicinal preparation (pharmaceutical substance), previously registered in the Republic of Belarus (amendments shall be presented in tabular form), shall comply with the following requirements:

1.6.1. When introducing a new indication and (or) a new mode of application (administration) to the instruction on medicinal preparation application and (or) information leaflet:

1.6.1.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.1.2. A draft of the new instruction on medicinal preparation application and (or) of the information leaflet (the instruction on medicinal preparation application and (or) information leaflet previously agreed (approved) by the Ministry of Health of the Republic of Belarus shall be enclosed to the draft) shall contain information specified in Sub-Clause 1.1.2 of Clause 1 of the present Resolution;

1.6.1.3. Copies of reports (for foreign-produced medicinal preparations) certified in accordance with the procedure established by the legislation or reports (for domestically-produced medicinal preparations) on medicinal preparation clinical trials for a new indication for medical application or a new mode of application (administration) in accordance with Good Clinical Practice for original medicinal preparations shall be submitted in accordance with Sub-clause 1.1.7 of Clause 1 of the present Resolution;

1.6.2. When excluding a previously approved indication for medical application and (or) mode of application (administration) from the instruction on medicinal preparation application and (or) from the information leaflet:
1.6.2.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.2.2. A draft of a new instruction on medicinal preparation application and (or) of an information leaflet shall contain information in accordance with Sub-Clause 1.1.2 of Clause 1 of the present Resolution;

1.6.2.3. The manufacturer’s document confirming the necessity of exclusion of a previously approved indication for medical application and (or) mode of application (administration) shall contain information on the reasons for making amendments: detected adverse reactions, results of medical use, clinical trials, a decision of an authority of the country, where the medicinal preparation is registered, to exclude any previously declared indications, modes of application (administration) from the instruction on medicinal preparation application and (or) from the information leaflet, other data on the medicinal preparation;

1.6.3. When making amendments to the sections of an instruction on medicinal preparation application and (or) an information leaflet, except for pharmacologic and clinical sections:

1.6.3.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.3.2. A draft of a new instruction on medicinal preparation application and (or) of an information leaflet shall contain information in accordance with Sub-Clause 1.1.2 of Clause 1 of the present Resolution;

1.6.4. When introducing, excluding or substituting the bulking, colouring, flavouring, stabilizing, preserving agents, components of the coat of a tablet or capsule in the medicinal preparation composition:

1.6.4.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.4.2. Draft amendments to a pharmacopoeial article for a domestically-produced medicinal preparation shall be executed in accordance with the Technical Code of Common Practice TCP 123-2008 (02040) “Pharmacopoeial Articles. The Procedure of Development and Approval”, and for a foreign-produced medicinal preparation draft amendments to the manufacturer’s regulatory document, containing factors and methods of control over the medicinal preparation quality, shall be submitted in accordance with Sub-clause 1.2.6 of Clause 1 of the present Resolution;

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

(see the text in the previous wording)

1.6.4.3. The manufacturer’s document containing stability test results for at least two batches of a medicinal preparation (a plan, a report, tables with test results) shall be submitted in accordance with Sub-clause 1.1.5 of Clause 1 of the present Resolution;
1.6.4.4. The manufacturer’s document confirming the quality of one batch of a medicinal preparation shall be executed in accordance with Sub-clauses 1.1.4 or 1.2.9 of Clause 1 of the present Resolution;

1.6.4.5. A draft instruction on medicinal preparation application and (or) draft information leaflet shall contain information in accordance with Sub-clause 1.1.2 of Clause 1 of the present Resolution;

1.6.4.6. The manufacturer’s document containing data on a new composition of a medicinal preparation with indication of amounts of all ingredients including excipients, colouring, flavouring, stabilizing agents and other components per dosage form, with reference to the regulatory document on their quality control (monographs or pharmacopoeial articles of the Pharmacopoeia, the manufacturer’s documents on quality control of the medicinal preparation), shall be submitted in accordance with Sub-clause 1.2.4 of Clause 1 of the present Resolution;

1.6.4.7. Package design with marking in the Russian or Belarusian language shall contain information on the marking of the package and label specified according to Appendix 4 hereto;

(in the wording of Resolution No. 129 of the Ministry of Health dated November 20, 2009)

(see the text in the previous wording)

1.6.5. When changing the text of a pharmacopoeial article or regulatory document of the manufacturer of a medicinal preparation (pharmaceutical substance) containing factors and methods of control over the quality of a medicinal preparation (pharmaceutical substance):

1.6.5.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.5.2. Draft amendments to a pharmacopoeial article for a domestically-produced medicinal preparation (pharmaceutical substance) or the manufacturer’s regulatory document for a foreign-produced medicinal preparation (pharmaceutical substance) containing factors and methods of control over the quality of a medicinal preparation (pharmaceutical substance) shall be submitted in accordance with Sub-clause 1.6.4.2 of Clause 1 of the present Resolution;

1.6.5.3. The manufacturer’s document confirming the quality of a medicinal preparation (pharmaceutical substance) shall be submitted according to Sub-Clauses 1.1.4 or 1.2.9 of Clause 1 of the present Resolution;

1.6.6. When changing medicinal preparation shelf life:

1.6.6.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.6.2. The manufacturer’s document containing stability test results for at least two batches of a medicinal preparation (a plan, a report, tables with test
results) shall be submitted in accordance with Sub-clause 1.1.5 of Clause 1 of the present Resolution;

1.6.6.3. A draft instruction on medicinal preparation application and (or) a draft information leaflet shall contain information in accordance with Sub-clause 1.1.2 of Clause 1 of the present Resolution;

1.6.6.4. Package design with marking in the Russian or Belarusian language shall contain information on the marking of the package and label specified according to Appendix 4 hereto;

(in the wording of Resolution No. 129 of the Ministry of Health dated November 20, 2009)

(see the text in the previous wording)

1.6.6.5. The manufacturer’s document confirming the medicinal preparation quality shall be executed in accordance with Sub-clauses 1.1.4 or 1.2.9 of Clause 1 of the present Resolution;

1.6.7. When changing medicinal preparation storage conditions:

1.6.7.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.7.2. The manufacturer’s document containing stability test results for at least two batches of a medicinal preparation under new storage conditions (a plan, a report, tables with test results) shall be submitted in accordance with Sub-clause 1.1.5 of Clause 1 of the present Resolution;

1.6.7.3. A draft instruction on medicinal preparation application and (or) a draft information leaflet shall contain information in accordance with Sub-clause 1.1.2 of Clause 1 of the present Resolution;

1.6.7.4. Package design with marking in the Russian or Belarusian language shall contain information on the marking of the package and label specified according to Appendix 4 hereto;

(in the wording of Resolution No. 129 of the Ministry of Health dated November 20, 2009)

(see the text in the previous wording)

1.6.7.5. The manufacturer’s document confirming the medicinal preparation quality shall be executed in accordance with Sub-clauses 1.1.4 or 1.2.9 of Clause 1 of the present Resolution;

1.6.8. When changing methods of control over the quality of a medicinal preparation and (or) pharmaceutical substance:

1.6.8.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.8.2. Copies of the reports on validation of the new quality control methods of a medicinal preparation and (or) pharmaceutical substance, certified in accordance with the procedure established by the legislation, shall be submitted in accordance with Sub-clause 1.2.8 of Clause 1 of the present Resolution;
1.6.8.3. Draft amendments to a pharmacopoeial article for a domestically-produced medicinal preparation (pharmaceutical substance) or the manufacturer’s regulatory document for a foreign-produced medicinal preparation (pharmaceutical substance) containing factors and methods of control over the quality of a medicinal preparation (pharmaceutical substance) shall be submitted in accordance with Sub-clause 1.6.4.2 of Clause 1 of the present Resolution;

1.6.8.4. The manufacturer’s document confirming the quality of a medicinal preparation (pharmaceutical substance) shall be executed in accordance with Sub-clauses 1.1.4 or 1.2.9 of Clause 1 of the present Resolution;

1.6.9. When changing the material or type of primary package of a medicinal preparation (pharmaceutical substance):

1.6.9.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.9.2. The manufacturer’s document confirming that the primary package material of a medicinal preparation (pharmaceutical substance) and its quality parameters are identical to the previous ones, or the regulatory document on quality control of the new packaging material shall be executed in the form of a comparative table;

1.6.9.3. The manufacturer’s document containing stability test results for at least two batches of a medicinal preparation (a plan, a report, tables with test results) shall be submitted in accordance with Sub-clause 1.1.5 of Clause 1 of the present Resolution;

1.6.10. When making changes in the production process of a medicinal preparation (pharmaceutical substance):

1.6.10.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.10.2. The manufacturer’s document containing the description of a new production process of a medicinal preparation (pharmaceutical substance), a brief scheme of manufacturing shall be submitted in accordance with Sub-clause 1.1.3 of Clause 1 of the present Resolution;

1.6.10.3. Draft amendments to the pharmacopoeial article for a domestically-produced medicinal preparation (pharmaceutical substance) or the manufacturer’s regulatory document for a foreign-produced medicinal preparation (pharmaceutical substance) containing factors and methods of control over the quality of a medicinal preparation (pharmaceutical substance), in case the quality parameters of the medicinal preparation (pharmaceutical substance) have changed, shall be submitted in accordance with Sub-clause 1.6.4.2 of Clause 1 of the present Resolution;

1.6.10.4. The manufacturer’s document confirming the quality of one batch of a medicinal preparation (pharmaceutical substance) shall be submitted in
1.6.11. When making changes in the marking of package or label of a medicinal preparation (pharmaceutical substance):

1.6.11.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.11.2. Package design with the new marking shall contain information on the marking of the package and label specified according to Appendix 4 hereto;

(in the wording of Resolution No. 129 of the Ministry of Health dated November 20, 2009)

(see the text in the previous wording)

1.6.12. When changing dose number per package in the process of filling a medicinal preparation (pharmaceutical substance):

1.6.12.1. An application shall be executed on the form according to Appendix 8 hereto;

1.6.12.2. A draft instruction on medicinal preparation application and (or) draft information leaflet shall contain information in accordance with Sub-clause 1.1.2 of Clause 1 of the present Resolution;

1.6.12.3. Draft amendments to the pharmacopoeial article for a domestically-produced medicinal preparation or the manufacturer’s regulatory document for a foreign-produced medicinal preparation containing factors and methods of medicinal preparation quality control shall be executed in accordance with Sub-clause 1.6.4.2 of Clause 1 of the present Resolution;

1.6.12.4. The manufacturer’s document confirming the quality of one batch of a medicinal preparation shall be executed in accordance with Sub-clauses 1.1.4 or 1.2.9 of Clause 1 of the present Resolution;

1.6.12.5. Package design with marking in the Russian or Belarusian language shall contain information on the marking of the package and label specified according to Appendix 4 hereto.

(in the wording of Resolution No. 129 of the Ministry of Health dated November 20, 2009)

(see the text in the previous wording)


3. The present Resolution shall enter into force upon its official publication.
APPLICATION for state registration (renewal of registration) of a medicinal preparation

1. Applicant, address ________________________________
2. Manufacturer, address ________________________________
   Including:
   carrying out production of a finished drug dosage form ________________________________
   carrying out filling and (or) packaging ________________________________
   carrying out quality control ________________________________
   other participants of the medicinal preparation manufacturing and quality control

3. Manufacturer of a pharmaceutical substance, address ________________________________
4. Name of medicinal preparation ________________________________
5. International non-proprietary name (INN) ________________________________
6. Composition of the medicinal preparation (specifying the names and amounts of active substances and excipients) ________________________________
7. Drug dosage form specifying the dose of active substance (for single-component or two-component medicinal preparation) ________________________________
8. Standard package (primary and secondary) specifying the dose number per package (filling) ________________________________
9. Mode of medicinal preparation administration (internal, external, parenteral and so on) ________________________________
10. Basic clinical and pharmacological group (according to ATC-code (Anatomical Therapeutic Chemical Classification)) ________________________________
11. Shelf life ________________________________
12. Storage conditions ________________________________
13. Whether any changes have occurred since the date of medicinal preparation registration; specify the kind of changes (to be filled in when renewing medicinal preparation registration) ________________________________
14. Protection with patents in the Republic of Belarus (patent holder, number, date of issue, period of validity) ________________________________
15. Price of the medicinal preparation in the country of origin and estimated price for delivery to the Republic of Belarus ________________________________
The application shall be submitted on the applicant’s letter headed paper, shall be signed by an authorized person of the applicant with indication of his/her position, surname and initials. All the fields provided for in the application form shall be filled in.

The applicant shall assume the responsibility for efficacy, safety and quality of the medicinal preparation, as well as guarantee reliability of the information in the registration dossier and the present application.

The applicant shall guarantee that the rights of a third party protected by the patent are not infringed in connection with the registration of the medicinal preparation.

"__" ____________ 200__   ___________________________   ____________________

(signature of the applicant or its representative)     (initials, surname)

Contact person acting on behalf of the applicant (to be filled in upon availability of a contact person) __________________________________________

(initials, surname)

Address, telephone _________________________________________________________

Appendix 1-

Appendix 1-1

to Resolution No.52

of the Ministry of Health

of the Republic of Belarus
dated May 8, 2009

INFORMATION CONTAINED IN THE REPORT ON NONCLINICAL STUDY OF A MEDICINAL PREPARATION IN THE PROCESS OF MEDICINAL PREPARATION REGISTRATION

(introduced by Resolution No. 124 of the Ministry of Health dated September 13, 2010)

1. A report on nonclinical study of a medicinal preparation in the process of registration of a medicinal preparation contains the following sections:

   Pharmacological studies;
   Pharmacokinetic studies;
   Toxicological studies;
   Studies of local tolerance;
   Additional toxicity studies;
   Studies of mechanisms of action;
   Studies of induction of drug dependence;
   Studies of metabolites and impurities;
   Other studies;
Literature source references.

In case some section (subsection) of a report on nonclinical study of a medicinal preparation in the process of medicinal preparation registration is missing, its absence shall be justified with references to publications in peer-reviewed scientific medical press or regulatory documents.

2. The “Pharmacological Studies” section consists of the following subsections: “Primary Pharmacodynamics”, “Secondary Pharmacodynamics”, “Safety Pharmacodynamics”, “Pharmacodynamic Interactions”, and includes reports on:

   Potential toxicity of a medicinal preparation;

   Dangerous or undesirable toxic reactions that may occur when using a medicinal preparation in humans (assessment of these reactions shall be made taking into account peculiarities of pathological conditions in humans);

   Qualitative and quantitative indicators of pharmacological properties of a medicinal preparation obtained using the methods of mathematical and statistical processing of results, at a given confidence level;

   Toxicological and therapeutic potential of a medicinal preparation with a view to its further clinical study.


4. The “Toxicological Studies” section covers single dose toxicity, repeated dose toxicity, genotoxicity in vitro, genotoxicity in vivo (including additional assessment of toxicokinetics); carcinogenicity (long-term studies, short-term studies or medium-term studies, further studies); reproductive toxicity; impact on fertility and early embryonic development, embryotoxicity, prenatal and postnatal toxicity, studies with introduction to immature offspring.

5. The section “Studies of Local Tolerance” contains the results of research of a dosage form of a given medicinal preparation developed for use in humans; comparative analysis of results and their comparison with the data obtained in the control group of animals injected with the bulking agent (dissolvent) for introduction of the investigational medicinal product and (or) excipients (if needed, this section also includes data obtained in the group of positive control or reference substance); evaluation of sensitizing potential for medicinal preparations, which are applied topically, using at least one test system (study on guinea pigs or local lymph nodes or other validated test systems).

6. The “Additional Toxicity Studies” section consists of “Antigenicity” and “Immunotoxicity” subsections. For medicinal preparations of biological origin it is necessary to submit documents confirming that all studies requiring repeated administration of a medicinal preparation were planned taking into
account probable stimulation of antibody formation, as well as the effect of these antibodies on the body.

7. The “Study of Mechanisms of Action” section covers results obtained from evaluation of quantitative indicators based on “dose-effect”, “time-effect” curves or other functional dependence, which explicitly quantifies the change in effect.

8. The “Studies of Induction of Drug Dependence” section includes assessment of potential ability of a medicinal preparation to induce psychological and physiological drug dependence.

9. The “Studies of Metabolites and Impurities” section contains results of assessment of the impact of metabolites and impurities on realization of the final pharmacological effect of a medicinal preparation and its expected safety profile.

10. The “Other Studies” section includes evaluation results of other studies, which are not reflected in Clauses 1-8 of the present Appendix.

11. The “Literature Source References” section contains a list of publications in peer-reviewed scientific medical press on the results of studies specified in Clauses 1-9 of the present Appendix.

For medicinal preparations of biological origin it is necessary to substantiate the expediency of conducting studies of reproductive function, embryonic (fetal) and perinatal toxicity, possible mutagenic and carcinogenic effects. In case the cause of these types of toxicity is not an active substance, but an auxiliary component whose presence in a medicinal preparation can be reliably excluded, these studies are not presented.

For medicinal preparations containing a new excipient, which is used in pharmaceutical practice for the first time, the report on nonclinical study of a medicinal preparation in the process of medicinal preparation registration shall include data on toxicological and pharmacokinetic studies of this excipient.

For medicinal preparations with a likelihood of significant decay of a medicinal preparation during its storage, the report on nonclinical studies of a medicinal preparation in the process of medicinal preparation registration shall include the results of toxicological studies of decay products.

Sections of the report on nonclinical study of a medicinal preparation in the process of medicinal preparation registration concerning general specific pharmacological activity:

Use validated research methodologies, recognized by the Ministry of Health of the Republic of Belarus or by a competent authority of the country, where they are applied;

Present detailed descriptions of new methodologies, ensuring their reproduction;

Present and prove statistical validity of the data;
Offer comparative analysis of the results and their comparison with the data characterizing a substance(s) with the same therapeutic effect (absence of comparative trials shall be justified separately);

Present data on the main pharmacological properties of the active substance with indication of its direct and indirect effect on the basic functions of human body physiological systems. In case the doses of a medicinal preparation causing adverse drug reactions are close to the doses recommended for medical use, these studies shall be conducted in-depth;

Substantiate study of pharmacodynamic interaction of fixed combinations of active substances based either on pharmacological premises, or on indications for their application followed by experimental verification of therapeutic significance of such interaction and possible adverse reactions associated with their use.

A report on nonclinical study of a medicinal preparation in the process of medicinal preparation registration may be presented in the form of one report containing all sections, or in the form of individual reports on each section.

Appendix 2 to Resolution No.52 of the Ministry of Health of the Republic of Belarus dated May 8, 2009

INFORMATION CONTAINED IN THE DRAFT INSTRUCTION ON MEDICINAL PREPARATION APPLICATION

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

A draft instruction on medicinal preparation application contains the following sections:
Name of medicinal preparation;
General characteristics;
Medicinal preparation composition;
Pharmaceutical form;
Classification code of medicinal preparation;
Pharmacologic properties;
Indications for administration;
1. The “Name of Medicinal Preparation” section shall contain information about an international non-proprietary name (if any), if:

   The manufacturer (applicant) uses the trade name of a medicinal preparation other than the international non-proprietary name (hereinafter “the INN”), and if the medicinal preparation contains only one active ingredient;

   A medicinal preparation is produced in several dosage forms and (or) forms varying in strength (for newborns, children, elderly people), then the dose size shall be specified next to the trade name of a medicinal preparation.

2. The “General Characteristics” section shall include:

   the INN or chemical name for a medicinal preparation containing one active substance in case there is no INN for this compound; basic properties of a drug dosage form shall contain a brief characteristic of the finished dosage form including physical and chemical properties (information shall comply with the “Description” section of the regulatory document on quality control) and immunological properties.

3. The “Medicinal Preparation Composition” section shall specify the active substance in the form of its INN or common name and its quantitative content per dose, per unit of weight, volume or an individual package, the list of excipients.

4. The “Pharmaceutical Form” section shall contain information on the dosage form in which the medicinal preparation is manufactured.

5. The “Classification Code of Medicinal Preparation” section shall contain information on its belonging to a specific group according to International Anatomical Therapeutic Chemical Classification (ATC).
6. The “Pharmacologic Properties” section shall consist of “Pharmacodynamics”, “Pharmacokinetics” sub-sections and shall contain the following data:

The “Pharmacodynamics” sub-section shall describe basic mechanisms which determine therapeutic properties of a medicinal preparation and its proved and predictable adverse reactions, other peculiarities of the medicinal preparation influence on human body;

The “Pharmacokinetics” sub-section shall contain information on bioavailability, organ and tissue distribution of a medicinal preparation, peculiarities of metabolism and elimination, peculiarities of pharmacokinetic processes in patients with elimination dispragia (liver, kidneys) and cardiovascular system disorders, as well as in patients of different age groups (newborns, children, elderly people), pregnant women.

7. The “Indications for Administration” section shall specify all nosological forms, syndromes and symptoms for which a medicinal preparation has a proved (scientifically grounded) therapeutic effect, as well as recommendations on the use of a medicinal preparation in terms of its preventive action, diagnostic effect or modification of body function.

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

(see the text in the previous wording)

8. The “Mode of Administration and Dosage” section shall specify routes of administration, doses (single, daily, maximum permissible; if required, course dose, toxic dose and other), frequency of administration specifying (if required) correlation with specific day time and meal, course duration, possibility and advisability of breaks between courses, number of refresher courses of treatment, for children: specific doses related to body weight or body surface area, or age-dependent dose gradation.

9. The “Adverse Reaction” section shall specify undesirable adverse reactions and complications which were detected during pharmacotherapy, or could develop in patients in the course of treatment with the medicinal preparation based on its pharmacological properties.

10. The “Contraindications” section shall list all possible, foreseen and predictable conditions under which administration of the medicinal preparation is forbidden.

11. The “Overdose” section shall describe basic clinical evidence at overdosing or body hypersensitivity and measures to be taken in case of overdose (emergency (acute) medical assistance, use of specific antidotes, pathogenetic or symptomatic therapy).

12. The “Precautionary Measures” section contains information regarding different aspects of body-drug interaction requiring special attention during pharmacotherapy or nonstandard procedures: peculiarities of administration,
application, safety control in certain patient populations (children, pregnant and nursing women), potential influence on behaviour or body functional indicators, interaction with alcohol, tobacco, food products.

If a medicinal preparation is intended for treatment of very rare diseases (less than 5 cases per 10,000 population), as well as if current scientific methods make it impossible to provide full information on efficacy and safety of a medicinal preparation, or obtaining such information conflicts with the accepted principles of medical ethics, it is necessary to include information about the need to dispense the medicinal preparation only by doctor’s prescription, application of the medicinal preparation under close medical supervision or patient’s stay in hospital conditions, and information that the description of this medicinal preparation is incomplete.

(Second part of Clause 12 is introduced by Resolution No. 124 of the Ministry of Health dated September 13, 2010)

13. The “Interaction with Other Medicinal Preparations” section contains data on permissibility of product’s simultaneous use with other medicinal preparations and on end-point clinical effect of their interaction.

14. The “Storage Conditions and Shelf Life” section points at the necessity to observe specific storage conditions including precise temperature limits (parameters) of the medicinal preparation storage for preservation of its pharmacological properties, a warning against visual signs of medicinal preparation inadequateness (if required), medicinal preparation shelf life, a warning against using the medicinal preparation after the expiry date, necessity to keep it out of reach of children.

(In the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

(See the text in the previous wording)

15. The “Pharmacy Purchasing Terms” section contains information on the procedure for dispensing the medicinal preparation, i.e. on prescription or without prescription.

16. The “Package” section contains information on dose number per package and medicinal preparation package type.

17. The “Information on Manufacturer (Applicant)” section contains data on the manufacturer’s (applicant’s) name, its address, as well as data on the person representing the interests of the manufacturer (applicant), his/her address, telephone and other information (if available).

(In the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

(See the text in the previous wording)

17-1. Homeopathic medicinal preparations shall contain the following statement: “homeopathic medicinal preparation without approved therapeutic (medical) indications for use”.

17-1. Homeopathic medicinal preparations shall contain the following statement: “homeopathic medicinal preparation without approved therapeutic (medical) indications for use”.
(Clause 17-1 is introduced by Resolution No. 124 of the Ministry of Health dated September 13, 2010)

18. Information text of a draft instruction on medicinal preparation application shall be submitted in the printed form on A4-sized paper with a margin of at least 1.5 cm on the perimeter and font size of at least 12 pt.

The font size of a draft instruction on medicinal preparation application, which will subsequently be attached to each individual package of a medicinal preparation, shall be at least 8 pt.

Appendix 3
to Resolution No.52
of the Ministry of Health
of the Republic of Belarus
dated May 8, 2009

INFORMATION CONTAINED IN THE DRAFT INFORMATION LEAFLET OF A MEDICINAL PREPARATION

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

1. Name of a medicinal preparation with reference to the international non-proprietary name (hereinafter “the INN”), if the manufacturer (applicant) uses a trade name of the medicinal preparation other than the INN, or in case the medicinal preparation contains only one active ingredient.

2. Dose size shall be indicated next to the trade name of a medicinal preparation, if the medicinal preparation is produced in several dosage forms and (or) in dosage forms varying in strength (for newborns, children, elderly people).

3. Name of the dosage form.

4. Brief characteristics of the finished dosage form, including physical and chemical properties (the information shall comply with the “Description” section of the manufacturer’s regulatory document on quality control, except for description of the capsule contents, tablet core).

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)
(see the text in the previous wording)
5. Composition of a medicinal preparation with indication of the active substance in the form of its INN or common name and its quantitative content per dose, per unit of weight, volume or per one individual package, list of excipients.

Excipients, including colouring agents, shall be indicated in the form of a complete INN, and in case of its absence – in the form of a common name with reference to the index of International Classification (E) (if any).

(the second part of Clause 5 is introduced by Resolution No. 124 of the Ministry of Health dated September 13, 2010)

6. Information on medicinal preparation’s belonging to a certain pharmacotherapeutic group or its pharmacological action using terminology intelligible for a patient.

7. Information on indications for administration of a medicinal preparation in the form of list of illnesses and conditions for which it is applied.

8. Information on proper use of a medicinal preparation including contraindications, precautions for application, interaction with other medicinal preparations and other types of interactions (with tobacco, alcohol, food products) which can affect the action of the medicinal preparation, special instructions for use of the medicinal preparation.

9. Information on peculiarities of medicinal preparation use by certain patient populations (children, pregnant or nursing women, elderly people, patients with specific pathologies).

10. Information on the influence of a medicinal preparation on human behaviour, ability to drive or to operate mechanisms (if required).

11. Information on excipients that are important for safe and effective use of a medicinal preparation.

12. Information on proper administration of a medicinal preparation including dose size, mode and route of administration, frequency of administration, specifying, if required, day time when the medicinal preparation should be taken and correlation with meals, as well as, if required, depending on the properties of the medicinal preparation, duration of use without medical control if it is limited.

13. Information on manifestations of the medicinal preparation overdose and measures to be taken in such cases (measures of emergency (acute) medical assistance and symptomatic therapy).

14. Information on actions to be taken by the patient in case one or more doses have not been taken, specifying (if required) the risk of development of drug withdrawal effect.

15. Description of adverse reactions that may occur when the medicinal preparation is administered in therapeutic or preventive doses, instruction to seek medical advice upon their onset, as well as when an adverse reaction not mentioned in an information leaflet occurs.
16. Information on observing specific storage conditions including precise temperature limits (parameters) of medicinal preparation storage for preservation of its pharmacological properties, a warning against visual signs of medicinal preparation inadequateness (if required), medicinal preparation shelf life, a warning against using a medicinal preparation after the expiry date, necessity to keep it out of reach of children.

17. Information on the procedure for dispensing a medicinal preparation, i.e. on prescription or without prescription.

18. Information on dose number per package and medicinal preparation package type.

19. Information on the manufacturer’s (applicant’s) name, its address as well as data on the person representing the interests of the manufacturer (applicant), his/her address, telephone and other information (if any).

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

(see the text in the previous wording)

20. Information text of a draft instruction on medicinal preparation application shall be submitted in printed form on A4-sized paper with a margin of at least 1.5 cm on the perimeter and font size of at least 12 pt.

The font size of a draft instruction on medicinal preparation application which will subsequently be attached to each individual package of a medicinal preparation shall be at least 8 pt.

Appendix 4 to Resolution No.52 of the Ministry of Health of the Republic of Belarus dated May 8, 2009

INFORMATION CONTAINED ON THE MARKING OF THE PACKAGE AND LABEL OF A MEDICINAL PREPARATION

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

1. The following data in the Belarusian or Russian language (information is given in several languages provided that the texts are identical, which is confirmed by translation into Russian or Belarusian certified by the applicant in
accordance with the procedure established. Information in the Russian of Belarusian language on the package of a medicinal preparation used for treatment of rare diseases may be placed in the form of a sticker) shall be specified on the secondary package of a medicinal preparation (12 colour samples of secondary package and label for each filling and dosage specifying the Pantone colours and scale of secondary package and label shall be submitted), and in case of its absence the data shall be specified on the primary package (label):

Name of the manufacturer (applicant), country, its trade mark (if any) (if two or more manufacturers participate in the production process, then it is allowed to specify the name of one manufacturer performing the final control over the finished medicinal preparation quality and bearing responsibility for its quality);

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

(see the text in the previous wording)

Trade name of a medicinal preparation;

International generic name (it is allowed to provide it in English or Latin) or, in case of its absence – common name (if the medicinal preparation contains one active substance);

(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)

(see the text in the previous wording)

Dosage form;

Dose and dose number per package, weight, volume (for undosed medicinal preparations);

Name and quantitative content of active ingredients per medicinal dose and for undosed medicinal preparations - per unit of weight or volume of medicinal preparations, per individual package;

Complete list of excipients for medicinal preparations designated for parenteral infusion, ophthalmologic administration and external and local application;

Mode of administration (may not be specified for tablets and capsules intended for ingestion; mode of administration shall be specified for parenteral medicinal preparations, then it is allowed to indicate the mode of administration “for injection” if the medicinal preparation can be introduced by three and more modes);

Storage conditions with indication of temperature limits;

Notice of the necessity to keep a medicinal preparation out of reach of children, shake before use, avoid freezing and others;

Batch number;

Expiry date.
The statement “No antibodies to immunodeficiency virus” shall be present on the package (label) of medicinal preparations obtained from blood, blood plasma as well as human organs and tissues; the statement “Product has passed radiation control” shall be present on the package (label) of medicinal preparations obtained from herbal raw material (integral or powdered and packed herbal raw material, tea, plant tea); “sterile” shall be stated on the package (label) of sterile medicinal preparations; “homeopathic medicine” shall be stated on the package (label) of homeopathic medicinal preparations.

A medical application instruction (information leaflet) in the Belarusian or Russian language shall be attached to each individual package. It is allowed to put the full text of a medical application instruction (information leaflet) directly on the primary or secondary package of a medicinal preparation dispensed without a prescription.

It is not allowed to place advertising information on the package or information not corresponding to the medical application instruction (information leaflet).

Package design, marked with an item number in the form of an identification bar code, shall be supplemented with its decoding (the decoding shall be attached to colour samples specified in the first paragraph of Part 1 of the present Clause).

(The fifth part is introduced by Resolution No. 124 of the Ministry of Health dated September 13, 2010)

The colour scheme of secondary package design and in case of its absence the labels of primary package shall be different for medicinal preparations with different amounts of the active component in the same dosage form.

2. The same information shall be indicated on both primary and secondary package, except for the following cases:

2.1. The following information is necessarily stated on strip cellular or non-cellular package (blister, strip) placed into the secondary package:
Manufacturer’s (applicant’s) name and (or) its trade mark (if any);
(in the wording of Resolution No. 124 of the Ministry of Health dated September 13, 2010)
(see the text in the previous wording)
Trade name of a medicinal preparation;
Content of the active ingredient per medicinal dose;
Batch number;
Expiry date;

2.2. The following information is indicated on the primary package (label) of a small size (with the area of one side not exceeding 10 square centimetres):
Trade name of a medicinal preparation;
Content of the active ingredient;
Weight, volume or quantity of dose units of the package contents;
Mode of administration (for parenteral medicinal preparations it is allowed not to state the mode on the package with volume of 1 ml and less);
Batch number;
Expiry date.
2.3. The following information is indicated on the primary tube-package:
Manufacturer’s (applicant’s) name and (or) its trade mark (if any);
Trade name of a medicinal preparation;
Dosage form;
Content of the active ingredient;
Mode of administration:
Quantity per package;
Storage conditions;
Batch number;
Expiry date.
(Sub-clause 2.3 is introduced by Resolution No. 124 of the Ministry of Health, dated September 13, 2010)
3. Primary and secondary package of medicinal preparations containing radionuclides shall be marked in accordance with the legislation.
The label on a shielding container shall be designed in accordance with Clause 1 of the present Appendix.
In addition the marking on a shielding container shall fully explain the coding on the primary package and may indicate the value of radionuclide(s) activity in a medicinal preparation, contained in dose or primary package at the specified date, and if necessary – time and number of capsules or liquid amount in millilitres, contained in primary package.
Marking shall contain the following information:
Manufacturer’s name and (or) its trade mark (if any);
Name or code of a medicinal preparation, including the name or symbol of a chemical element with the radionuclide index;
Batch number and expiry date;
International symbol of radioactivity;
Radionuclide(s) activity in a medicinal preparation (indicated in accordance with the third part of the present Clause).
(Clause 3 is introduced by Resolution No. 124 of the Ministry of Health dated September 13, 2010)
COMPOSITION
of a medicinal preparation specifying the amounts of all constituent ingredients, including excipients, colouring, flavouring, stabilizing agents and other components per dosage form, with reference to the regulatory document on quality control (pharmacopoeial articles, pharmacopoeia’s monographs, manufacturer’s regulatory documents)

Trade name of a medicinal preparation___________________________________
Manufacturer's name_____________________________________________________
Drug dosage form _______________________________________________________
Dose of a medicinal preparation, if the medicinal preparation contains one active ingredient_______________________________________________________

<table>
<thead>
<tr>
<th>Name of ingredient</th>
<th>Amount</th>
<th>Purpose of the ingredient</th>
<th>Reference to the regulatory document on quality control</th>
</tr>
</thead>
</table>

The amounts of all ingredients shall be specified per dosage form, and for undosed medical preparations - per unit of weight or volume, per one individual package.

For medicinal preparations in the form of capsules the composition of the coat and of its contents shall be specified separately, and for the coated tablets the composition of the core and the composition of the coat shall be specified separately.

If active substances are presented in the form of compounds and derivatives, it is necessary to specify their quantification, total mass, and if required – the mass of the active part of a molecule.

If a medicinal preparation contains an active substance for the first time declared in the medicinal preparation composition, the quantitative characteristic of an active substance that is a salt or hydrate shall be specified in terms of the mass of the active part of a molecule.

Excipients shall be specified and marked in such a way as to preclude mistaking them for excipients of close chemical structure (for example, starch, sodium starch glycolate, pregelatinized starch).
# LIST OF SWEETENERS AND SYNTHETIC ORGANIC COLOURING AGENTS ALLOWED IN THE COMPOSITION OF MEDICINAL PREPARATIONS

<table>
<thead>
<tr>
<th>No.</th>
<th>Name of colouring agent. Type of sweetener</th>
<th>Index of International Classification (E)</th>
<th>Maximum admissible amount of intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tartrazine</td>
<td>E 102</td>
<td>7.5 mg/kg/day</td>
</tr>
<tr>
<td>2</td>
<td>Quinoline yellow</td>
<td>E 104</td>
<td>500 mcg/kg/day</td>
</tr>
<tr>
<td>3</td>
<td>Orange yellow</td>
<td>E 110</td>
<td>2.5 mg/kg/day</td>
</tr>
<tr>
<td>4</td>
<td>Azorubine (carmoisine)</td>
<td>E 122</td>
<td>1.25 mg/kg/day</td>
</tr>
<tr>
<td>5</td>
<td>Cochineal red Ponceau 4R</td>
<td>E 124</td>
<td>125 mcg/kg/day</td>
</tr>
<tr>
<td>6</td>
<td>Red charming</td>
<td>E 129</td>
<td>7 mg/kg/day</td>
</tr>
<tr>
<td>7</td>
<td>Patent blue V</td>
<td>E 131</td>
<td>12.5 mg/kg/day</td>
</tr>
<tr>
<td>8</td>
<td>Indigo carmine</td>
<td>E 132</td>
<td>2.5 mg/kg/day</td>
</tr>
<tr>
<td>9</td>
<td>Brilliant blue</td>
<td>E 133</td>
<td>12.5 mg/kg/day</td>
</tr>
<tr>
<td>10</td>
<td>Brilliant black PN</td>
<td>E 151</td>
<td>2.5 mg/kg/day</td>
</tr>
</tbody>
</table>

## Sweeteners

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Index of International Classification (E)</th>
<th>Maximum admissible amount of intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sorbite</td>
<td>E 420</td>
<td>not rated</td>
</tr>
<tr>
<td>2</td>
<td>Mannite</td>
<td>E 421</td>
<td>50 mg/kg/day</td>
</tr>
<tr>
<td>3</td>
<td>Acesulfame potassium</td>
<td>E 950</td>
<td>15 mg/kg/day (not used in medicinal preparations for children)</td>
</tr>
<tr>
<td>4</td>
<td>Aspartame</td>
<td>E 951</td>
<td>40 mg/kg/day</td>
</tr>
<tr>
<td>5</td>
<td>Cyclamic acid and its sodium and calcium salts</td>
<td>E 952</td>
<td>11 mg/kg/day</td>
</tr>
<tr>
<td>6</td>
<td>Saccharin and its sodium, potassium and calcium salts</td>
<td>E 954</td>
<td>5 mg/kg/day</td>
</tr>
<tr>
<td>7</td>
<td>Maltitol</td>
<td>E 965</td>
<td>not rated</td>
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Appendix 7
to Resolution No.52 of the Ministry of Health of the Republic of Belarus dated May 8, 2009
APPLICATION
for state registration (renewal of registration) of a pharmaceutical substance

1. Applicant, country ________________________________________________
2. Manufacturer, country _____________________________________________
3. Name of the pharmaceutical substance ______________________________
4. Shelf life __________________________________________________________
5. Storage conditions ________________________________________________
6. Package ___________________________________________________________
7. Whether any changes have occurred since the date of registration; specify the kind of changes (to be filled in when performing renewal of registration of the substance) __________________________________________
8. Protection with patents in the Republic of Belarus (patent holder, number, date of issue, period of validity) _______________________________
9. Price of the pharmaceutical substance in the country of origin and estimated price for delivery to the Republic of Belarus __________________

The application shall be submitted on the applicant’s letter headed paper, shall be signed by an authorized person of the applicant with indication of his/her position, surname and initials. All the fields provided for in the application form shall be filled in.

The applicant shall assume the responsibility for efficacy, safety and quality of the medicinal preparation, as well as guarantee reliability of the information in the registration dossier and the present application.

The applicant shall guarantee that the rights of a third party protected by the patent are not infringed in connection with the registration of the medicinal preparation.

"__" ____________ 200__   ___________________________   ____________________
   (signature of the applicant or its representative)     (initials, surname)

Contact person acting on behalf of the applicant (to be filled in upon availability of a contact person) ______________________________
   (initials, surname)

Address, telephone _______________________________________________________

Appendix 8
to Resolution No.52
of the Ministry of Health of the Republic of Belarus
dated May 8, 2009

APPLICATION
for making amendments to the registration dossier of a medicinal preparation (pharmaceutical substance), previously registered in the Republic of Belarus
1. Applicant, address_________________________________________________

2. Manufacturer, address____________________________________________
   Including:
   carrying out production of a finished drug dosage form________________
   carrying out filling and (or) packaging_______________________________
   carrying out quality control________________________________________
   other participants of the medicinal preparation manufacturing and quality
   control ___________________________________________________________

3. Manufacturer of a pharmaceutical substance, address________________

4. Name of medicinal preparation____________________________________

5. International non-proprietary name (INN) __________________________

6. Composition of the medicinal preparation (specifying the names and
   amounts of active substances and excipients) __________________________

7. Drug dosage form specifying the dose of active substance (for single-
   component or two-component medicinal preparation) _____________________

8. Standard package (primary and secondary) specifying the dose number
   per package (filling) _______________________________________________

9. Mode of medicinal preparation administration (internal, external,
   parenteral and so on) _____________________________________________

10. Basic clinical and pharmacological group (according to ATC-code
    (Anatomical Therapeutic Chemical Classification)) _____________________

11. Shelf life_______________________________________________________

12. Storage conditions________________________________________________

13. Sections of the registration dossier whereto amendments (addenda)
    will be made ______________________________________________________
    (composition, marking, package etc.)

The application shall be submitted on the applicant’s letter headed paper,
shall be signed by an authorized person of the applicant with indication of
his/her position, surname and initials. All the fields provided for in the
application form shall be filled in.

The applicant shall assume the responsibility for efficacy, safety and
quality of the medicinal preparation, as well as guarantee reliability of the
information in the registration dossier and the present application.

"__" ____________ 200________________________ (signature of the applicant
or its representative) (initials, surname)

Contact person acting on behalf of the applicant (to be filled in upon
availability of a contact person) _____________________________ (initials, surname)

Address, telephone _____________________________