Text consolidated by Valsts valodas centrs (State Language Centre) with amending regulations of:

20 February 2007 [shall come into force on 24 February 2007];

4 August 2008 [shall come into force on 9 August 2008];

8 October 2013 [shall come into force on 15 October 2013];

11 August 2015 [shall come into force on 1 October 2015];

25 September 2018 [shall come into force on 28 September 2018];

15 January 2019 [shall come into force on 18 January 2019];

4 March 2021 [shall come into force on 9 March 2021];

7 December 2021 [shall come into force on 9 December 2021].

If a whole or part of a paragraph has been amended, the date of the amending regulation appears in square brackets at the end of the paragraph. If a whole paragraph or sub-paragraph has been deleted, the date of the deletion appears in square brackets beside the deleted paragraph or sub-paragraph.

Republic of Latvia

CabinetRegulation No. 304

Adopted 18 April 2006

**Regulations Regarding the Procedures for the Manufacture and Control of Medicinal Products, the Requirements for the Qualification and Professional Experience of a Qualified Person and the Procedures for the Issuance of the Certificate of Good Manufacturing Practice to a Medicinal Product Manufacturing Undertaking**

*Issued pursuant to*

*Section 5, Clauses 3 and 13 and Section 52 of the Pharmaceutical Law*

**I. General Provisions**

1. The Regulation prescribes the procedures for the manufacture and control of medicinal products, the requirements for the qualification and professional experience of a qualified person and the procedures for the issuance of the certificate of good manufacturing practice to a medicinal product manufacturing undertaking.

2. The Regulation shall apply to:

2.1. medicinal products for human use manufactured industrially or prepared using a method which includes an industrial process;

2.2. all medicinal products for human use which are manufactured in the Republic of Latvia, including medicinal products intended for export, or which are imported;

2.3. intermediate products,

2.4. homeopathic medicinal products;

2.5. herbal medicinal products which comply with the criteria for traditional herbal medicinal products specified in regulations regarding the registration of medicinal products;

2.6. investigational drugs;

2.7. the quality control of medicinal products prepared in a pharmacy;

2.8. active substances and excipients.

[*8 October 2013; 25 September 2018*]

2.1The following shall apply to investigational drugs:

2.11. Chapter IX of Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC (hereinafter – Regulation No 536/2014);

2.12. the principles of and guidelines for good manufacturing practice referred to in Article 63 of Regulation No 536/2014 in accordance Commission Delegated Regulation (EU) 2017/1569 of 23 May 2017 supplementing Regulation (EU) No 536/2014 of the European Parliament and of the Council by specifying principles of and guidelines for good manufacturing practice for investigational medicinal products for human use and arrangements for inspections, and also detailed relevant guidelines for good manufacturing practice of medicinal products which are included in the European Commission Guidelines referred to Section 51.1of the Pharmaceutical Law which have been published by the European Commission in Volume 4 of The rules governing medicinal products in the European Union and which are available on the website of the State Agency of Medicines;

2.13. Paragraphs 5 and 7, Sub-paragraph 8.5, Paragraph 9, Chapter III, Paragraph 30, Chapter V, Paragraphs 78, 79, 80, 81, 82, 83, 93, and 94 of this Regulation.

[*25 September 2018; 31 January 2022 / See Paragraph 99.2*]

2.2 The Commission Delegated Regulation (EU) No 1252/2014 of 28 May 2014 supplementing Directive 2001/83/EC of the European Parliament and of the Council with regard to the principles and guidelines of good manufacturing practice for active substances for medicinal products for human use (hereinafter – Regulation No 1252/2014), and the detailed guidelines for active substances which are included in the European Commission Guidelines for good manufacturing practice referred to in Section 51.1 of the Pharmaceutical Law which have been published by the European Commission in Volume 4 of The rules governing medicinal products in the European Union and which are available on the website of the State Agency of Medicines shall apply to active substances.

[*25 September 2018*]

3. The Regulation shall not apply to:

3.1. radionuclides (radioactive isotopes) in the form of sealed radiation sources;

3.2. whole blood, plasma or blood cells of human origin, except for industrially prepared plasma.

4. For the purpose of this Regulation:

4.1. [8 October 2013];

4.2. dividing up is the dividing of finished medicinal products and substances into a certain amount of units;

4.3. a finished product is a medicinal product to which all the stages of manufacture are applicable, including packaging in its final container;

4.4. packaging is any operation for turning a bulk product into a finished product, also filling and labelling;

4.5. a starting material is any substance used for the manufacture of medicinal products, except for the packaging material;

4.6. qualification is an operation by which it is confirmed and documented that any equipment used for the manufacture of medicinal products is appropriately installed, operates correctly and ensures the expected results. Qualification is a part of validation but the performance of qualification of separate stages does not mean the process validation;

4.7. good manufacturing practice is a part of the medicinal products quality assurance system which ensures that medicinal products are consistently produced, imported and controlled in accordance with the quality requirements appropriate to their intended use;

4.8. a batch is a defined quantity of a homogenous (with specified tolerances) medicinal product or intermediate product that is obtained in a separate manufacturing process or in several processes. In case of continuous manufacture, a batch may be a certain part of an amount manufactured. A batch size is a certain specified amount or amounts manufactured during a specified period of time;

4.9. specification is a detailed description of the requirements for the products and materials used or obtained in the manufacturing process;

4.10. an intermediate product is a partly processed material, also a starting material, which is subject to the further manufacturing steps (stages) of a medicinal product before it becomes a bulk product;

4.11. validation is a documented programme the implementation of which allows to affirm with great certainty that a certain process, method or system used in the manufacture or control of a medicinal product works constantly, ensuring the results which comply with the previously specified criteria;

4.12. the medicinal product manufacturer is a person which is carrying out manufacturing activities and in accordance with the laws and regulations regarding the procedures for licensing pharmaceutical activity has obtained a special permit (licence) for the manufacture of medicinal products or importation with permitted activity – manufacture of medicinal products (hereinafter – the special permit (licence) for the manufacture of medicinal products);

4.13. the pharmaceutical quality system shall be the organisational measures taken in order to ensure the conformity of the quality of medicinal products with their intended use.

[*4 August 2008; 11 August 2015; 25 September 2018*]

**II. Requirements for the Manufacture of Medicinal Products**

5. The medicinal product manufacturer shall carry out the manufacturing activities laid down in the laws and regulations governing pharmaceutical activities in accordance with good manufacturing practice and conditions of the special permit (licence) for the manufacture and importation of medicinal products. This provision shall also apply to the medicinal products which are intended only for export.

[*25 September 2018; 4 March 2021*]

6. The special permit (licence) for the manufacture of medicinal products is required for the performance of both total and partial manufacturing process as well as for different dividing up, packaging, and presentation processes of a finished product.

7. The special permit (licence) for the manufacture of medicinal products shall not be required for preparation, dividing up, changes in the packaging or presentation of medicinal products carried out by a pharmacist or pharmacist’s assistant at a pharmacy.

[*11 August 2015*]

7.1 Officials of the State Agency of Medicines which are referred to in Paragraph 33 of this Regulation shall, before issue of the special permit (licence) for the manufacture and importation of medicinal products or in relation to re-registration of the special permit (licence), carry out conformity assessment inspections in order to assess the conformity of the relevant premises, equipment, installations, staff and documents with the requirements which are laid down in this Regulation for good manufacturing practice and conditions for a special operation. A control report (Annex 1) shall be drawn up after the inspection.

[*4 March 2021*]

8. A medicinal product manufacturer shall ensure implementation of the following requirements:

8.1. personnel with adequate qualifications are engaged in the manufacture and control of the medicinal products and such personnel ensures the compliance with the requirements for the manufacture and control in accordance with the Regulation;

8.2. acts with medicinal products and investigational drugs in accordance with the Pharmaceutical Law and also with the requirements laid down in this Regulation and laws and regulations regarding the distribution and quality control of medicinal products;

8.3. in accordance with the laws and regulations regarding licensing regulations of pharmaceutical activity, notifies the State Agency of Medicines of all changes in the data which are submitted for the issue of the special permit (licence) for the manufacture and importation of medicinal products or re-registration thereof and, where necessary, submits updated description of the site, and also immediately (but not later than within five working days) informs if the responsible official referred to in Section 52 of the Pharmaceutical Law (hereinafter – the qualified person) is substituted;

8.4. ensures a possibility for the officials of the State Agency of Medicines to visit all the premises of the medicinal product manufacturer at any time;

8.5. ensures a possibility for the qualified person to fulfil the duties referred to in Paragraphs 10 and 11 of this Regulation, for example, by placing at his or her disposal all the necessary facilities;

8.6. complies with the principles of and guidelines for good manufacturing practice for medicinal products and uses only such active substances as starting materials which are manufactured in accordance with the requirements laid down in Regulation No 1252/2014 and guidelines for active substances which are included in the European Commission Guidelines referred to in Section 51.1 of the Pharmaceutical Law which have been published by the European Commission in Volume 4 of The rules governing medicinal products in the European Union and which are available on the website of the State Agency of Medicines. The manufacture of active substances includes both total and partial manufacturing or importation of active substances, and also different types of dividing up, packaging and presentation operations which are performed before the inclusion thereof in the composition of the medicinal products, including re-packaging or re-labelling performed by the distributor of the starting materials;

8.7. [4 March 2021];

8.8. carries out all the manufacturing or importation activities for the registered medicinal products (the medicinal products submitted for registration) in accordance with the information which is provided for in the submission for registration of medicinal products and registration documentation;

8.9. uses in manufacture of medicinal products only such active substances which are distributed in accordance with good distribution practice of active substances which is laid down in the European Commission Guidelines of 19 March 2015 on principles of Good Distribution Practice of active substances for medicinal products for human use (2015/C 95/01) (available on the website of the State Agency of Medicines) referred to in Section 22, Paragraph three of the Pharmaceutical Law and guidelines for active substances which are included in the European Commission Guidelines referred to in Section 51.1 of the Pharmaceutical Law which have been published by the European Commission in Volume 4 of The rules governing medicinal products in the European Union and which are available on the website of the State Agency of Medicines. A medicinal product manufacturer shall verify whether the active substance manufacturer and distributors have complied with good manufacturing practice and good distribution practice by auditing the sites of manufacturers of active substances and sites of operation of distributors of active substances. A medicinal product manufacturer shall verify such conformity itself or via intermediation of a third person with which the medicinal product manufacturer has entered into the contract;

8.10. ensures that excipients would be suitable for use in manufacture of medicinal products by establishing the conformity with good manufacturing practice which is assessed in accordance with the guidelines on official risk assessment in order to determine suitable good manufacturing practice for excipients which are included in the European Commission Guidelines referred to in Section 51.1 of the Pharmaceutical Law which have been published by the European Commission in Volume 4 of The rules governing medicinal products in the European Union and which are available on the website of the State Agency of Medicines. The requirements of other corresponding quality systems and also the source of excipients and intended use thereof, and previous quality deficiencies established shall be taken into account in such risk assessment. A medicinal product manufacturer shall ensure that corresponding good manufacturing practice found out in such way is applied and provide documentation for the measures which have been taken in accordance with this Sub-paragraph;

8.11. verifies the registration of manufacturers, importers, and wholesalers of active substances in the EudraGMDP database;

8.12. verifies the quality and authenticity of active substances and excipients;

8.13. reviews manufacturing methods on a regular basis in conformity with the scientific and technical development. If variations to the registration documentation of medicinal products are necessary, the variations shall be carried out in accordance with the procedures laid down in conformity with Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products;

8.14. obligations of the medicinal product manufacturer laid down in Chapters II, III, and IV and Article 31(1) and (5), Article 33, Article 35(1)(b) and (4), and Article 38(1) of Commission Delegated Regulation (EU) 2016/161 of 2 October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for the safety features appearing on the packaging of medicinal products for human use (hereinafter – Delegated Regulation No 2016/161).

[*4 August 2008; 8 October 2013; 25 September 2018; 15 January 2019; 4 March 2021*]

8.1 The safety features of medicinal products which are referred to in Article 3(2)(a) and (b) of Delegated Regulation No 2016/161 shall not be removed or covered, partially or fully, except for the following cases:

8.11. they can be removed or covered by the holder of a special permit (licence) for the manufacture of medicinal products which before that inspects, in conformity with Articles 16 and 17 of Delegated Regulation No 2016/161, whether they are authentic and have not been tampered with;

8.12. the holder of the special permit (licence) for the manufacture of medicinal products shall replace the abovementioned safety features of the medicinal products with equivalent safety features in respect of the possibility to inspect authenticity, identity of the medicinal products and obtain evidence on integrity of the medicinal products by complying with the safety requirements defined in the laws and regulations regarding labelling of medicinal products. Such replacement shall be carried out without opening the primary packaging. The safety features shall be regarded to be equivalent if:

8.12.1. they are equally efficient, allowing to inspect authenticity and identity of medicinal products and providing evidence on integrity thereof;

8.12.2. the unique identifier which is referred to in Article 3(2)(a) of Delegated Regulation No 2016/161 (hereinafter – the unique identifier) complies with the requirements which are laid down in Articles 4, 5, 6, and 7 of Delegated Regulation No 2016/161;

8.13. the replacement of the safety features is carried out in conformity with the principles of good manufacturing practice for medicinal products referred to in Sub-paragraph 8.6 of this Regulation.

[*15 January 2019 / Paragraph shall be applied from 9 February 2019 by complying with the transitional measures laid down in Articles 48 and 50 of Delegated Regulation No 2016/161. See Paragraph 99.3*]

8.2 In addition to Paragraph 8.1 of this Regulation, the anti-tampering device referred to in Article 3(2)(b) of Delegated Regulation No 2016/161 (hereinafter – the anti-tampering device), upon justified request in which the previous and new anti-tampering device is described and also labelling pictures and drafts are appended and upon coordination with the State Agency of Medicines, may be replaced with a new equivalent anti-tampering device by ensuring that the new anti-tampering device completely closes packaging and covers any parts of the previous anti-tampering device.

[*15 January 2019 / Paragraph shall be applied from 9 February 2019 by complying with the transitional measures laid down in Articles 48 and 50 of Delegated Regulation No 2016/161. See Paragraph 99.3*]

8.3 The unique identifier is allowed to be attached in the form of a sticker in one of the following cases:

8.31. there are no other possibilities in the manufacturing process or technically possible alternatives to print the unique identifier on the packaging (shall not apply to a parallel importer);

8.32. the State Agency of Medicines, upon registering medicinal products, has permitted to do it for parallel imported medicinal products, and also by protecting health of inhabitants and ensuring continuous delivery of medicinal products if the following provisions have been complied with:

8.32.1. a sticker on which the unique identifier is printed is the part of secondary or primary packaging and it is safe against falsification, it is not possible to remove it without damaging the packaging, the sticker itself or without leaving visible signs of damage;

8.32.2. a sticker on which the unique identifier is printed shall be attached by a medicinal product manufacturer in conformity with good manufacturing principles for medicinal products referred to in Sub-paragraph 8.6 of this Regulation;

8.32.3. secondary and primary packaging on which a sticker is attached shall, in addition to the requirements in respect of the unique identifier, comply with the requirements which are laid down for labelling in accordance with the laws and regulations regarding labelling of medicinal products.

[*15 January 2019 / Paragraph shall be applied from 9 February 2019 by complying with the transitional measures laid down in Articles 48 and 50 of Delegated Regulation No 2016/161. See Paragraph 99.3*]

8.4 Attaching of the unique identifier to the packaging in the form of a sticker is not permitted if:

8.41. it deteriorates legibility of data – data are not easily legible, clearly understandable and indelible;

8.42. the sticker on which the unique identifier is printed may be detached from the packaging without damaging packaging or sticker itself or without leaving visible signs of damage;

8.43. the sticker on which the unique identifier is printed is intended for the placement on the existing sticker thus causing confusion and suspicion of possible falsification.

[*15 January 2019 / Paragraph shall be applied from 9 February 2019 by complying with the transitional measures laid down in Articles 48 and 50 of Delegated Regulation No 2016/161. See Paragraph 99.3*]

9. A medicinal product manufacturer shall ensure that at least one qualified person the education and practical experience of whom complies with the qualification and professional requirements specified in Chapter III of this Regulation and who is mainly responsible for the fulfilment of the duties referred to in Paragraphs 10 and 11 of this Regulation is at his or her disposal permanently and continuously. If the medicinal product manufacturer complies with the conditions referred to in Paragraph 13 of this Regulation, he or she himself or herself may take responsibility and fulfil the duties of the qualified person.

10. Without prejudice to his or her relationship with the medicinal product manufacturer, the qualified person shall be responsible for the compliance of the manufacture and control of each batch of the medicinal product with the requirements of this Regulation and with the methods indicated in the registration documentation of the medicinal product. If investigational drugs are manufactured, the qualified person shall be responsible for the compliance of the manufacture and verification of each batch of the medicinal products with the principles and guidelines of good manufacturing practice, the documents and information of the product specification that the sponsor has indicated in the submission to the State Agency of Medicines for the receipt of the permit for clinical trials.

11. The qualified person shall in all cases (especially if the medicinal products are released for sale) certify the finished product, making accurate entries in the register or another equivalent document intended for such purpose and attesting with his or her signature that each batch of the medicinal product is manufactured and controlled in accordance with the requirements referred to in Paragraph 10 of this Regulation. After the specified operations the register or the relevant document shall be supplemented and retained in the undertaking for at least 5 years since the last entry made, ensuring the accessibility to the abovementioned register or document for the officials of the State Agency of Medicines.

11.1 If medicinal products are intended to be placed on the market in the European Union, the qualified person shall ensure that the safety features of medicinal products which are referred to in Article 3(2)(a) and (b) of Delegated Regulation No 2016/161 are on the packaging of medicinal products.

[*15 January 2019 / Paragraph shall be applied from 9 February 2019 by complying with the transitional measures laid down in Articles 48 and 50 of Delegated Regulation No 2016/161. See Paragraph 99.3*]

12. Such requirements shall be complied with in the manufacture of narcotic and psychotropic medicinal products which are laid down in the Law on the Legal Trade of Narcotic and Psychotropic Substances and Medicinal Products, and also Precursors and in the relevant laws and regulations which determine the requirements for the use of narcotic and psychotropic substances and medicinal products and also precursors in medicinal product manufacturing undertakings.

[*4 March 2021*]

12.1 A medicinal product manufacturer shall immediately inform the Health Inspectorate and marketing authorisation holder if the information is at its disposal that the medicinal products which it manufactures on the basis of the special permit (licence) referred to in Paragraph 5 of this Regulation and granted to it for the manufacture of medicinal products are falsified or it has suspicions that they may be falsified, regardless of whether these medicinal products are distributed in a legal supply chain or by illegal means, including by purchasing medicinal products by intermediation of a website.

[*8 October 2013*]

**III. Qualification and Professional Experience Requirements for the Qualified Person**

13. The qualified person shall meet the following qualification and professional experience requirements:

13.1. the qualified person shall possess a diploma, certificate or other evidence of the qualification awarded upon completion of the study programme of a higher education institution (university), or completion of such programme which in accordance with the procedures specified in laws and regulations is recognised as equal to the university study programme in Latvia and which includes at least four years of theoretical and practical studies in one of the following fields of science: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology. The minimum duration of studies at a university may be three and a half years if followed by the theoretical and practical studies of at least one year that include the training of at least six months in a general-type pharmacy and at the end of which an examination is taken in conformity with the requirements specified in the university study programme;

13.2. the study programme referred to in Sub-paragraph 13.1 of this Regulation shall include the theoretical and practical studies in which at least the following study courses are acquired:

13.2.1. physics;

13.2.2. general and inorganic chemistry;

13.2.3. organic chemistry;

13.2.4. analytical chemistry;

13.2.5. pharmaceutical chemistry, including the analysis of medicinal products;

13.2.6. general and medical biochemistry;

13.2.7. physiology;

13.2.8. microbiology;

13.2.9. pharmacology;

13.2.10. pharmaceutical technology;

13.2.11. toxicology;

13.2.12. pharmacognosy (the study of the composition of the active substances of plant and animal origin and the effects of the active substances);

13.3. at least two years of practical experience in one or several undertakings which have the special permit (licence) for the manufacture of medicinal products in such areas as the qualitative analysis of medicinal products, the quantitative analysis of active substances as well as testing and inspecting that are necessary to ensure the quality of medicinal products. The practical experience may be reduced by one year if the duration of studies at a university is at least 5 years and by a year and a half if the duration of studies is at least 6 years.

14. Studies of the study courses referred to in Sub-paragraph 13.2 of this Regulation shall be in such proportion as to enable the relevant person to fulfil the obligations of the qualified person specified in Paragraphs 10 and 11 of this Regulation.

[*4 August 2008*]

15. If diplomas, certificates or other official evidences of the qualification do not conform to the criteria specified in Sub-paragraph 13.1 of this Regulation, the State Agency of Medicines shall request that the relevant person submits the certification issued by the higher education institution regarding the completion of the study courses referred to in Sub-paragraph 13.2 of this Regulation.

**IV. Principles and Guidelines of Good Manufacturing Practice for Medicinal Products**

15.1 The guidelines which are included in the European Commission Guidelines referred to in Section 51.1 of the Pharmaceutical Law which have been published by the European Commission in Volume 4 of The rules governing medicinal products in the European Union and which are available on the website of the State Agency of Medicines shall be taken into account for the interpretation of the principles and guidelines of good manufacturing practice.

[*25 September 2018*]

16. A medicinal product manufacturer shall establish, implement, and maintain efficient pharmaceutical quality system which includes active participation of higher level management and staff of different structural units. Within the framework of good manufacturing practice, the pharmaceutical quality system shall apply to all processes, starting from the manufacture of investigational drugs, transfer of technologies, and commercial manufacture to the discontinuation of manufacture of medicinal products. In respect of manufacture of medicinal products, the pharmaceutical quality system shall ensure that:

16.1. the sale of the product is achieved by creating, planning, implementing, maintaining, and continuously improving the system which allows consistent supply of the products with appropriate quality indicators;

16.2. all the cycles of the product and that of the process related thereto are supervised and knowledge management is implemented in all the stages;

16.3. the medicinal products are created and developed by taking into account the requirements of good manufacturing practice;

16.4. manufacturing and control activities are clearly specified and good manufacturing practice is introduced;

16.5. management responsibilities are clearly specified;

16.6. the measures are taken for starting material and packaging material manufacturing, supply and use, selection and supervision of suppliers by making sure that each supply has been made from an approved supply chain;

16.7. the processes which ensure outsourcing management have been developed;

16.8. the control system within the framework of which efficient supervision and control system is developed and used has been established and maintained in order to ensure the process performance and product quality;

16.9. the results of the product and process supervision are taken into account during the process of batch release and also in order to investigate deviations and carry out preventive actions by avoiding potential deviations in the future;

16.10. all the necessary inspections of intermediate products and all inspections and validations of the process are performed;

16.11. quality improvements are constantly introduced which comply with the present knowledge level about the process and product;

16.12. the measures have been taken for the perspective assessment and approval of the planned variations, where necessary, by informing the relevant competent authority and receiving its approval before introduction of the variations;

16.13. after introduction of any variations, the assessment shall be carried out in order to approve that quality objectives have been reached and that there are no accidental harmful impacts on the product quality;

16.14. when investigating deviations, the possible product defects, and other problems, the analysis of reasons shall be carried out. The reasons shall be identified by using quality risk management principles. If it is not possible to identify the actual reason, it shall be tried to identify and rectify the most possible reason. If there are suspicions of human error or it is identified as a reason, it shall be justified and ensured that errors or problems of processes, procedures or system based errors or problems, if any, are not ignored. Appropriate corrective and preventive actions (CAPA) shall be identified and carried out during the investigation process. Such activity shall be managed and assessed in accordance with the quality risk management principles;

16.15. medicinal products are sold or supplied only after the qualified person referred to in Paragraph 9 of this Regulation has verified that all the batches of the medicinal products are manufactured and inspected in accordance with the registration documentation and other provisions of this Regulation which apply to the manufacture, control, and release of medicinal products;

16.16. the measures are taken for ensuring quality of medicinal products during their distribution and storage;

16.17. the self-control inspection and quality auditing process has been introduced in accordance with which the efficiency and suitability of pharmaceutical quality system are assessed on a regular basis.

[*25 September 2018*]

17. A medicinal product manufacturer shall ensure the compliance with the following requirements in respect of the personnel:

17.1. at each manufacturing or import site, there is sufficient number of employees with the necessary qualification which complies with the requirements laid down for the staff in the guidelines referred to in Paragraph 15.1 of this Regulation in order to ensure achievement of the objectives of a pharmaceutical quality system;

17.2. the duties of the management and supervision staff responsible for the implementation and operation of good manufacturing practice, including the duties of the qualified person referred to in Paragraph 9 of this Regulation, shall be defined in the position description. The hierarchy of staff relationship shall be defined in a structural scheme. The structural scheme and position descriptions shall be approved in accordance with the internal procedures laid down by the manufacturer;

17.3. the staff referred to in Sub-paragraph 17.2 of this Regulation shall be given certain authority for the performance of their duties;

17.4. the initial and permanent training of the staff shall be ensured by especially including acquisition of theory and concepts of quality assurance and good manufacturing practice and application thereof in practice, and the practical efficiency of the training shall be assessed on a regular basis;

17.5. hygiene programmes adjusted to the actions to be performed shall be developed by especially emphasising the procedures which refer to the health of the staff, personal hygiene and working clothes, and the requirements laid down therein shall be complied with.

[*25 September 2018*]

18. Premises and equipment shall, in addition to the construction requirements specified in laws and regulations, comply with the following requirements:

18.1. premises and manufacturing equipment shall be located, designed, constructed, adapted, and maintained to suit the intended operations;

18.2. premises and manufacturing equipment shall be laid out, designed, and operated in such a way as to minimise the risk of error and to permit effective cleaning and maintenance in order to avoid contamination, cross contamination of medicinal products and starting materials (contamination of a material or finished product with another material or product) and any adverse effect on the quality of the product;

18.3. premises and equipment which are used for manufacturing and importation activities which are critical for the quality of medicinal products shall be duly qualified and validated.

[*25 September 2018*]

19. A medicinal product manufacturer has established and maintains the documentation system which is based on specifications, manufacturing formulas, processing and packaging instructions, procedures and notes which apply to different manufacturing activities carried out. The documentation system shall ensure data quality and integrity. Documents are clear, without mistakes and are updated in a timely manner. The procedures determined previously in respect of general manufacturing activities and conditions and also special documents regarding manufacture of each batch are available. The abovementioned set of documents shall ensure the possibility to track the manufacturing history of each batch.

[*25 September 2018 / New wording of the Paragraph shall come into force on 31 January 2022. See Paragraph 2 of Amendments*]

20. For a medicinal product, the batch documentation shall be retained for at least 1 year after the expiry date of the batch to which it relates or for at least 5 years after the certification of the finished product referred to in Paragraph 11 of this Regulation, whichever is the longer period.

21. For an investigational drug, the batch documentation shall be retained for at least 5 years after the completion or formal discontinuation of the last clinical trial in which the batch was used. The sponsor or marketing authorisation holder, if different, shall be responsible for ensuring that such batch records are retained which are required for the subsequent registration of medicinal products in accordance with the laws and regulations regarding the registration of medicinal products.

22. When electronic, photographic or other data processing systems are used instead of written documents, the medicinal product manufacturer shall first validate the system to ensure that the data will be stored during the anticipated period of storage. Data which are stored in such systems shall be understandable, legible and easily accessible and they shall be issued to the officials of the State Agency of Medicines and Health Inspectorate upon request. Electronically stored data shall be protected against illegal access, data loss or damage by duplicating them or making backup copies thereof and transferring them to another storage system and also by saving audit trails.

[*25 September 2018 / Amendment regarding the new wording of the second and third sentence shall come into force on 31 January 2022. See Paragraph 2 of Amendments*]

23. The manufacturing process of medicinal products shall comply with the following requirements:

23.1. production operations shall be carried out in accordance with pre-established instructions, procedures and with the requirements of good manufacturing practice;

23.2. sufficient resources required shall be made available for the manufacturing process control;

23.3. all manufacturing process deviations and product defects shall be documented and thoroughly investigated;

23.4. appropriate technical or organisational measures shall be taken to avoid cross contamination and mix-ups of medicinal products and starting materials;

23.5. any new manufacturing process of medicinal products or important variations of a manufacturing process shall be validated. The critical phases of manufacturing processes shall be validated repeatedly on a regular basis.

23.6. [25 September 2018].

[*25 September 2018 / New wording of Sub-paragraphs 23.4 and 23.5 shall come into force on 31 January 2022. See Paragraph 2 of Amendments*]

24. The quality control shall meet the following requirements:

24.1. a medicinal product manufacturer shall establish and maintain the quality control system. The system shall be supervised by the person who has the required qualification which complies with the requirements laid down in the position description and who is not involved in the manufacturing;

24.2. one or several quality control laboratories are at the disposal of the person referred to in Sub-paragraph 24.1 of this Regulation with appropriate staff and equipment in order to carry out the necessary inspection tests of starting material and packaging materials and testing of intermediate product and final product of medicinal products, or such laboratory is available to the abovementioned person;

24.3. the laboratories with which a contract has been entered into and the requirements referred to in Paragraphs 25, 26, and 27 of this Regulation have been complied with may be used for quality control testing of medicinal products (including imported medicinal products);

24.4. [25 September 2018 / See Paragraph 2 of Amendments];

24.5. during the final control of the finished product before release of medicinal products for sale or distribution, in addition to the analytical testing results, other essential information such as the manufacturing conditions, the results of the manufacturing process inspections, the inspection of the manufacturing documents, and also the conformity of the finished product and packaging thereof with specifications shall be taken into account in the quality control system;

24.6. samples of each batch of a finished medicinal product shall be retained for at least 1 year after the expiry date;

24.7. [25 September 2018 / See Paragraph 2 of Amendments];

24.8. samples of starting materials, other than solvents, gases or water, used in the manufacturing process shall be retained for at least 2 years after the release of the product. The storage period of the samples may be shortened if the period of stability of the material, as indicated in the relevant specification, is shorter;

24.9. the State Agency of Medicines shall be notified of the storage place of medicinal products and starting materials and its officials shall be provided with a possibility to access samples at any time;

24.10. if medicinal products are manufactured for an individual order or in small quantities, or if the storage of the samples of medicinal products and starting materials is difficult because of their properties, other sampling and storing conditions may be specified upon agreement with the State Agency of Medicines.

[*25 September 2018 / New wording of Sub-paragraph 24.5 shall come into force on 31 January 2022. See Paragraph 2 of Amendments*]

25. If any manufacturing operation or operation linked thereto or quality control is carried out by another person (hereinafter – the contract acceptor), the medicinal product manufacturer and contract acceptor shall enter into a written contract regarding the performance of certain work. The contract shall clearly define the obligations of the parties, in particular the obligation of the contract acceptor to comply with the principles and guidelines for good manufacturing or importation practice and also the way in which the qualified person referred to in Paragraph 9 of this Regulation who is responsible for the certification of each batch shall fulfil his or her obligations.

[*25 September 2018*]

26. The contract acceptor shall ensure the fulfilment of the following requirements:

26.1. shall not subcontract any of the work entrusted to him or her under the contract referred to in Paragraph 25 of this Regulation without a written permission from the medicinal product manufacturer;

26.2. the contract acceptor who performs a part of the manufacturing operations under the contract on behalf of the initial manufacturer may be only the medicinal product manufacturer who has the special permit (licence) for the manufacture of medicinal products;

26.3. shall comply with the principles and guidelines for good manufacturing practice specified in this Regulation which are to be applied to the relevant activities, and also submit to the control carried out by the State Agency of Medicines.

[*25 September 2018*]

27. Prior to entering into an agreement regarding the performance of the quality control, a medicinal product manufacturer shall ensure that the officials of the State Agency of Medicines carry out the inspection and provide a statement regarding the compliance of the laboratory with the requirements of good manufacturing practice.

28. A medicinal product manufacturer shall ensure the compliance with the following requirements in respect of complaints and recall of medicinal products:

28.1. implement a system for recording and reviewing complaints received regarding the medicinal products together with an effective operation of such system on the basis of which the medicinal products which have already entered the distribution network may be recalled promptly and at any time. The medicinal product manufacturer shall record and investigate any complaint concerning a defect of medicinal products. The medicinal product manufacturer shall inform the State Agency of Medicines, the Health Inspectorate, and marketing authorisation holder within 24 hours after the establishment of the fact of any defect or complaint that could result in a recall or abnormal restriction on supply and, in so far as it is possible, indicate also the countries of destination;

28.2. any recall of medicinal products shall be made in accordance with the requirements specified in the laws and regulations regarding the distribution of medicinal products;

28.3. [25 September 2018 / See Paragraph 2 of Amendments];

28.4. [25 September 2018 / See Paragraph 2 of Amendments];

28.5. [25 September 2018 / See Paragraph 2 of Amendments];

28.6. [25 September 2018 / See Paragraph 2 of Amendments];

[*25 September 2018 / New wording of the introductory part shall come into force on 31 January 2022. See Paragraph 2 of Amendments*]

29. A medicinal product manufacturer shall ensure repeated self-control inspections as a part of the pharmaceutical quality system in order to supervise the implementation of and compliance with good manufacturing practice and suggest necessary corrective activities and preventive measures. Such inspections and any corrective actions subsequently taken shall be documented and such records shall be kept for at least five years.

[*25 September 2018*]

30. [25 September 2018]

31. A medicinal product manufacturer manufacturing medicinal products derived from human blood and plasma shall:

31.1. ensure that the manufacturing and purifying processes used in the manufacture of the medicinal products derived from human blood or human plasma are properly validated in order to attain batch-to-batch consistency and guarantee protection from contamination with specific viruses (hepatitis B surface antigen (HBs Ag), HIV 1 and HIV 2 antibodies (anti-HIV ½) hepatitis C virus antibody (anti-HCV));

31.2. notify the State Agency of Medicines of the methods used to reduce or eliminate pathogenic viruses liable to be transmitted by such medicinal products;

31.3. use such starting materials (human blood and plasma) for the manufacture of these medicinal products which are received from such blood preparation institutions where the collection, testing, processing, storage, and distribution of human blood and blood components is carried out in accordance with the laws and regulations regarding the quality and safety standards for collection, testing, processing, storage, and distribution of the human blood and blood components.

[*4 August 2008; 25 September 2018*]

**V. Procedures for Issuing the Certificate of Good Manufacturing Practice for Medicinal Products and Active Substances**

[*8 October 2013*]

32. In order to ensure that a manufacturer of medicinal products and active substances complies with the principles of good manufacturing practice laid down in this Regulation and also in order to make sure whether the manufacturers comply with the requirements of the Pharmaceutical Law and laws and regulations governing the field of manufacture of medicinal products and active substances in their operations, the State Agency of Medicines shall carry out inspections, where necessary, also unannounced inspections. Sample inspections shall be carried out at the laboratory of the State Agency of Medicines or at another official medicines control laboratory of the country of the European Economic Area. Inspections may be carried out in cooperation with the European Medicines Agency (the cooperation shall take the form of information exchange about both the planned and carried out inspections, also inspection coordination in third countries). The State Agency of Medicines shall:

32.1. carry out good manufacturing practice inspections (inspecting) at least once in three years for medicinal product manufacturers and at least once in five years for active substance manufacturers;

32.2. agree with a medicinal product manufacturer on the time when the inspection of good manufacturing practice will be commenced and notify the manufacturer thereof in writing not later than 10 working days before the commencement of the inspection (shall not apply to unannounced inspections);

32.3. inspect repeatedly medicinal product manufacturers which are located in Latvia or third countries;

32.4. establish supervision system by including therein inspections with regularity corresponding to risk and efficient follow-up inspections at the premises of active substance manufacturers, importers, and distributors located in Latvia;

32.5. if it has justified suspicions of non-compliance with the requirements referred to in the Pharmaceutical Law, in this Regulation, including good manufacturing practice and also good distribution practice, it may carry out inspections:

32.5.1. at the premises of an active substance manufacturer or distributor in third countries;

32.5.2. at the premises of a manufacturer or importer of excipients;

32.6. is entitled to carry out inspections at the premises of a marketing authorisation holder;

32.7. is entitled to carry out inspection of an active substance manufacturer on the basis of the submission of such active substance manufacturer registered in Latvia or medicinal product manufacturer located in Latvia which uses the relevant active substances for the manufacture of medicinal products if the active substance manufacturer is located in third countries, or the submission of the importer registered in Latvia or such marketing authorisation holder the registered medicinal products of which contain the relevant active substances;

32.8. is entitled to carry out the inspections referred to in Sub-paragraphs 32.3, 32.4, and 32.6 of this Regulation also upon request of another Member State of the European Union or country of the European Economic Area, the European Commission or European Medicines Agency;

32.9. is entitled to request the competent authority of another European Union Member State to carry out the inspection of the manufacturer registered in a third country;

32.10. is entitled to carry out the inspection of the manufacturer of active substances and excipients upon request of the European Directorate for the Quality of Medicines if the relevant active substance or excipient is included in the monograph of the European Pharmacopoeia and it has been issued with the certificate for the conformity with the requirements of the monograph of the European Pharmacopoeia.

[*8 October 2013; 25 September 2018*]

33. The State Agency of Medicines shall authorise competent officials for the performance of the inspection referred to in Paragraph 32 of this Regulation who have been trained to perform the control and supervision of the compliance with the requirements of good manufacturing practice and who have the following rights:

33.1. to inspect the manufacturing undertakings of medicinal products or substances used as starting materials and all the laboratories which are used by the medicinal product manufacturer in order to determine whether the medicinal products are manufactured and controlled in accordance with the good manufacturing practice and the manufacturing and control methods indicated in the documents submitted for the registration of the medicinal products. The abovementioned shall also apply to the inspection of contract acceptors who have entered into the agreement referred to in Paragraph 25 of this Regulation with a medicinal product manufacturer for the performance of separate manufacturing stages or the quality control;

33.2. to take samples in order to perform independent testing at the official medicines control laboratory of a country of the European Economic Area or at the laboratory of the State Agency of Medicines. Expenses connected with the testing of medicinal products shall be covered by the person controlled in accordance with the price list of paid services provided by the State Agency of Medicines;

33.3. to review all the documentation of the object to be inspected;

33.4. to inspect whether the manufacturing processes used in the manufacture of immunological preparations (vaccines, toxins, allergenic products) are properly validated and attain batch-to-batch consistency.

[*8 October 2013; 11 August 2015; 25 September 2018*]

33.1 The State Agency of Medicines and Health Inspectorate shall establish and implement duly developed quality system which is complied with by the management and officials who carry out the inspections. The quality system shall be updated accordingly.

[*25 September 2018 / Paragraph shall come into force on 31 January 2022. See Paragraph 2 of Amendments*]

34. A medicinal product manufacturer shall provide to the officials of the State Agency of Medicines the following data during the control:

34.1. information on the control of the finished medicinal products and control of the ingredients and control carried out at the intermediate stages of the manufacturing process in accordance with the documentation of the registration of the medicinal products;

34.2. on the immunological preparations and medicinal products obtained from human blood and plasma – copies of the certificates of all the finished products issued by the qualified person.

35. The authorised officials of the State Agency of Medicines during the inspections of medicinal product manufacturing undertakings shall take into account the Compilation of Community Procedures on Inspections and Exchange of Information published on behalf of the European Commission. In order to interpret the principles and guidelines of good manufacturing practice, also the principles of good manufacturing practice for active substances, the guidelines of the European Commission shall be taken into account.

36. Authorised officials of the State Agency of Medicines shall, after each inspection referred to in Paragraph 32 of this Regulation, prepare an inspection report (Annex 1) where it is indicated whether the medicinal product manufacturer complies with the requirements of good manufacturing practice. The State Agency of Medicines shall, within three working days after drawing up the report, send the control report to the inspected person in the form of an electronic document to his or her electronic mail address or, upon request, in the form of a printed document, and shall ensure a possibility to provide comments. One copy of the control report shall be sent to the medicinal product manufacturer where the inspection had been carried out, the other copy, if necessary, to the authority which requested the inspection. If the investigational drug manufacturer or importer is inspected, one copy of the control report shall be sent also to the sponsor of clinical research by ensuring the compliance with confidentiality. The State Agency of Medicines may make available the control report of the investigational drug manufacturer or importer to other Member States, clinical medicinal product investigation ethics committee or the European Medicines Agency upon the justified request thereof.

[*8 October 2013; 4 March 2021*]

37. Expenses related to the inspection of good manufacturing practice of a medicinal product manufacturing undertaking and the sample testing shall be covered by the medicinal product manufacturer in accordance with the price list of paid services provided by the State Agency of Medicines.

[*11 August 2015*]

38. The State Agency of Medicines shall, on the basis of the report referred to in Paragraph 36 of this Regulation and information provided by the manufacturer on rectification of deficiencies, take the relevant decision:

38.1. to issue the certificate if the conformity with the principles and guidelines for good manufacturing practice has been established during the inspection;

38.2. to postpone the issuance of the certificate, indicating the reasons and time period during which the necessary measures shall be carried out. In determining the period of time, it shall be taken into account that the final time period for the issuance of the certificate of good manufacturing practice may not exceed 90 days after the carrying out of the inspection referred to in Paragraph 32 of this Regulation;

38.3. to refuse to issue the certificate.

[*8 October 2013; 4 March 2021*]

39. The State Agency of Medicines shall take the decision to refuse to issue a certificate if the following has been established in the control report and in the assessment of information provided by the manufacturer on rectification of deficiencies:

39.1. the manufacture of medicinal products at the specific manufacturing site does not comply with the principles and guidelines for good manufacturing practice specified in this Regulation;

39.2. there is no qualified person at the medicinal product manufacturing undertaking;

39.3. the duties of the qualified person are carried out by a person whose qualification and experience does not comply with the requirements specified in this Regulation.

[*4 March 2021*]

40. The State Agency of Medicines shall, not later than within five days after taking the relevant decision, notify in writing the medicinal product manufacturer thereof.

41. The State Agency of Medicines shall:

41.1. issue the certificate of good manufacturing practice compliance of a manufacturer (Annex 2) to the inspected medicinal product or active substance manufacturer or medicinal product importer (a person which is involved in the activities for the performance of which, in accordance with the laws and regulations regarding the procedures for bringing in and out of the medicinal products, a special permit (licence) for the manufacture or importation of medicinal products which is issued by the State Agency of Medicines in accordance with laws and regulations regarding the procedures for licensing pharmaceutical activity is required) if the activity of the inspected person complies with the requirements for good manufacturing practice. The certificate shall be issued in the form of an electronic document by sending it to the electronic mail address of the inspected person within three working days after the relevant medicinal product or active substance manufacturer or medicinal product importer has paid the specified charge for the assessment of the documents and inspection of good manufacturing practice in accordance with the price list of paid services provided by the State Agency of Medicines. If the good manufacturing practice compliance assessment is associated with travel, the manufacturer shall cover the travel (transport) expenses of the State Agency of Medicines to the undertaking and return, expenditures for the preparation of a visa, expenditures for the hotel (lodging), health insurance expenses and daily allowance in conformity with the laws and regulations regarding the procedures by which expenditures associated with official trips and work trip of employees shall be compensated. A certificate in the form of a printed document (including a duplicate) shall be issued within three working days after receipt of a request, and an additional charge shall be taken for the abovementioned service in accordance with the price list of paid services provided by the State Agency of Medicines;

41.2. if the decision referred to in Sub-paragraph 38.3 of this Regulation has been taken, take, in conformity with the laws and regulations regarding the procedures for licensing pharmaceutical activity, the decision to suspend the operation of the special permit (licence) for the manufacture of medicinal products up to the rectification of deficiencies referred to in the control report. The decision to suspend the operation of the special permit (licence) for the manufacture of medicinal products shall not be taken if:

41.2.1. medicinal products are classified to be critical due to their possible non-availability;

41.2.2. non-compliance with the requirements of good manufacturing practice is established but immediate threats to the public health are not caused thereby, and an agreement on the plan for measures for the rectification of deficiencies has been reached;

41.3. include the information on the issued certificate of good manufacturing practice compliance of a manufacturer in the EudraGMDP database;

41.4. enter the information in the EudraGMDP database if the result of the carried out inspection referred to in Paragraph 32 of this Regulation indicates that the manufacturer of a medicinal product, active substance or excipient fails to comply with the requirements laid down in the Pharmaceutical Law and in this Regulation and the requirements of good manufacturing practice have not been complied with.

[*8 October 2013; 11 August 2015; 25 September 2018*]

**VI. Quality Control of Medicinal Products Prepared in a Pharmacy**

42. The quality control requirements specified in this Chapter shall apply to medicinal products prepared in a pharmacy in accordance with a prescription (*formula magistralis*) or a written request of a medical treatment institution (*formula officinalis*).

43. The head of a pharmacy shall be liable for the quality of medicinal products prepared in the pharmacy. The same person may not prepare medicinal products and carry out the quality control of these medicinal products.

44. The following control shall be mandatory for medicinal products prepared in a pharmacy:

44.1. in accordance with Paragraphs 61 and 64 of this Regulation (by documenting the results in writing);

44.2. in accordance with Paragraphs 66 and 67 of this Regulation – the inspection of the aggregate state, uniformity of mass, colour, taste, and odour of the medicinal products as well as the inspection of solutions in order to specify particulate matter (hereinafter – the organoleptic control);

44.3. in accordance with Paragraphs 74, 75 and 76 of this Regulation – when dispensing medicinal products.

45. The following shall be performed for medicinal products prepared in a pharmacy, if necessary (on the basis of instructions of the head of the pharmacy):

45.1. the physical control – in accordance with Paragraphs 68 and 69 of this Regulation;

45.2. the chemical control – in accordance with Paragraphs 70, 71, and 72 of this Regulation;

45.3. the questioning control – in accordance with Paragraph 73 of this Regulation.

46. In order to perform the quality control of the medicinal products prepared, a specially equipped workplace with devices, apparatus, and equipment used in analytical work shall be present in a pharmacy. Taking into account the specific nature of the pharmacy work, the head of a pharmacy shall develop the list of devices, apparatus, and equipment required for the analytical work. Annex 3 to this Regulation shall be used in drawing up this list. The list shall be co-ordinated with the State Agency of Medicines.

47. The head of a pharmacy shall approve the list of nomenclature of the concentrates and semi-finished products used in the pharmacy.

48. The head of a pharmacy shall approve the list of those persons who perform the following duties in a pharmacy:

48.1. a person who inspects the starting materials purchased as well as performs the duties specified in Paragraphs 53, 54, 55, 56, 57, 58, and 59 of this Regulation;

48.2. a person who accepts prescriptions and dispenses medicinal products (hereinafter – the dispensing chemist) as well as performs the duties specified in Paragraphs 61, 64, 74, 75, 76, and 77 of this Regulation;

48.3. a person who prepares medicinal products and performs the duties specified in Paragraphs 62 and 63 of this Regulation;

48.4. a person who tests medicinal products and performs the duties specified in Paragraphs 66, 67, 68, 69, 70, 71, and 72 of this Regulation.

49. The measuring instruments calibrated and verified in accordance with the legal acts issued pursuant to the law On Uniformity of Measurements shall be used in a pharmacy.

50. The results of the control performed in a pharmacy shall be registered in the relevant register (Annex 4).

51. Before making the first entry, the pages of the register referred to in Paragraph 50 of this Regulation shall be numbered, the register shall be sewn through and approved with the seal of the pharmacy and the signature of the head of the pharmacy. The register shall be kept in the pharmacy for a year after making the last entry.

52. A pharmacy shall submit the annual report on the quality control of medicinal products in the pharmacy (Annex 5) to the State Agency of Medicines until 1 February of the next year.

53. The head of a pharmacy shall ensure incoming control of starting materials intended for the preparation of medicinal products in the pharmacy. The control shall include the following measures:

53.1. the inspection of the existence of the documents attesting to the quality of the starting materials;

53.2. the inspection of the leakproofness and labelling of the packaging;

53.3. the organoleptic control (if possible).

54. If there are any doubts or suspicions, a pharmacy shall send the samples of starting materials to the State Agency of Medicines for the performance of full chemical analysis. These starting materials shall be placed in the quarantine zone up to the final ascertaining of the matter. If, in performing analysis, the non-compliance with the quality requirements has been established, the State Agency of Medicines shall notify thereof also the Health Inspectorate.

[*4 August 2008*]

55. Starting materials shall be stored in accordance with the storage requirements specified for the relevant substance.

56. A labelling shall be placed on flat-bottomed vessels in which starting materials are stored, indicating the name, manufacturing batch number, expiry date, and filling date of the starting materials. If the highly potent substances referred to in Annex 6 of this Regulation are being stored in a flat-bottomed vessel, the maximum single and daily doses referred to in this Annex shall also be indicated on the labelling. The given name, surname, and signature of the person who filled in starting materials shall be indicated on the label of a flat-bottomed vessel. Flat-bottomed vessels which are intended for starting materials used for the manufacture of sterile forms of medicinal products shall have the indication “Sterilajām zāļu formām”[For sterile pharmaceutical forms].

57. Liquids shall be kept in the flat-bottomed vessels equipped with calibrated droppers or pipettes on which the number of drops of a certain liquid per one millilitre is indicated.

58. A flat-bottomed vessel shall be refilled only after the utilisation of the previous content thereof and the treatment of a container in accordance with the instruction.

59. Crude herbal medicinal plants collected by inhabitants shall be inspected in a pharmacy by the external features, specifying their identity, the samples shall be taken and the following inspections shall be ensured:

59.1. the microscopic inspection in order to specify the identity thereof;

59.2. the determination of heavy metals (lead, cadmium);

59.3. the qualitative and quantitative analysis (if necessary).

60. All prescriptions by which medicinal products are prepared shall be registered in a pharmacy in the prescription register which is drawn up in accordance with Annex 7 of this Regulation. A separate register shall be created for the registration of requests of medical treatment institutions. The prescription registers and registers of requests of medical treatment institutions shall be stored in the pharmacy for the current and previous year.

61. The dispensing chemist shall carry out the following operations:

61.1. inspect the compliance of the prescription type with the content of the medicinal product prescribed;

61.2. inspect the compliance of the drawing up of the prescription with the laws and regulations determining the procedures for drawing up prescriptions;

61.3. inspect the term of validity of the prescription;

61.4. inspect the compliance of the single and daily doses of the highly potent substances referred to in Annex 6 of this Regulation, which are specified on the prescription, with the patient’s age;

61.5. inspect whether, in accordance with the laws and regulations determining the procedures for drawing up prescriptions, the amount of a certain substance is not exceeded which is allowed to be prescribed on one prescription, if the composition of the prescribed medicinal product includes ethyl alcohol, narcotic and equivalent psychotropic substances referred to in the Schedule II of narcotic and psychotropic substances and precursors permitted in Latvia, and psychotropic substances referred to in the Schedule III of narcotic and psychotropic substances and precursors permitted in Latvia;

61.6. assess the composition of the prescribed medicinal products from the point of view of the chemical and psychical compatibility in order to ascertain that the medicinal products to be prepared are effective and safe;

61.7. calculate the price of the medicinal products;

61.8. fill in the prescription register, issue a completed receipt to the customer and inform the customer orally of the time when he or she may receive the finished medicinal product, indicating the time up to which the medicinal product must be taken;

61.9. attach the receipt number to the prescription and hand over the prescription for the preparation of the medicinal product.

62. A person who prepares medicinal products shall observe the instructions on the prescription and the time when the medicinal products have to be prepared.

63. During the preparation of medicinal products or immediately after the preparation of medicinal products, if it is not necessary to make calculations previously, the person who prepares the medicinal products shall fill in a control counterfoil in which the information referred to in Annex 8 to this Regulation shall be indicated.

64. The person who prepares medicinal products shall hand over a completed control counterfoil together with the prepared and inspected medicinal products and the prescription (request) to the dispensing chemist. The dispensing chemist shall:

64.1. compare the data on the control counterfoil and the prescription (request);

64.2. inspect the correctness of the calculations made;

64.3. inspect the suitability of the packaging of the medicinal products with the physical and chemical features of the ingredients included in the composition of the medicinal products;

64.4. ensure that the prepared and inspected medicinal products are stored in accordance with their physical and chemical features up to the dispensing to the patient or medical treatment institution.

65. Control counterfoils shall be kept in a pharmacy for 3 months after completing thereof. The signatures of those persons who have prepared the medicinal product, who have packed the medicinal product (if the medicinal product has been packed by a person other than the person who has prepared it) and who has inspected the medicinal product as well as the signature of the dispensing chemist shall be on the control counterfoil. The analysis number of the medicinal product shall also be indicated on the control counterfoil.

66. For medicinal products to be used orally which are intended for children, the taste shall be inspected for each preparation, but for medicinal products which are intended for adults it shall be inspected randomly.

67. In order to specify particulate matter in ophthalmological solutions, the organoleptic control shall be carried out in compliance with the following requirements:

67.1. the control shall be carried out after the filtration of the solution and filling in the direct packaging;

67.2. the control shall be performed in a specially arranged workplace which is protected from direct sunlight and is equipped with a device for the determination of particulate matter in solutions. It is allowed to use the white and black display which is illuminated in such a way that the light does not shine into the eyes of a controller;

67.3. the control shall be carried out by screening the packaging units filled with a solution against the white and black background which is illuminated with a 60 watts mat bulb or a 20 watts fluorescent light bulb. For coloured solutions 100 watts and 30 watts bulbs shall be used respectively. The distance from the eyes to the screening object shall be from 25 to 30 cm but the angle between the optical axis of screening and the light direction shall be around 90°;

67.4. the visual acuity of the controller shall be 1.0 (if necessary, it shall be corrected with optical devices);

67.5. the surface of the packaging unit to be screened shall be clean and dry;

67.6. the packaging unit shall be placed in the control area, turned upside down and screened against the black and white background. Then, avoiding sharp motions, it shall be turned back to the initial state and screened again against the black and white background;

67.7. if particulate matter is established, the solution shall be filtered and controlled again.

68. The physical control shall be carried out randomly taking into account all the types of medicinal products prepared. In performing the physical control, the total weight and volume of the medicinal products, the weight and volume of the separate dosage units shall be inspected taking into account the permissible deviations in accordance with Annex 9 to this Regulation.

69. The concentration of a solution may be calculated using the formula in which the refractive index determined with a refractometer is used.

70. In order to determine the identity of the substances included in the composition of medicinal products (the qualitative analysis) and the amount thereof (the quantitative analysis), the chemical control shall be carried out.

71. The qualitative analysis shall be carried out for:

71.1. the purified water obtained in a pharmacy. The analysis shall be carried out once a day prior to preparation of medicinal products, taking the water from each container, or, if a pipeline is used, at each workplace, inspecting the presence of calcium, magnesium, chloride ions and sulphate ions in accordance with the requirements of the European Pharmacopoeia. The presence of oxidisable substances and ammonium ions shall be also inspected in the water intended for the preparation of solutions and eye drops for newborn children. Once in a half year a pharmacy shall send the purified water to the State Agency of Medicines for carrying out the full chemical analysis;

71.2. the starting materials upon the receipt thereof at the premises of the preparation. For the highly potent substances referred to in Annex 6 to this Regulation if any doubts or suspicions have arisen – also upon receipt in a pharmacy.

[*4 August 2008*]

72. The qualitative and quantitative analysis shall be carried out for:

72.1. the eye drops and eye ointments containing narcotic substances, tetracaine hydrochloride (dicaine) or atropine sulphate;

72.2. the medicinal products intended for newborn children up to the age of 1 month;

72.3. the hydrochloric acid solution for internal use, atropine sulphate, mercury dichloride and silver nitrate solutions;

72.4. all concentrates and semi-finished products, including triturations;

72.5. the ethyl alcohol solution if it is diluted in a pharmacy, determining the concentration in percentage by volume with an alcoholmeter or by density with an aerometer or a hydrometer, or a pycnometer, using the pharmacopoeia tables (if necessary, also upon receipt in a pharmacy);

72.6. all types of the prepared medicinal products randomly, paying special attention to the medicinal products intended for children.

73. The questioning control may be performed in a pharmacy randomly and in the case of doubts. A person who carries out the questioning control shall name the first ingredient of the medicinal product to be inspected, then the person who prepared the medicinal product shall name all the ingredients taken and the amounts thereof.

74. When dispensing medicinal products prepared in a pharmacy to a patient or medical treatment institution, the control thereof shall be performed.

75. When dispensing medicinal products, the dispensing chemist shall inspect the following:

75.1. the compliance of the information indicated on the receipt and the labelling with the prescription (request);

75.2. the time of submission of the prescription (request) and the time of the preparation of the medicinal product;

75.3. the compliance of the labelling of the medicinal products with the laws and regulations regarding the labelling of medicinal products.

76. When dispensing medicinal products, the dispensing chemist shall sign on the prescription, indicating the date of dispensing the medicinal products, and shall fill in the prescription register.

77. When dispensing medicinal products to a customer, the dispensing chemist shall remind how the medicinal products are to be used by indicating that the medicinal products may not be used for a longer period of time than is specified by the doctor, and recommend to observe the expiry date of the medicinal products and the storage indications.

**VII. Supervision and Sanctions**

78. The supervision of manufacture of medicinal products laid down in this Regulation after the relevant special permit (licence) for the manufacture and importation of medicinal products is issued, and also the supervision of replacement of the requirements for the manufacture of active substances and excipients and safety features of medicinal products shall be ensured by the State Agency of Medicines by carrying out the inspections (inspecting) referred to in Paragraph 32 of this Regulation. The Health Inspectorate shall supervise the compliance with the quality control requirements of the medicinal products manufactured at a pharmacy.

[*4 March 2021*]

79. Upon request of the Member States of the European Union, the countries of the European Economic Area, the European Commission or the European Medicines Agency, the State Agency of Medicines shall authorise officials for carrying out the inspections referred to in Paragraph 32 of this Regulation at the medicinal product manufacturer who is located in the third countries and Latvia.

[*8 October 2013*]

80. The State Agency of Medicines shall inspect whether the qualification of the qualified person complies with the requirements laid down in this Regulation and notify the Health Inspectorate of non-conformity. The Health Inspectorate is entitled to suggest a medicinal product manufacturer to suspend temporarily or remove the qualified person from the office if he or she fails to fulfil the duties referred to in Paragraphs 10 and 11 of this Regulation.

[*25 September 2018*]

81. The State Agency of Medicines is entitled to send the control report referred to in Paragraph 36 of this Regulation to the Health Inspectorate for taking the decision regarding the suspension of the manufacture of medicinal products if it has been established during the inspection and it is indicated in the control report that:

81.1. the manufacturing is carried out in the premises not referred to in the submission for the receipt of the special permit (licence) for the manufacture of medicinal products;

81.2. such medicinal products or dosage forms are manufactured which have not been referred to in the submission for the receipt of the special permit (licence) for the manufacture of medicinal products;

81.3. the medicinal product manufacturer does not ensure compliance with the requirements specified in Paragraph 8 of this Regulation;

81.4. the qualified person does not perform the duties specified in Paragraphs 10 and 11 of this Regulation;

81.5. the medicinal product manufacturer does not present during the control the data and documentation specified in Paragraph 34 of this Regulation.

[*4 August 2008*]

82. After receipt of the control report of the State Agency of Medicines referred to in Paragraph 81 of this Regulation, the Health Inspectorate shall take the decision regarding the suspension of the manufacture of medicinal products in accordance with the Pharmaceutical Law.

[*4 August 2008*]

83. If the suspension of the manufacture of medicinal products is connected with the violations regarding the use of narcotic and psychotropic substances and precursors in the manufacture of medicinal products specified in the Law on the Legal Trade of Narcotic and Psychotropic Substances and Medicinal Products, and also Precursors, and also in Regulation (EC) No 273/2004 of the European Parliament and of the Council of 11 February 2004 on drug precursors, Council Regulation (EC) No 111/2005 of 22 December 2004 laying down rules for the monitoring of trade between the Community and third countries in drug precursors, and Commission Delegated Regulation (EU) 2015/1011 of 24 April 2015 supplementing Regulation (EC) No 273/2004 of the European Parliament and of the Council on drug precursors and Council Regulation (EC) No 111/2005 laying down rules for the monitoring of trade between the Union and third countries in drug precursors, and repealing Commission Regulation (EC) No 1277/2005, the Health Inspectorate shall notify the law enforcement institutions thereof.

[*4 March 2021*]

84. The Health Inspectorate shall, at least once a year, carry out the inspections in pharmacies owning a specific permit (licence) for opening (operation) of a general-type pharmacy or for opening (operation) of a closed-type pharmacy with a condition of specific operation – preparation of medicinal products.

[*4 August 2008*]

85. If there are substantiated suspicions or doubts, the Health Inspectorate is entitled to take samples of the medicinal products prepared, the purified water obtained, the concentrates and semi-finished products to be used for the preparation of medicinal products in a pharmacy and send them to the laboratory for the examination, including for microbiological testing. Expenses of the testing shall be covered by the person controlled in accordance with the price list of the paid services provided by the State Agency of Medicines.

[*4 August 2008; 11 August 2015*]

86. When taking samples of medicinal products for the quality control, the official of the Health Inspectorate shall draw up the sampling record in accordance with the laws and regulations which determine the procedures by which the market supervision institutions shall request and take samples of products. The sampling record shall contain the following additional information:

86.1. the number of the prescription or the request of the medical treatment institution;

86.2. the composition of the medicinal product;

86.3. the position, given name and surname of the person who prepared the medicinal product;

86.4. the position, given name and surname of the person who inspected the medicinal product.

[*4 August 2008*]

87. The Health Inspectorate shall hand over the samples to the State Agency of Medicines for carrying out the expert-examination by drawing up the document regarding the handing over of the samples for the expert-examination in accordance with the laws and regulations regarding the procedures by which the market supervision institutions shall request and receive samples of products.

[*4 August 2008*]

88. The State Agency of Medicines shall carry out the organoleptic testing, physical testing and full chemical testing – the qualitative and quantitative analysis – of the samples of the medicinal products submitted for the expert-examination.

89. The State Agency of Medicines shall prepare and submit the opinion of the expert-examination regarding the control results – the testing report – to the Health Inspectorate in accordance with the laws and regulations regarding the procedures by which the market supervision institutions shall request and receive samples of products.

[*4 August 2008*]

90. A pharmacy shall, upon request of the State Agency of Medicines, provide any information connected with the preparation, quality control, and documentation of the medicinal products.

91. If it is determined during the testing of samples that the quality of the medicinal products prepared in a pharmacy does not comply with the requirements specified in the documentation of the technical norms (for example, in the pharmacopoeia, technical rules), the Health Inspectorate shall notify the pharmacy thereof in writing within three days. The head of the pharmacy shall identify the reasons for non-compliance of the quality of the medicinal products and implement measures in order to prevent and not to allow such violations in future as well as shall, within a month, notify the Health Inspectorate in writing of the measures taken. If the quality of the medicinal products has been affected by inappropriate quality of the starting materials, the head of the pharmacy shall ensure that the medicinal products prepared from these starting materials are recalled.

[*4 August 2008*]

92. If violations which may affect the quality of the manufactured medicinal products are established repeatedly within a year, the Health Inspectorate shall notify the State Agency of Medicines thereof.

[*4 August 2008; 8 October 2013*]

93. The State Agency of Medicines and the Health Inspectorate shall ensure, according to their competence, prompt information exchange for the promotion of the enforcement of this Regulation and shall provide law enforcement institutions and the Ministry of Health with information on the circumstances that are evidence of the diversion of medicinal products to illegal circulation.

[*4 August 2008*]

94. The Ministry of Health, the State Agency of Medicines, the Health Inspectorate, and other authorities shall not disclose information related to the commercial secret of a medicinal product manufacturer and which has become known to the authorities in the course of enforcing this Regulation.

[*4 August 2008*]

**VIII. Closing Provisions**

95. The following are repealed:

95.1. Cabinet Regulation No. 432 of 12 December 2000, Regulations Regarding the Manufacture and Control of Medicinal Products (*Latvijas Vēstnesis*, 2000, No. 454/457; 2003, No. 114);

95.2. Cabinet Regulation No. 396 of 11 September 2001, Procedures for Issue of Medicinal Product Good Manufacturing Practice Conformity Assessments and Medicinal Product Good Manufacturing Practice Certificates to Medicinal Product Manufacturing Undertakings (*Latvijas Vēstnesis*, 2001, No. 131; 2003, No. 167).

96. A person who fulfilled the duties of the qualified person up to 16 December 2000 but whose qualification and professional experience do not conform to the requirements referred to in this Regulation has the right to continue the fulfilment of the abovementioned duties in the European Union and in the countries of the European Economic Area. In the field connected with investigational drugs, such person has the right to continue the performance of the duties of the qualified person in the Republic of Latvia.

97. If a person has a diploma, a certificate or another attestation regarding the qualification granted prior to 16 December 2000 for completion of a programme or study courses at a higher education institution which is recognised in Latvia as being equivalent to what is referred to in Paragraph 13 of this Regulation, such person may perform the duties of the qualified person if he or she has at least 2 years’ experience in one or more medicinal product manufacturing undertakings that have the special permit (licence) for the manufacture of medicinal products in a field related to the supervision of the manufacture of medicinal products, the qualitative and quantitative analysis of active substances as well as to the performance of inspections required for the quality assurance of finished medicinal products under direct control of the qualified person. If the practical work experience of the relevant person exceeds 10 years but during the last 2 years he or she has not been employed in the supervision of manufacturing, i.e. in the medicinal product quality control under direct supervision of the qualified person, such person shall work for at least 1 year in the supervision of manufacturing, i.e. in the medicinal product quality control under direct supervision of the qualified person in order to obtain the right to work as the qualified person.

[*4 August 2008*]

98. In respect of herbal medicinal products which comply with the traditional herbal medicinal product criteria specified in the regulations regarding the registration of medicinal products and which are on the market on the day of coming into force of this Regulation, the requirements of this Regulation shall be implemented by 20 May 2011.

99. Until receipt of the special permit (licence) referred to in Paragraph 5 of this Regulation for the manufacture/importation of medicinal products, but no longer than until 31 December 2006, the merchants to whom the special permit (licence) has been issued for the following types of pharmaceutical operations on the day of coming into force of this Regulation are entitled to perform the manufacturing operations of medicinal products referred to in Paragraph 6 of this Regulation:

99.1. the opening (operation) of a medicinal product manufacturing undertaking;

99.2. the manufacture of medicinal products in a pharmacy;

99.3. the manufacture (re-packaging and re-dividing up) of medicinal products at a medicinal product wholesale facility.

99.1 The conditions of Sub-paragraph 41.1 of this Regulation regarding issue of a certificate of good manufacturing practice compliance or duplicate thereof to a medicinal product or active substance manufacturer in a paper document format for additional fee shall come into force on 1 July 2014.

[*8 October 2013*]

99.2 Paragraph 2.1 of this Regulation shall come into force after six months from the day when the notification referred to in Article 82(3) of Regulation No 536/2014 is published in the Official Journal of the European Union. After publication of the notification, the Ministry of Health shall send it for publication in the official gazette *Latvijas Vēstnesis*.

[*25 September 2018 / See notification*]

99.3 Sub-paragraph 8.14, Paragraphs 8.1, 8.2, 8.3, 8.4, and 11.1 of this Regulation shall be applied from 9 February 2019 by having regard to the transitional measures laid down in Articles 48 and 50 of Delegated Regulation No 2016/161.

[*15 January 2019*]

99.4Until 31 December 2022 and before issue of the relevant special permit (licence) for the manufacture and importation of medicinal products or re-registration thereof in order to assess the conformity of the relevant premises, equipment, installations, staff and documents with the requirements laid down in this Regulation and conditions for special activity at the site or location where manufacture or importation control and control on the basis of a risk assessment will be carried out, the State Agency of Medicines may carry out the conformity assessment inspections of manufacturers and importers of medicinal products remotely. If inspections are carried out remotely, the State Agency of Medicines shall indicate in the control report the conditions in conformity with the process and results of the inspection.

[*7 December 2021*]

99.5Until 31 December 2022, after issue of the relevant special permit (licence) for the manufacture and importation of medicinal products, the State Agency of Medicines may postpone the inspections of good manufacturing practice of medicinal products or active substances referred to in Paragraph 32 of this Regulation or carry out them remotely on the basis of a risk assessment and having regard to the Communication from the European Commission on legal regulation issues of medicinal products during COVID-19 pandemic. The State Agency of Medicines may postpone the abovementioned inspections if the changes which broaden the scope of the relevant licence for the manufacture or importation of medicinal products or the registration of an active substance manufacturer or importer and which must be indicated in the certificate of good manufacturing practice (for example, new installations, new premises, manufacture of new medicinal products) are not intended, and also the competent supervisory authority has not carried out activities which affect the validity of the particular certificate of good manufacturing practice for a manufacture located outside the European Economic Area country.

[*7 December 2021*]

99.6If the State Agency of Medicines postpones the inspections in the case referred to in Paragraph 99.5 of this Regulation, it shall be regarded that the certificate of good manufacturing practice is valid until 31 December 2022.

[*7 December 2021*]

99.7 If the State Agency of Medicines carries out the inspection of good manufacturing practice of the manufacturers of the medicinal products or active substances referred to in Paragraph 32 of this Regulation remotely (partly remotely), the conditions shall be indicated in the certificate of good manufacturing practice which is issued after the inspection in conformity with the process and results of the inspection.

[*4 March 2021*]

99.8Until 31 December 2022, a medicinal product manufacturer may carry out remotely the inspections of good manufacturing practice and good distribution of the manufacturers and distributors of the active substances referred to in Sub-paragraph 8.9 of this Regulation by auditing the sites of the manufacturers of active substances and locations of activity of the distributors of active substances.

[*7 December 2021*]

99.9Until 31 December 2022, the qualified person may carry out the certification of finished products which is referred to in Paragraph 11 of this Regulation remotely if the holder of the special permit (licence) for the manufacture or importation of medicinal products ensures that the qualified person has access to all the information necessary for the certification of a batch.

[*7 December 2021*]

100. The Regulation shall come into force on 1 July 2006.

**Informative Reference to European Union Directives**

[*4 August 2008; 8 October 2013; 25 September 2018*]

The Regulation contains legal norms arising from:

1) [25 September 2018 / See Paragraph 2 of Amendments];

2) Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use;

3) [25 September 2018 / See Paragraph 2 of Amendments];

4) Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use;

5) Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use;

6) [25 September 2018 / See Paragraph 2 of Amendments];

7) Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC;

8) Directive 2011/62/EU of the European Union and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products;

9) Commission Directive (EU) 2017/1572 of 15 September 2017 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards the principles and guidelines of good manufacturing practice for medicinal products for human use.

Prime Minister A. Kalvītis

Minister for Health G. Bērziņš

**Annex 1**

Cabinet Regulation No. 304

18 April 2006

**Inspection Control Report of Good Manufacturing Practice**

[*8 October 2013; 4 March 2021*]

|  |
| --- |
| **Report No.** |
| **Name of the product(-s) and dosage form(-s)** | *It is significant to indicate for the inspections which are carried out upon request of the European Medicines Agency, in other cases it is necessary to indicate only for the inspections related to certain products* |
| **Inspected site(-s)** | *The name of the object and full address, including precise location and designation of the inspected site.**EudraGMDP reference number.**Site location identifier (DUNS number/GPS coordinates)* |
| **Manufacturing activities carried out** |  | *Medicinal products for human use* | *Veterinary medicinal products* | *Investigational drugs* |
| *Manufacture of finished products:**sterile products**non-sterile products**biological products* |     |     |     |
| *Sterilisation of intermediate product, active substance or medicinal product* |   |   |   |
| *Primary packaging* |   |   |   |
| *Secondary packaging* |   |   |   |
| *Performance of quality control inspections* |   |   |   |
| *Importation* |   |   |   |
| *Batch certification* |   |   |   |
| *Storage and distribution* |   |   |   |
| *Manufacture of active substance* |   |   |   |
| *Other \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_* |   |   |   |
| **Date(-s) of the inspection** | *Day(-s), month, year* |
| **Inspector(-s) and expert(-s)** | *Given name, surname of the inspector(-s)* |
| *Given name, surname of the expert (assessor) (if applicable)* |
| *Name of the responsible authority(-ies)* |
| **References** | *Medicinal product marketing authorisation number and/or the number of the special permit (licence) for the manufacture of medicinal products.**Reference number(-s) of the European Medicines Agency (if the inspection is carried out upon request of the European Medicines Agency)* |
| **Introductory part** | *Short description of the undertaking and entrepreneurial activities* |
| *If the inspection is performed in a country other than the European Economic Area country, it shall be indicated whether the responsible authority of the relevant country is informed of the inspection and whether this authority has participated in the inspection* |
| *Date of the previous inspection* |
| *Given name(-s), surname(-s) of the inspector(-s) who participated in the previous inspection* |
| *Significant changes since the previous inspection* |
| **Brief layout of inspecting activities undertaken** |  |
| Scope of the inspection | *Short description of the inspection (the inspection of the product, the inspection of the process, and/or the general inspection of good manufacturing practice). Indicate the reason for the inspection, for example, a new application for the registration of medicinal products, repeated (routine) inspection, the investigation of the defect of the product* |
| Area(-s) inspected and main actions/process of the inspection | *Indicate each area inspected* |
| **Activities not inspected** | *If necessary, indicate the area or operations which were not inspected* |
| **Personnel met during the inspection** | *Indicate the given name, surname, position of the key personnel encountered (the list shall be attached in annex to the report)* |
| **Observations of inspectors in relation to the inspection and deficiencies established** | *This section may be linked to the section regarding the deficiencies established in order to explain their classification.**The description of this section may be reduced if controlling persons recognise a Site Master File submitted to the responsible authority to be acceptable* |
| *Chapter headings to be used**Relevant new headings of chapters may be introduced* | *Overview of inspection findings from the last inspection and the measures for rectification of deficiencies taken* |
| *Quality management* |
| *Personnel* |
| *Premises and installations* |
|  | *Documentation* |
| *Production* |
| *Quality control* |
| *Contract manufacturing and fulfilment of the quality control on the basis of the contract* |
| *Complaints and recall of production* |
| *Self-inspection* |
| *Distribution and transportation (shipment)* | *For example, compliance with good distribution practice* |
| *Issues which apply to the assessment of the application for the registration of medicinal products* | *For example, an inspection before the registration (authorisation) of medicinal products* |
| *Other specific issues identified* | *For example, important variations in future announced by the undertaking* |
| *Site Master File* | *Evaluation of the Site Master File, if any. Date of the Site Master File* |
| **Miscellaneous information**Samples taken |  |
| **Annexes appended** | *List of annexes appended* |
| **List of deficiencies classified as critical, major and other** | *All the deficiencies shall be listed and the relevant reference to the requirements of the laws and regulations governing the field of manufacture of medicinal products in respect of good manufacturing practice shall be provided. All the deficiencies which have been detected shall be indicated, also if they have been rectified immediately.**If the deficiencies are related to the assessment of the application for the registration of medicinal products, it shall be clearly specified.**The undertaking shall be requested to inform the responsible authorities of the deadlines for and progress of measures for rectification of deficiencies* |
| **Comments of the inspector on replies of the manufacturer in relation to that established during the inspection** | *For example, whether replies are acceptable* |
| **Comments of the inspector regarding the issues/aspects established in the assessment report** |  |
| **Recommendations for further activities** | *For the authority upon request of which the inspection is carried out or for the responsible authority of the state where the inspected site is located* |
| **Summary and conclusions** | *Inspector(-s) shall indicate whether the manufacturer/importer is operating or is not operating in the inspected field in accordance with the requirements of Directive(-s) 2003/94/EC and/or 91/412/EEC and whether the manufacturer/importer is acceptable in relation to the particular product (it applies to the situations when certain non-conformity has been established but an agreement on the plan for the measures for rectification of deficiencies has been reached and inspector has no grounds to assume that it will not be implemented, and also to the situations when immediate harm to the public health is not caused)* |
| **Given name(-s), surname(-s)****Signature(-s)****Authority(-ies)****Date**Sending of the report | *The inspection control report shall be signed and dated by all inspectors/experts who participated in the inspection.**If the inspection is carried out upon request of the European Medicines Agency (EMA), the inspection control report shall be forwarded to the EMA* |

Notes.

Definitions of significant deficiencies:

1. Critical deficiencies – the deficiencies due to which a product harmful to human and animal health has been produced or there is a significant risk to produce such product, or a product which leaves harmful residual substances in animal bodies from which food products of animal origin are obtained.

2. Major deficiencies – deficiencies which are not critical deficiencies and:

2.1. due to which a product non-complying with the registration documentation has been produced or such product may be produced;

2.2. which indicate to great deviations from the principles of good manufacturing practice of the European Union;

2.3. which indicate to great deviations from the conditions of the special permit (licence) for manufacture of medicinal products (within the scope of the European Union);

2.4. which indicate that satisfactory procedures are not carried out for the batch release or (within the scope of the European Union) the qualified person fails to fulfil the official duties thereof;

2.5. combination of various other deficiencies from which each individual deficiency is not significant but together they may cause significant deficiency; therefore, they must be explained and they should be notified as a significant deficiency.

3. Other deficiencies – deficiencies which may not be classified as critical or major but which point towards deviations from the principles of good manufacturing practice. Deficiencies may be classified as “other deficiencies” if they are evaluated as non-significant or there is not sufficient information to classify them as major or critical.

4. The detail of the document “signature” need not be completed if the electronic document has been prepared in accordance with the laws and regulations regarding drawing up of electronic documents.

The time when the electronic document was signed is the date and time when the time stamp was added.

**Annex 2**

Cabinet Regulation No. 304

18 April 2006

[*8 October 2013; 4 March 2021; 25 September 2018 / Amendment regarding the replacement of words and figures shall come into force on 31 January 2022. See Paragraph 2 of Amendments*]

|  |  |
| --- | --- |
| LATVIJAS REPUBLIKAZĀĻU VALSTS AĢENTŪRA\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_(adrese, reģistrācijas numurs, tālruņa numurs, faksa numurs, e-pasta adrese) | REPUBLIC OF LATVIASTATE AGENCY OF MEDICINES\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_(address, registration number, phone, fax number, e-mail) |

Sertifikāts Nr. \_ \_ \_/\_ \_ \_/\_ \_ \_

*Certificate No.*

**RAŽOTĀJA LABAS RAŽOŠANAS PRAKSES ATBILSTĪBAS SERTIFIKĀTS**

***CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER***

**1.daļa**

***Part 1***

|  |
| --- |
| Izdots pēc oficiālas pārbaudes (inspekcijas) saskaņā ar Direktīvas 2001/83/EK 111.panta 5.punktu vai Direktīvas 2001/82/EK 80.panta 5.punktu, vai Direktīvas 2001/20/EK 15.pantu\**Issued following an inspection in accordance with Art. 111(5) of Directive 2001/83/EC or Art. 80(5) of Directive 2001/82/EC or Art. 15 of Directive 2001/20/EC\**vai / *or*Izdots saskaņā ar Savstarpējās atzīšanas līgumu starp Eiropas Savienību un [Savstarpējās atzīšanas līguma partnervalsts]\**Issued under the provisions of the Mutual Recognition Agreement between the European Union and [MRA Partner]\**Latvijas kompetentā iestāde − Zāļu valsts aģentūra apliecina:*Competent authority of Member State − State*Agency of Medicines confirms the following:Zāļu ražotājs / *The manufacturer*\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Ražošanas vietas adrese / *Site address*\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Ir oficiāli pārbaudīts nacionālās uzraudzības un kontroles programmas ietvaros attiecībā uz atbilstību speciālajai atļaujai (licencei) zāļu ražošanai Nr. \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ saskaņā ar Direktīvas 2001/83/EK 40.pantu / Direktīvas 2001/82/EK 44.pantu / Direktīvas 2001/20/EK 13.pantu\*, kas pārņemts šādos Latvijas Republikas tiesību aktos:*Has been inspected under the national inspection programme in connection with manufacturing authorisation No. \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ in accordance with Art. 40 of Directive 2001/83/EC / Art. 44 of the Directive 2001/82/EC / Art. 13 of Directive 2001/20/EC\* transposed in the following national legislation:*\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\*vai / *or*Ir oficiāli pārbaudīts attiecībā uz zāļu reģistrācijas apliecību(-ām) norādītiem ražotājiem, kas atrodas ārpus Eiropas Ekonomikas zonas, saskaņā ar Regulas (EK) Nr. 726/2004 8.panta 2.punktu / 33.panta 2.punktu / 19.panta 3.punktu / 44.panta 3.punktu\* vai Direktīvas 2001/83/EK 111.panta 4.punktu / Direktīvas 2001/82/EK 80.panta 4.punktu\*, kas pārņemts šādos Latvijas Republikas tiesību aktos:*Has been inspected in connection with marketing authorisation(s) listing manufacturers located outside of the European Economic Area in accordance with Art. 8(2)/33(2)/19(3)/44(3)\* of Regulation (EC) 726/2004 or Art. 111(4) of Directive 2001/83/EC/ Art. 80(4) of Directive 2001/82/EC transposed in the following national legislation:*\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\*un/vai\* / *and/or\**Ir aktīvo vielu ražotājs, kas ir oficiāli pārbaudīts saskaņā ar Direktīvas 2001/83/EK 111.panta 1.punktu / Direktīvas 2001/82/EK 80.panta 1.punktu, kas pārņemts šādos Latvijas Republikas tiesību aktos:*Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC/ Art. 80(1) of Directive 2001/82/EC transposed in the following national legislation:*\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\* |
| un/vai *and/or\**Ir palīgvielu ražotājs, kas ir pārbaudīts saskaņā ar Direktīvas 2001/83/EK 111.panta 1.punktu, kas pārņemts šādos Latvijas Republikas tiesību aktos:*Is an excipient manufacturer that has been inspected in accordance with Art. 111 (1) of Directive 2001/83/EC\* transposed in the following national legislation:*\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\*vai / orCits (norādīt):*Other (please specify):*\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\* |

Ražotāja oficiālajās pārbaudēs, no kurām pēdējā tika veikta ../../…. [datums], iegūtā informācija ļauj uzskatīt, ka tas atbilst labas ražošanas prakses prasībām, kas noteiktas Savstarpējās atzīšanas līgumā starp Eiropas Savienību un *[Savstarpējās atzīšanas līguma partnervalsts]*/ labas ražošanas prakses principiem un pamatnostādnēm, kas noteiktas Direktīvā 2003/94/EK1/ Direktīvā 91/412/EEK1/ aktīvo vielu labas ražošanas prakses principiem1, kas noteikti Direktīvas 2001/83/EK 47. pantā / Direktīvas 2001/82/EK 51. pantā\*. Atbilstošs labas ražošanas prakses līmenis, kas noteikts Direktīvas 2001/83/EK 46(f) pantā (1Šīs prasības atbilst Pasaules veselības organizācijas (PVO) labas ražošanas prakses ieteikumiem). *From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on …../...…/...… [date], it is considered that it complies with the Good Manufacturing Practice requirements referred to in the Agreement of Mutual Recognition between the European Union and [MRA partner]/The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC 1)/ Directive 91/412/EEC 1)/ The principles of GMP for active substances 1)referred to in Article 47 of Directive 2001/83/EC/Article 51 of Directive 2001/82/EC.\* an appropriate level of GMP as referred to in Article 46 (f) of Directive 2001/83/EC (1)− These requirements fulfil the GMP recommendations of WHO)*

Šis sertifikāts atspoguļo ražošanas vietas statusu iepriekš minētās oficiālās pārbaudes laikā, un tas nevar atspoguļot atbilstības statusu, ja ir pagājuši vairāk nekā trīs gadi kopš oficiālās pārbaudes, kad tika izsniegts šis sertifikāts. Taču šis derīguma termiņš var tikt saīsināts vai pagarināts, piemērojot riska vadības regulējošos principus un veicot ierakstu ierobežojumiem un paskaidrojumiem paredzētajā vietā.

*This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection, after which time the issuing authority should be consulted. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field.*

Šis sertifikāts ir derīgs tikai pilnā apjomā, uzrādot visas lapas un abas dokumenta daļas (1. un 2. daļu).

*This certificate is valid only when presented with all pages and both Parts 1 and 2.*

Sertifikāta autentiskumu var pārbaudīt EudraGMDP datubāzē. Ja tas datubāzē neparādās, sazinieties ar Zāļu valsts aģentūru.

*The authenticity of this certificate may be verified in EudraGMDP database. If it does not appear, please contact the issuing authority.*

**2.daļa**

***Part 2***

|  |  |
| --- | --- |
| Cilvēkiem paredzētās zāles \**Human medicinal products* |  |
| Veterinārās zāles\**Veterinary medicinal products* |  |
| Cilvēkiem paredzētās pētāmās zāles\**Human investigational medicinal products* |  |

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| --- |
| **1. RAŽOŠANAS DARBĪBAS – ZĀLES\******MANUFACTURING OPERATIONS − MEDICINAL PRODUCTS\**** |
| 1.1. | Sterilās zāļu formas*Sterile products* |
| 1.1.1. Aseptiski ražotas (ražošanas darbības ar šādām zāļu formām)*Aseptically prepared (processing operations for the following dosage forms)*1.1.1.1. Šķidrumi liela tilpuma iepakojumā*Large volume liquids*1.1.1.2. Liofilizāti*Lyophilisates*1.1.1.3. Mīkstās zāļu formas*Semi-solids*1.1.1.4. Šķidrumi maza tilpuma iepakojumā*Small volume liquids*1.1.1.5. Cietās zāļu formas un implanti*Solids and implants*1.1.1.6. Citi aseptiski ražoti produkti (brīvs uzskaitījums)*Other aseptically prepared products (free text)*1.1.2. Sterilizētas (ražošanas darbības ar šādām zāļu formām)*Terminally sterilised (processing operations for the following dosage forms)*1.1.2.1. Šķidrumi liela tilpuma iepakojumā*Large volume liquids*1.1.2.2. Mīkstās zāļu formas*Semi-solids*1.1.2.3. Šķidrumi maza tilpuma iepakojumā*Small volume liquids*1.1.2.4. Cietās zāļu formas un implanti*Solids and implants*1.1.2.5. Citi sterilizēti produkti (brīvs uzskaitījums)*Other terminally sterilised products*1.1.3. Sērijas sertifikācija*Batch certification* |
| 1.2. | Nesterilās zāļu formas*Non − sterile products* |
|   | 1.2.1. Nesterilās zāļu formas (ražošanas darbības ar šādām zāļu formām)*Non-sterile products (processing operations for the following dosage forms)*1.2.1.1. Cietās kapsulas*Capsules, hard shell*1.2.1.2. Mīkstās kapsulas*Capsules, soft shell*1.2.1.3. Košļājamās gumijas*Chewing gums*1.2.1.4. Impregnētās matrices*Impregnated matrices*1.2.1.5. Ārīgi lietojami šķidrumi*Liquids for external use*1.2.1.6. Iekšķīgi lietojami šķidrumi*Liquids for internal use*1.2.1.7. Medicīniskās gāzes*Medicinal gases*1.2.1.8. Citas cietās zāļu formas*Other solid dosage forms*1.2.1.9. Aerosolu preparāti (zem spiediena)*Pressurised preparations*1.2.1.10. Radionuklīdu ģeneratori*Radionuclide generators*1.2.1.11. Mīkstās zāļu formas*Semi-solids*1.2.1.12. Supozitoriji*Suppositories*1.2.1.13. Tabletes*Tablets*1.2.1.14. Transdermālie plāksteri*Transdermal patches*1.2.1.15. Intraruminālās ierīces*Intraruminal devices*1.2.1.16. Lopbarības piedevas*Veterinary premixes*1.2.1.17. Citas nesterilās zāļu formas (brīvs uzskaitījums)*Other non-sterile medicinal product (free text)*1.2.2. Sērijas sertifikācija*Batch certification* |
| 1.3. | Bioloģiskas izcelsmes zāles*Biological medicinal products* |
|   | 1.3.1. Bioloģiskas izcelsmes zāles*Biological medicinal products*1.3.1.1. No cilvēka asinīm un plazmas iegūtas zāles*Blood products*1.3.1.2. Imunoloģiskie preparāti*Immunological products*1.3.1.3. Šūnu terapijas preparātii*Cell therapy products*1.3.1.4. Gēnu terapijas preparāti*Gene therapy products*1.3.1.5. Biotehnoloģiskie preparāti*Biotechnology products*1.3.1.6. No cilvēka vai dzīvnieku materiāliem izdalīti preparāti*Human or animal extracted products*1.3.1.7. No audiem veidoti produkti*Tissue engineered products*1.3.1.8. Citas bioloģiskas izcelsmes zāles (brīvs uzskaitījums)*Other biological medicinal products (free text)*1.3.2. Sērijas sertifikācija (zāļu veidu saraksts)*Batch certification (list of product types)*1.3.2.1. No cilvēka asinīm un plazmas iegūtas zāles*Blood products*1.3.2.2. Imunoloģiskie preparāti*Immunological products*1.3.2.3. Šūnu terapijas zāles*Cell therapy products*1.3.2.4. Gēnu terapijas zāles*Gene therapy products*1.3.2.5. Biotehnoloģiskie preparāti*Biotechnology products*1.3.2.6. No cilvēka vai dzīvnieku materiāliem izdalīti preparātii*Human or animal extracted products*1.3.2.7. No audiem veidoti produkti*Tissue engineered products*1.3.2.8. Citas bioloģiskas izcelsmes zāles (brīvs uzskaitījums)*Other biological medicinal products (free text)* |
| 1.4. | Citi produkti vai ražošanas darbības*Other products or processing activity* |
|   | 1.4.1. Ražošana:*Manufacture of*1.4.1.1. Augu izcelsmes zāles*Herbal products*1.4.1.2. Homeopātiskās zāles*Homoeopathic products*1.4.1.3. Citi (brīvs uzskaitījums)*Other (free text)*1.4.2. Aktīvo vielu / palīgvielu / galaprodukta sterilizācija:*Sterilisation of active substances / excipients / finished product*1.4.2.1. Filtrēšana*Filtration*1.4.2.2. Sterilizācija ar karstu, sausu gaisu*Dry heat*1.4.2.3. Sterilizācija ar ūdens tvaiku*Moist heat*1.4.2.4. Ķīmiskā sterilizācija*Chemical*1.4.2.5. Apstarošana ar gamma stariem*Gamma irradiation*1.4.2.6. Apstarošana ar elektronu kūli*Electron beam*1.4.3. Citi (brīvs uzskaitījums)s)*Other (free text)* |
| 1.5. | Iepakošana*Packaging* |
|   | 1.5.1. Primārā iepakošana*Primary packing*1.5.1.1. Cietās kapsulas*Capsules, hard shell*1.5.1.2. Mīkstās kapsulas*Capsules, soft shell*1.5.1.3. Košļājamās gumijas*Chewing gums*1.5.1.4. Impregnētās matrices*Impregnated matrices*1.5.1.5. Šķidrumi ārīgai lietošanai*Liquids for external use*1.5.1.6. Šķidrumi iekšķīgai lietošanaiai*Liquids for internal use*1.5.1.7. Medicīniskās gāzes*Medicinal gases*1.5.1.8. Citas cietās zāļu formas*Other solid dosage forms*1.5.1.9. Aerosolu preparāti (zem spiediena)*Pressurised preparations*1.5.1.10. Radionuklīdu ģeneratori*Radionuclide generators*1.5.1.11. Mīkstās zāļu formas*Semi-solids*1.5.1.12. Supozitoriji*Suppositories*1.5.1.13. Tabletes*Tablets*1.5.1.14. Transdermālie plāksteri*Transdermal patches*1.5.1.15. Intraruminālās ierīces*Intraruminal devices*1.5.1.16. Lopbarības piedevas*Veterinary premixes*1.5.1.17. Citas nesterilās zāļu formas (brīvs uzskaitījums)*Other non-sterile dosage forms (free text)*1.5.2. Sekundārā iepakošana\**Secondary packing* |
| 1.6. | Kvalitātes kontroles testēšana*Quality control testing* |
|   | 1.6.1. Mikrobioloģiskā: sterilitāte*Microbiological: sterility*1.6.2. Mikrobioloģiskā: nesterilo zāļu formu tīrība*Microbiological: non-sterility*1.6.3. Ķīmiskā / fizikālā*Chemical / physical*1.6.4. Bioloģiskā*Biological* |

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| **2. ZĀĻU IMPORTĒŠANA\******IMPORTATION OF MEDICINAL PRODUCTS*** |
| 2.1. | Importēto zāļu kvalitātes kontroles testēšana*Quality control testing of imported medicinal products* |
|   | 2.1.1. Mikrobioloģiskā: sterilitāte*Microbiological: sterility*2.1.2. Mikrobioloģiskā: nav sterilitātes (nesterilas zāļu formas)*Microbiological: non-sterility*2.1.3. Ķīmiskā / fizikālā*Chemical / physical*2.1.4. Bioloģiskā*Biological* |
| 2.2. | Importēto zāļu sērijas sertifikācija*Batch certification of imported medicinal products* |
|   | 2.2.1. Sterilās zāļu formas*Sterile products*2.2.1.1. Aseptiski ražotas*Aseptically prepared*2.2.1.2. Sterilizētas*Terminally sterilised*2.2.2. Nesterilās zāļu formas*Non-sterile products*2.2.3. Bioloģiskas izcelsmes zāles*Biological medicinal products*2.2.3.1. No cilvēka asinīm un plazmas iegūtas zāles*Blood products*2.2.3.2. Imunoloģiskie preparāti*Immunological products*2.2.3.3. Šūnu terapijas preparāti*Cell therapy products*2.2.3.4. Gēnu terapijas preparāti*Gene therapy products*2.2.3.5. Biotehnoloģiskie preparāti*Biotechnology products*2.2.3.6. No cilvēka vai dzīvnieku materiāliem izdalīti preparāti*Human or animal extracted products*2.2.3.7. No audiem veidoti produkti*Tissue engineered products*2.2.3.8. Citi bioloģiskas izcelsmes produkti (brīvs uzskaitījums)*Other biological medicinal products (free text)* |
| 2.3. | Citas importēšanas darbības*Other importation activities* |
|   | 2.3.1. Faktiskā importēšanas vieta*Site of physical importation*2.3.2. Starpprodukta importēšana, ar kuru tiek veiktas turpmākās ražošanas darbības*Importation of intermediate which undergoes further processing*2.3.3. Citi (brīvs uzskaitījums)*Other (free text)* |

Jebkādi ierobežojumi vai paskaidrojumi saistībā ar šā sertifikāta jomu\*:

*Any restrictions or clarifying remarks related to the scope of this certificate:*

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| **3. RAŽOŠANAS DARBĪBAS − AKTĪVĀS VIELAS*****MANUFACTURING OPERATIONS − ACTIVE SUBSTANCES***Aktīvā(-ās) viela(-as):*Active substance(s):* |
| 3.1. | Ķīmiski sintezēto aktīvo vielu ražošana*Manufacture of active substance by chemical synthesis* |
|   | 3.1.1. Aktīvo vielu starpproduktu ražošana*Manufacture of active substance intermediates*3.1.2. Tehnisko (neattīrīto) aktīvo vielu ražošana*Manufacture of crude active substance*3.1.3. Sāļu iegūšana / attīrīšanas posmi: (brīvs uzskaitījums) (piemēram, kristalizācija)*Salt formation/ Purification steps: (free text) (e.g. crystallisation)*3.1.4. Citas darbības (brīvs uzskaitījums)*Other (free text)* |
| 3.2. | Aktīvo vielu izdalīšana no dabiskiem avotiem*Extraction of active substance from natural sources* |
|   | 3.2.1. Vielas izdalīšana no augu valsts avotiem*Extraction of substance from plant source*3.2.2. Vielas izdalīšana no dzīvnieku valsts avotiem*Extraction of substance from animal source*3.2.3. Vielas izdalīšana no materiāla, kas ņemts no cilvēka*Extraction of substance from human source*3.2.4. Vielas izdalīšana no minerālu avotiem*Extraction of substance from mineral source*3.2.5. Izdalītās vielas modifikācija (norādiet avotu 1,2,3,4)*Modification of extracted substance (specify source 1,2,3,4)*3.2.6. Izdalītās vielas attīrīšana (norādiet avotu 1,2,3,4)*Purification of extracted substance (specify source 1,2,3,4)*3.2.7. Cits (brīvs teksts)*Other (free text)* |
| 3.3. | Aktīvo vielu ražošana, izmantojot bioloģiskos procesus*Manufacture of active substance using biological processes* |
|   | 3.3.1. Fermentācija*Fermentation*3.3.2. Šūnu kultūras (norādiet šūnu tipu) (piemēram, zīdītāju/baktēriju)*Cell culture (specify cell type) (e.g. mammalian / bacterial)*3.3.3. Atdalīšana / attīrīšana*Isolation / Purification*3.3.4. Modifikācija*Modification*3.3.5. Cits (brīvs uzskaitījums)*Other (free text)* |
| 3.4. | Sterilo aktīvo vielu ražošana (attiecīgi aizpildot 3.1., 3.2., 3.3.sadaļu)*Manufacture of sterile active substance (sections 3.1, 3.2, 3.3 to be completed as applicable)* |
|   | 3.4.1. Aseptiski sagatavotas*Aseptically prepared*3.4.2. Sterilizētas*Terminally sterilised* |
| 3.5. | Vispārīgie nobeiguma posmi*General finishing steps* |
|   | 3.5.1. Fizikālās apstrādes posmi (norādiet) (piemēram, žāvēšana, malšana / mikronizēšana, sijāšana)*Physical processing steps (specify) (e.g. drying, milling / micronisation, sieving)*3.5.2. Pirmējā iepakošana (aktīvo vielu ievietošana / noslēgšana iepakojumā, kurš atrodas tiešā kontaktā ar aktīvo vielu)*Primary packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)*3.5.3. Sekundārā iepakošana (noslēgtā pirmējā iepakojuma ievietošana sekundārā iepakojumā vai konteinerā. Tas iekļauj arī jebkuru materiāla marķēšanu, kas var tikt izmantota aktīvās vielas identifikācijai vai izsekojamībai (sērijas numurs))*Secondary packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)*3.5.4. Citi (brīvs teksts) (darbībām, kas nav aprakstītas iepriekšējos punktos)*Other (free text) (for operations not described above)* |
| 3.6. | Kvalitātes kontroles veikšana*Quality control testing* |
|   | 3.6.1. Fizikāli vai ķīmiski*Physical / Chemical testing*3.6.2. Mikrobioloģiski (izņemot sterilitātes testus)*Microbiological testing (excluding sterility testing)*3.6.3. Mikrobioloģiski (ietverot sterilitātes testus)*Microbiological testing (including sterility testing)*3.6.4. Bioloģiski*Biological testing* |

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| **4. CITAS DARBĪBAS − AKTĪVĀS VIELAS*****OTHER ACTIVITIES − ACTIVE SUBSTANCES***(brīvs uzskaitījums)*(free text)* |

Jebkādi ierobežojumi vai paskaidrojumi saistībā ar šā sertifikāta jomu\*:

*Any restrictions or clarifying remarks related to the scope of this certificate:*

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| ……/……/……*(datums / date)* | Zāļu valsts aģentūras pilnvarotās amatpersonas vārds, uzvārds un paraksts*Name and signature of the authorised person of the Competent Authority of Latvia*\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_*(vārds, uzvārds, amats, atbildīgā iestāde, tālruņa un faksa numurs / name, surname, position, national authority, phone & fax number)* |

Piezīmes.

1. \* Izdzēst neatbilstošo.

*Delete that which does not apply.*

2. Šis sertifikāts attiecas arī uz importētāju.

*This certificate applies also to the importer.*

3. Dokumenta rekvizītu "Paraksts" neaizpilda, ja elektroniskais dokuments ir sagatavots atbilstoši normatīvajiem aktiem par elektronisko dokumentu noformēšanu.

*Document property "Signature" is not filled in if the document is prepared in accordance with the laws of electronic documents.*

Par elektroniskā dokumenta parakstīšanas laiku uzskata laika zīmoga pievienošanas datumu un laiku.

*The time when the electronic document was signed is the date and time when the time stamp was added.*

**Annex 3**

Cabinet Regulation No. 304

18 April 2006

**Devices, Apparatus, Equipment, and Reagents to be Used for Analytical Work in a Pharmacy**

1. Devices and apparatus:

1.1. a photoelectrical colorimeter:

1.2. a device for the particulate matter control in solutions;

1.3. a laboratory thermometer from 0 °C to 100 °C (with the graduation value up to 1 °C);

1.4. a laboratory water bath;

1.5. a test tube stand;

1.6. a pH meter;

1.7. a refractometer;

1.8. hand scales (for weighing of reagents) with the weighing limitation:

1.8.1. from 0.02 g to 1 g

1.8.2. from 0.1 g to 5 g;

1.8.3. from 1 g to 20 g;

1.8.4. from 5 g to 100 g;

1.9. an alcohol burner;

1.10. a stand for the fixation of laboratory vessels and devices;

1.11. a set of glass alcoholmeters;

1.12. technical scales and a set of technical weights from 10 mg to 0.5 kg;

1.13. an ultraviolet irradiator for the determination of vitamins in a solution;

1.14. a cabinet dryer with a thermometer from 0 °C to 200 °C.

2. Laboratory vessels:

2.1. a pharmacy pipette with an outlet tube with a capacity of 3 ml and 6 ml;

2.2. indicator and reagent droppers;

2.3. calcium chloride pipes with a ball-shaped part (for protection of purified water against the carbon dioxide);

2.4. flasks, cone-shaped with a capacity of 50 ml, 100 ml, 200 ml;

2.5. a flask with a ground stopper with a capacity of 100 ml;

2.6. chemical test tubes;

2.7. measuring cylinders with ground stoppers with a capacity of 10 ml, 25 ml, 50 ml, 100 ml;

2.8. graduated cylinders with a capacity of 10 ml, 25 ml, 50 ml, 100 ml, and 250 ml;

2.9. volumetric flasks with ground stoppers with a capacity of 25 ml, 50 ml, 100 ml;

2.10. microburettes with a capacity of 3 ml and 5 ml;

2.11. Moor’s pipettes with a capacity of 5 ml and 10 ml;

2.12. a mortar and pestle;

2.13. funnels;

2.14. graduated pipettes with a capacity of 1 ml, 2 ml, 5 ml, and 10 ml;

2.15. porcelain evaporating dishes with a capacity of 25 ml, 50 ml, 100 ml;

2.16. porcelain crucibles;

2.17. bottles for the storage of reagents;

2.18. glass or porcelain spot plates with or without wells for the analysis of drops;

2.19. syringe-flask;

2.20. separatory funnels with a capacity of 50 ml and 100 ml;

2.21. a burette with a tap;

2.22. flat-bottomed vessels.

3. Ancillary materials:

3.1. eye pipettes;

3.2. eye spatula;

3.3. goggles;

3.4. brushes for washing of test tubes and flasks;

3.5. filter paper;

3.6. a flame needle or a graphite pin;

3.7. a rubber balloon for microburettes and pipettes;

3.8. test tube rack;

3.9. a permanent marker;

3.10. forceps;

3.11. glass rods;

3.12. spreading rods;

3.13. crucible tongs;

3.14. cotton wool, hygroscopic.

4. Titrated solutions:

|  |  |  |  |
| --- | --- | --- | --- |
| No. | Solution name | Molar concentration | Normal concentration |
| 4.1. | Ammonium thiocyanate solution | 0.1 M | 0.1 N |
| 4.2. | Sodium ethylene diamine tetra acetate (trilon B) solution | 0.05 M | - |
| 4.3. | Mercury (II) nitrate solution | 0.05 M | 0.1 N |
| 4.4. | Hydrochloric acid solution | 0.1 M | 0.1 N |
| 4.5. | Iodine solution | 0.05 M | 0.1 N |
| 4.6. | Potassium bromate solution | 0.0167 M | 0.1 N |
| 4.7. | Potassium permanganate solution | 0.02 M | 0.1 N |
| 4.8. | Sodium hydroxide solution | 0.1 M | 0.1 N |
| 4.9. | Sodium nitrite solution | 0.1 M | - |
| 4.10. | Sodium thiosulphate solution | 0.1 M | 0.1 N |
| 4.11. | Silver nitrate solution | 0.1 M | 0.1 N |

Note. Titrated solutions shall be kept at a temperature of 18 °C – 20 °C in tightly closed bottles in a dark place. Iodine, potassium bromate, potassium permanganate, sodium nitrite and silver nitrate solutions shall be kept in dark glass bottles. Sodium hydroxide and sodium thiosulphate solution shall be protected from exposure to air carbon dioxide. Titrated solutions shall be received from the State Agency of Medicines.

5. Indicators:

|  |  |  |
| --- | --- | --- |
| 5.1. | Ammonium ferrous sulphate solution | 30 % |
| 5.2. | Bromphenol blue solution | 0.1 % |
| 5.3. | Bromothymol blue solution | 0.1 % |
| 5.4. | Starch solution | 1 % |
| 5.5. | Eriochrome black |  |
| 5.6. | Phenolphthalein solution | 1 % |
| 5.7. | Acid chrome dark blue |  |
| 5.8. | Potassium chromate solution | 5 % |
| 5.9. | Methylene blue solution | 0.15 % |
| 5.10. | Methyl red solution | 0.1 % |
| 5.11. | Methyl orange solution | 0.1 % |
| 5.12. | Sodium eosinate solution | 0.1 % and 0.5 %; |
| 5.13. | Tropaeoline 00 solution | 0.1 % |

6. Indicator paper:

|  |  |  |
| --- | --- | --- |
| No. | Name | Colour transition pH |
| 6.1. | Red litmus paper | > 8.0 |
| 6.2. | Blue litmus paper | < 5.0 |
| 6.3. | Universal indicator paper | pH 1.0–10.0 |
| 6.4. | Universal indicator paper for specification of basicity | pH 7.0–14.0 |

Note.

1. Indicator paper is used in order to specify pH of water solutions and suspensions with the precision of

1.0–2.0 pH units. pH shall be determined at a room temperature for solutions and suspensions which do not contain heavy oxidising substances, organic solvents and salts in large concentration.

2. Indicator paper shall be kept in a dry room, not contaminated with gases, protecting from the effects of light, humidity, acids vapours, ammonium and other chemically active compounds.

7. Reagents:

|  |  |  |
| --- | --- | --- |
| 7.1. | Activated carbon |  |
| 7.2. | Ammonium ferrous (III) sulphate |  |
| 7.3. | Ammonium molybdate solution in concentrated sulphuric acid (Froede’s reagent) |  |
| 7.4. | Ammonium oxalate solution | 4 % |
| 7.5. | Ammonium thiocyanate |  |
| 7.6. | Ammonium vanadate solution in hydrochloric acid |  |
| 7.7. | Ammonia buffer solution |  |
| 7.8. | Ammonia solution | 10 % |
| 7.9. | Barium hydroxide solution | 5 % |
| 7.10. | Barium chloride or barium nitrate solution | 5 % |
| 7.11. | b – naphthol alakaline solution | 2 % |
| 7.12. | Iron trichloride solution | 3 % |
| 7.13. | Acetic acid, diluted | 30 % |
| 7.14. | Fehling’s reagent I |  |
| 7.15. | Fehling’s reagent II |  |
| 7.16. | Formaldehyde solution (formalin) |  |
| 7.17. | Formaldehyde solution in concentrated sulphuric acid (Marquis reagent) |  |
| 7.18. | Formol mixture |  |
| 7.19. | Tosylchloramide sodium solution |  |
| 7.20. | Potassium dihydrogen phosphate |  |
| 7.21. | Potassium dichromate solution | 5 % |
| 7.22. | Potassium iodide |  |
| 7.23. | Potassium hexacyanoferrate (II) solution (yellow prussiate) | 1 %; 5 %; 20 % |
| 7.24. | Potassium hexacyanoferrate (III) solution (red prussiate) | 2 %; 5 %; 10 % |
| 7.25. | Potassium monohydrigenphosphate |  |
| 7.26. | Potassium permanganate |  |
| 7.27. | Cobalt chloride solution | 5 % |
| 7.28. | Cobalt nitrate alcoholic solution | 1 % |
| 7.29. | Cobalt nitrate solution | 5 % |
| 7.30. | Lugol reagent |  |
| 7.31. | Sodium hydrogencarbonate |  |
| 7.32. | Sodium hydroxide solution | 10 %; 2 M |
| 7.33. | Sodium carbonate solution | 1 %; 5 %; 10 % |
| 7.34. | Sodium nitrite |  |
| 7.35. | Sodium nitropruside solution | 1 %; 5 %; 10 % |
| 7.36. | Disodium sulphide solution | 2 % |
| 7.37. | Nesler’s reagent |  |
| 7.38. | Perhydrol |  |
| 7.39. | Hydrochloric acid | 25 % |
| 7.40. | Hydrochloric acid, diluted | 8.3 % |
| 7.41. | Sulphuric acid, diluted | 16 % |
| 7.42. | Sulphuric acid, concentrated |  |
| 7.43. | Nitric acid diluted | 16 % |
| 7.44. | Ammoniacal silver nitrate |  |
| 7.45. | Silver nitrate solution | 2 % |
| 7.46. | Sulphanilic acid solution |  |
| 7.47. | Lead diacetate solution | 10 % |
| 7.48. | Tannin solution | 0.1 %; 5 % |
| 7.49. | Hydrogen peroxide solution | 3 % |
| 7.50. | Vanillin |  |
| 7.51. | Cupric acetate solution | 5 % |
| 7.52. | Copper dinitrate solution | 5 % |
| 7.53. | Copper wire |  |
| 7.54. | Cupric sulphate |  |
| 7.55. | Tartaric acid solution | 20 % |

Note. Reagents shall be received from the State Agency of Medicines. If reagents are prepared in a pharmacy, the methodology, provisions for storage, and term of validity thereof shall be co-ordinated with the State Agency of Medicines.

8. Solvents:

8.1. acetone;

8.2. ethyl alcohol, 90 %; 95–96 %;

8.3. diethyl ether;

8.4. glycerol;

8.5. chloroform.

Minister for Health G. Bērziņš

**Annex 4**

Cabinet Regulation No. 304

18 April 2006

**Contents of the Register of the Medicinal Product Quality Control Results Performed in the Pharmacy**

[*4 August 2008*]

1. Register of the testing results of the medicinal products prepared on individual prescriptions (requests of medical treatment institutions)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Date | No.(also the analysis number) | Prescription or request number | Composition of the medicinal product | Testing results | Given name, surname of the manufacturer | Given name, surname, and signature of the tester |
| organoleptic | physical | qualitative | quantitative |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|  |  |  |  |  |  |  |  |  |  |

2. Register of the testing results of the purified water obtained in the pharmacy

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Date | No.(also the analysis number) | Testing results | Conclusion | Given name, surname, and signature of the tester |
| chloride ions | sulphate ions | calcium and magnesium ions | ammonium ions | reducing agents |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|  |  |  |  |  |  |  |  |  |

3. Register of the testing results of the concentrates, partially processed products, ethyl alcohol

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Date | No.(also the analysis number) | Name,concentration | Testing results | Given name of the manufacturersurname | Given name, surname, and signature of the tester |
| organoleptic | qualitative | quantitative |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|  |  |  |  |  |  |  |  |

4. Register of the inspection results of the starting materials identity

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Date | No.(also the analysis number) | Name | Manufactured batch number | Substance under analysis | Conclusion | Given name of the fillersurname and signature | Given name, surname, and signature of the tester |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|  |  |  |  |  |  |  |  |

Minister for Health G. Bērziņš

**Annex 5**

Cabinet Regulation No. 304

18 April 2006

**Report Regarding the Quality Control of Medicinal Products in the Pharmacy in 20\_\_\_**

|  |
| --- |
|  |
| (holder company of the special permit (licence) for pharmaceutical activities) |
|  |
|  |
| (legal address and the registration number in the Commercial Register) |
|  |
|  |
| (pharmacy name and address) |

|  |  |  |  |
| --- | --- | --- | --- |
| No. | Name of the site analysed | Number of analyses performed | Of them with dissatisfactory results |
| physical | qualitative | quantitative |
| 1. | Concentrates |  |  |  |  |
| 2. | Partially processed products |  |  |  |  |
| 3. | Purified water |  |  |  |  |
| 4. | Medicinal products prepared on individual prescriptions and requests of medical treatment institutions |  |  |  |  |
| 5. | Starting materials for the preparation of medicinal products |  |  |  |  |
|  | **Total** |  |  |  |  |

|  |  |  |
| --- | --- | --- |
| Head of the Pharmacy |  |  |
|  | (given name, surname, signature) |  |
| Date |  |  |

Minister for Health G. Bērziņš

**Annex 6**

Cabinet Regulation No. 304

18 April 2006

**Maximum One-time or Daily Doses of Highly Potent Substances which are Used for the Preparation of Medicinal Products in a Pharmacy**

1. Maximum one-time or daily doses of highly potent substances for children up to the age of 14, administering orally (the amounts of the substances are indicated in grams if other units of measurement are not specified)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No. | Drug substance name | Up to 6 months | From 6 months to 1 year | 2 years | 3–4 years | 5–6 years | 7–9 years | 10–14 years |
| single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
| 1. | *Acidum arsenicosum anhydricum* | \* | \* | \* | \* | 0.0002 | 0.0006 | 0.0003 | 0.001 | 0.0005 | 0.0015 | 0.00075 | 0.002 | 0.001 | 0.003 |
| 2. | *Acidum hydrochloricum dilutum* | 1 drop | 3 drops | 2 drops | 6 drops | 2 drops | 6 drops | 3 drops | 9 drops | 5 drops | 15 drops | 7–8 drops\*\* | 20 drops | 8–10 drops | 30 drops |
| 3. | *Acidum nicotinicum* | 0.005 | 0.015 | 0.008 | 0.024 | 0.01 | 0.03 | 0.015 | 0.045 | 0.025 | 0.075 | 0.03 | 0.09 | 0.05 | 0.15 |
| 4. | *Adonisidum* | 1 drop | 2 drops | 2 drops | 4 drops | 3 drops | 6 drops | 5 drops | 10 drops | 6 drops | 12 drops | 8 drops | 15 drops | 10–15 drops | 20–30 drops |
| 5. | *Aethylis aminobenzoas (Anaesthesinum)* | 0.025 | 0.075 | 0.04 | 0.12 | 0.06 | 0.18 | 0.08 | 0.24 | 0.12 | 0.36 | 0.16 | 0.5 | 0.2 | 0.6 |
| 6. | *Aethylmorphini hydrochloridum* | \* | \* | \* | \* | 0.003 | 0.01 | 0.005 | 0.015 | 0.006 | 0.018 | 0.0075 | 0.025 | 0.01 | 0.03 |
| 7. | *Ambenonii chloridum (Oxazylum)* | \* | \* | 0.0015 | 0.0015 | 0.0025 | 0.0025 | 0.003 | 0.003 | 0.004 | 0.004 | 0.006 | 0.006 | 0.0075–0.01 | 0.0075–0.01 |
| 8. | *Aminarsonum* | 0.04 | 0.12 | 0.08 | 0.24 | 0.1 | 0.3 | 0.15 | 0.45 | 0.15 | 0.45 | 0.2 | 0.5 | 0.25 | 0.75 |
| 9. | *Aminasinum* | 0.005–0.0075 | 0.01–0.015 | 0.01 | 0.02 | 0.015 | 0.03 | 0.025 | 0.05 | 0.05 | 0.1 | 0.075 | 0.15 | 0.1 | 0.2 |
| 10. | *Aminophenazonum (Amidopyrinum)\*\*\** | 0.025 | 0.075 | 0.05 | 0.15 | 0.05 | 0.15 | 0.075 | 0.2 | 0.1 | 0.3 | 0.15 | 0.45 | 0.2–0.3 | 0.6–0.9 |
| 11. | *Aminophyllinum (Euphyllinum)* | \* | \* | 0.01 | 0.03 | 0.02 | 0.06 | 0.03 | 0.09 | 0.05 | 0.15 | 0.075 | 0.25 | 0.1 | 0.3 |
| 12. | *Apomorphini hydrochloridum* | \* | \* | \* | \* | 0.001 | 0.003 | 0.0015 | 0.0045 | 0.002 | 0.006 | 0.0025 | 0.0075 | 0.003 | 0.009 |
| 13. | *Atropini sulfas* | 0.0001 | 0.0002 | 0.0002 | 0.0004 | 0.0002 | 0.0004 | 0.00025 | 0.0005 | 0.0003 | 0.0006 | 0.0004 | 0.0008 | 0.0005 | 0.001 |
| 14. | *Barbamylum* | 0.01 | 0.02 | 0.01 | 0.02 | 0.02 | 0.04 | 0.025–0.03 | 0.05–0.06 | 0.04 | 0.08 | 0.05–0.075 | 0.1–0.15 | 0.1–0.15 | 0.2–0.3 |
| 15. | *Barbitalum natricum* | 0.03 | 0.06 | 0.075 | 0.15 | 0.1 | 0.2 | 0.15 | 0.3 | 0.2 | 0.4 | 0.25 | 0.5 | 0.3 | 0.6 |
| 16. | *Bendazolum (Dibazolum)* | 0.001 | 0.001 | 0.001 | 0.001 | 0.002 | 0.002 | 0.004 | 0.004 | 0.005 | 0.005 | 0.006 | 0.006 | 0.008 | 0.008 |
| 17. | *Bromisovalum* | 0.05 | 0.1 | 0.1 | 0.2 | 0.15 | 0.3 | 0.2 | 0.4 | 0.25 | 0.5 | 0.3 | 0.6 | 0.3–0.4 | 0.6–0.8 |
| 18. | *Carbromalum* | \* | \* | 0.1 | 0.2 | 0.15 | 0.3 | 0.2 | 0.4 | 0.2 | 0.4 | 0.25 | 0.5 | 0.3–0.4 | 0.6–0.8 |
| 19. | *Chloramphenicolum (Laevomycetinum)* | one-time 0.02; daily 0.12 for 1 kg of child’s weight | 0.25 | 1.5 | 0.25 | 1.5 | 0.3 | 1.8 | 0.4 | 2.0 |
| 20. | *Chlorali hydras* | 0.1 | 0.3 | 0.15 | 0.45 | 0.2 | 0.6 | 0.25 | 0.75 | 0.3 | 0.9 | 0.4 | 1.2 | 0.5–0.75 | 1.5–2.0 |
| 21. | *Chlortetracyclini hydrochloridum* | 0.025 for 1 kg of child’s weight daily | 0.075 | 0.3 | 0.1 | 0.4 | 0.15 | 0.6 | 0.2–0.3 | 0.8–1.0 |
| 22. | *Codeinum* | \* | \* | \* | \* | 0.002 | 0.006 | 0.004 | 0.012 | 0.005 | 0.015 | 0.006 | 0.02 | 0.006–0.01 | 0.02–0.03 |
| 23. | *Codeini phosphas* | \* | \* | 0.0025 | 0.0075 | 0.004 | 0.012 | 0.005 | 0.015 | 0.006–0.008 | 0.02–0.025 | 0.01 | 0.03 | 0.015–0.02 | 0.045–0.06 |
| 24. | *Coffeinum* | \* | \* | \* | \* | 0.04 | 0.12 | 0.05 | 0.15 | 0.06 | 0.18 | 0.075 | 0.25 | 0.075–0.1 | 0.25–0.3 |
| 25. | *Coffeinum natrii – benzoas* | 0.05 | 0.15 | 0.06 | 0.18 | 0.07 | 0.2 | 0.08 | 0.25 | 0.1 | 0.3 | 0.15 | 0.5 | 0.15–0.2 | 0.5–0.6 |
| 26. | *Digalen – neo* | 1 drop | 3 drops | 2 drops | 6 drops | 4 drops | 12 drops | 6 drops | 18 drops | 7 drops | 21 drops | 8 drops | 24 drops | 10 drops | 30 drops |
| 27. | *Diphenhydraminum (Dimedrolum)* | 0.002 | 0.006 | 0.005 | 0.015 | 0.01 | 0.03 | 0.015 | 0.045 | 0.02 | 0.06 | 0.03 | 0.09 | 0.04 | 0.1 |
| 28. | *Ephedrini hydrochloridum* | 0.0025 | 0.0075 | 0.006 | 0.02 | 0.01 | 0.03 | 0.015 | 0.045 | 0.015 | 0.045 | 0.02 | 0.06 | 0.025 | 0.075 |
| 29. | *Erythromycinum* | 0.005–0.008 for 1 kg of child’s weight one-time | 0.125 | 0.5 | 0.15 | 0.6 | 0.2 | 0.8 | 0.25 | 1.0 |
| 30. | *Extractum Belladonnae siccum* | \* | \* | 0.0025 | 0.0075 | 0.003 | 0.009 | 0.004 | 0.012 | 0.005 | 0.015 | 0.0075 | 0.025 | 0.01–0.015 | 0.03–0.045 |
| 31. | *Extractum Filicis maris spissum* | \* | \* | \* | \* | 1.0 | 1.0 | 1.5–2.0 | 1.5–2.0 | 2.5–3.0 | 2.5–3.0 | 3.5–4.0 | 3.5–4.0 | 5.0 | 5.0 |
| 32. | *Extractum Opii siccum* | \* | \* | \* | \* | \* | \* | 0.0025 | 0.0075 | 0.005 | 0.015 | 0.0075 | 0.025 | 0.01 | 0.03 |
| 33. | *Folium Digitalis* | 0.005 | 0.02 | 0.01 | 0.04 | 0.02 | 0.08 | 0.03 | 0.12 | 0.04 | 0.16 | 0.05 | 0.2 | 0.05–0.075 | 0.2–0.3 |
| 34. | *Ftivazidum (Phthivasidum)* | 0.04 for 1 kg of child’s weight daily | 0.3 | 0.6 | 0.35 | 0.7 | 0.4 | 0.8 | 0.5–0.75 | 1.0–1.5 |
| 35. | *Herba Adonidis vernalis* | 0.03 | 0.12 | 0.05 | 0.2 | 0.1 | 0.4 | 0.15 | 0.6 | 0.2 | 0.8 | 0.3 | 1.2 | 0.3–0.5 | 1.2–2.0 |
| 36. | *Herba Thermopsidis* | 0.005 | 0.015 | 0.005 | 0.015 | 0.01 | 0.03 | 0.015 | 0.045 | 0.02 | 0.06 | 0.025 | 0.075 | 0.03–0.05 | 0.1–0.15 |
| 37. | *Lantosidum* | 1 drop | 3 drops | 2 drops | 6 drops | 3 drops | 9 drops | 5 drops | 15 drops | 6 drops | 18 drops | 10 drops | 30 drops | 15 drops | 45 drops |
| 38. | *Mepacrinum hydrochloridum (Acrichinum)* | 0.0125 | 0.025 | 0.0125 | 0.025 | 0.025 | 0.05 | 0.04 | 0.08 | 0.05 | 0.1 | 0.075 | 0.15 | 0.1–0.125 | 0.2–0.25 |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No. | Drug substance name | Up to 6 months | From 6 months to 1 year | 2 years | 3–4 years | 5–6 years | 7–9 years | 10–14 years |
| single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose | single dose administration | daily dose |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
| 39. | *Metamizolum natricum (Analginum)* | 0.025 | 0.075 | 0.05 | 0.15 | 0.1 | 0.3 | 0.15 | 0.45 | 0.2 | 0.6 | 0.25 | 0.75 | 0.3–0.5 | 0.9–1.5 |
| 40. | *Morphini hydrochloridum* | \* | \* | \* | \* | 0.001 | 0.002 | 0.0015 | 0.003 | 0.0025 | 0.0075 | 0.003 | 0.01 | 0.003–0.005 | 0.01–0.015 |
| 41. | *Neostigmini methylsulfas (Proserinum)* | \* | \* | 0.001 | 0.001 | 0.002 | 0.002 | 0.003 | 0.003 | 0.005 | 0.005 | 0.007 | 0.007 | 0.01 | 0.01 |
| 42. | *Nicethamidum (Cordiaminum)* | 2 drops | 6 drops | 3 drops | 9 drops | 4 drops | 12 drops | 5 drops | 15 drops | 6 drops | 18 drops | 7–8 drops | 20–25 drops | 10–15 drops | 30–40 drops |
| 43. | *Omnoponum* | \* | \* | \* | \* | 0.002 | 0.004 | 0.003 | 0.006 | 0.005 | 0.015 | 0.006 | 0.02 | 0.0075–0.01 | 0.02–0.03 |
| 44. | *Opium pulveratum* | \* | \* | \* | \* | \* | \* | 0.005 | 0.015 | 0.01 | 0.03 | 0.015 | 0.045 | 0.015–0.02 | 0.045–0.06 |
| 45. | *Oxytetracyclini dihydras* | 0.025 for 1 kg of child’s weight daily | 0.15 | 0.3 | 0.2 | 0.4 | 0.25 | 0.5 | 0.3 | 0.6 |
| 46. | *Papaverini hydrochloridum* | \* | \* | 0.005 | 0.01 | 0.01 | 0.02 | 0.015 | 0.03 | 0.02 | 0.04 | 0.03 | 0.06 | 0.05–0.06 | 0.15–0.2 |
| 47. | *Pentetrazolum (Corazolum)* | 0.02 | 0.04 | 0.02 | 0.06 | 0.03 | 0.09 | 0.05 | 0.15 | 0.06 | 0.18 | 0.075 | 0.2 | 0.08 | 0.25 |
| 48. | *Pentobarbitalum natrium (Aethaminalum natrium)* | 0.01 | 0.02 | 0.01 | 0.02 | 0.02 | 0.04 | 0.025–0.03 | 0.05–0.06 | 0.04 | 0.08 | 0.05–0.075 | 0.1–0.15 | 0.1–0.15 | 0.2–0.3 |
| 49. | *Phenasonum (Antipyrinum)* | \* | \* | 0.05 | 015 | 0.075 | 0.2 | 0.1 | 0.3 | 0.15 | 0.45 | 0.2 | 0.6 | 0.25–0.3 | 0.75–0.9 |
| 50. | *Phenobarbitalum* | 0.005 | 0.01 | 0.01 | 0.02 | 0.02 | 0.04 | 0.03 | 0.06 | 0.04 | 0.08 | 0.05 | 0.1 | 0.075 | 0.15 |
| 51. | *Phenylbutazonum (Butadionum)* | \* | \* | 0.01 | 0.03 | 0.02 | 0.06 | 0.03 | 0.09 | 0.04 | 0.12 | 0.05–0.06 | 0.15–0.18 | 0.08–0.1 | 0.24–0.3 |
| 52. | *Plasmocidum* | \* | \* | \* | \* | 0.005 | 0.01 | 0.0075 | 0.015 | 0.01 | 0.02 | 0.015 | 0.03 | 0.02–0.025 | 0.04–0.05 |
| 53. | *Platyphyllini hydrotartras* | 0.0004 | 0.0012 | 0.0006 | 0.0025 | 0.001 | 0.003 | 0.0015 | 0.0045 | 0.0025 | 0.0075 | 0.003 | 0.009 | 0.005 | 0.015 |
| 54. | *Prednisolonum* | 0.001 for 1 kg of child’s weight daily | - | 0.02 | - | 0.025–0.03 | - | 0.025–0.04 |
| 55. | *Prednisonum* | 0.001 for 1 kg of child’s weight daily | - | 0.02 | - | 0.025–0.03 | - | 0.025–0.04 |
| 56. | *Proguanili hydrochloridum (Bigumalum)* | 0.0125 | 0.025 | 0.0125 | 0.025 | 0.025 | 0.05 | 0.03–0.04 | 0.06–0.08 | 0.04–0.05 | 0.08–0.1 | 0.075 | 0.15 | 0.1–0.125 | 0.2–0.25 |
| 57. | *Solutio Iodi spirituosae 5 %* | \* | \* | \* | \* | \* | \* | \* | \* | 4 drops | 12 drops | 5 drops | 15 drops | 8 drops | 24 drops |
| 58. | *Strychnini nitras* | \* | \* | \* | \* | 0.00025 | 0.0005 | 0.0003 | 0.0006 | 0.0005 | 0.001 | 0.0006–0.00075 | 0.0012–0.0015 | 0.00075–0.001 | 0.0015–0.002 |
| 59. | *Sulfacetamidum natricum (Sulfacylum – natrium)* | 0.2 for 1 kg of child’s weight daily | 0.35 | 2.0 | 0.4 | 2.5 | 0.5 | 3.0 | 0.5 | 3.0 |
| 60. | *Sulfadimidinum (Sulfadimezinum)* | 0.2 for 1 kg of child’s weight daily | 0.35 | 2.0 | 0.4 | 2.5 | 0.5 | 3.0 | 0.5 | 3.0 |
| 61. | *Sulfaguanidinum* (*Sulginum*) | 0.2 for 1 kg of child’s weight daily | 0.35 | 2.0 | 0.4 | 2.5 | 0.5 | 3.0 | 0.5 | 3.0 |
| 62. | *Sulfanilamidum* (*Streptocidum*) | 0.2 for 1 kg of child’s weight daily | 0.35 | 2.0 | 0.4 | 2.5 | 0.5 | 3.0 | 0.5 | 3.0 |
| 63. | *Sulfathiasolum* (*Norsulfazolum*) | 0.2 for 1 kg of child’s weight daily | 0.35 | 2.0 | 0.4 | 2.5 | 0.5 | 3.0 | 0.5 | 3.0 |
| 64. | *Sulfaethidolum (Aethazolum)* | 0.2 for 1 kg of child’s weight daily | 0.35 | 2.0 | 0.4 | 2.5 | 0.5 | 3.0 | 0.5 | 3.0 |
| 65. | *Tetracyclinum* | 0.025 for 1 kg of child’s weight daily | 0.15 | 0.3 | 0.2 | 0.4 | 0.25 | 0.5 | 0.3 | 0.6 |
| 66. | *Theophyllinum* | \* | \* | \* | \* | 0.04 | 0.12 | 0.05 | 0.15 | 0.06 | 0.2 | 0.08 | 0.25 | 0.1 | 0.3 |
| 67. | *Thymolum* | \* | \* | \* | \* | 0.05 | 0.2 | 0.1 | 0.4 | 0.15 | 0.6 | 0.25 | 1.0 | 0.3 | 1.2 |
| 68. | *Thyreoidinum* | 0.01 | 0.03 | 0.02 | 0.06 | 0.03 | 0.09 | 0.05 | 0.15 | 0.075 | 0.25 | 0.1 | 0.3 | 0.15 | 0.45 |
| 69. | *Tinctura Belladonnae* | 1 drop | 3 drops | 1 drop | 3 drops | 2 drops | 6 drops | 3 drops | 9 drops | 3 drops | 9 drops | 4 drops | 12 drops | 4–6 drops | 12–18 drops |
| 70. | *Tinctura Opii simplex* | \* | \* | \* | \* | \* | \* | 1–2 drops | 2–4 drops | 3 drops | 6 drops | 4 drops | 8 drops | 5–7 drops | 10–15 drops |
| 71. | *Tinctura Strychni* | \* | \* | \* | \* | 1 drop | 2 drops | 2 drops | 4 drops | 3 drops | 6 drops | 4 drops | 8 drops | 5–6 drops | 10–12 drops |
| 72. | *Trimeperidini hydrochloridum (Promedolum)* | \* | \* | \* | \* | 0.005 | 0.01 | 0.0075 | 0.015 | 0.01 | 0.02 | 0.01 | 0.02 | 0.015 | 0.03 |
| 73. | *Vicasol (Vikasolum)* | 0.002–0.005 | 0.006–0.015 | 0.002–0.005 | 0.006–0.015 | 0.006 | 0.018 | 0.008 | 0.025 | 0.01 | 0.03 | 0.01 | 0.03 | 0.015 | 0.045 |

Notes.

\* Substance is not prescribed.

\*\* If two doses are indicated, the lower is applicable for younger children and the highest for older children.

\*\*\*In treating rheumatism, the daily dose of 0.15–0.2 for one year of life is permissible.

2. Maximum one-time or daily doses of highly potent substances for children from the age of 14 and adults (the amount of substances is indicated in grams if other units of measurement are not specified)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No. | Name of the highly potent substance | Routine of administration | Maximum one-time dose | Maximum daily dose |
| 1 | 2 | 3 | 4 | 5 |
| 1. | *Acetarsolum (Osarsolum)* | Orally | 0.25 | 1.0 |
| 2. | *Acidum arsenicosum anhydricum* | Orally | 0.005 | 0.015 |
| 3. | *Acidum hydrochloricum dilutum* | Orally |   | 2 ml (40 drops) |   | 6 ml (120 drops) |
| 4. | *Acidum nicotinicum* | Orally | 0.1 | 0.5 |
| 5. | *Adonisidum* | Orally |   | 40 drops | 120 drops |
| 6. | *Aethacridini lactas* | Orally | 0.05 | 0.15 |
| 7. | *Aether anaestheticus (Aether medicinalis)* | Orally | 0.33 ml (20 drops) |   | 1 ml (60 drops) |
| 8. | *Aethoxydum* | Orally | 1.5 | 4.5 |
| 9. | *Aethylis aminobenzoas (Anaesthesinum)* | Orally | 0.5 | 1.5 |
| 10. | *Aethylis biscoumacetas (Neodicumarinum)* | Orally | 0.3 | 0.9 |
| 11. | *Aethylmorphini hydrochloridum* | Orally | 0.03 | 0.1 |
| 12. | *Ambenonii chloridum (Oxazylum)* | Orally | 0.025 | 0.05 |
| 13. | *Aminarsonum* | Orally | 0.25 | 1.0 |
| 14. | *Aminophenazonum (Amidopyrinum)* | Orally | 0.5 | 2.0 |
| 15. | *Aminophyllinum (Euphyllinum)* | Orally | 0.5 | 1.5 |
| 16. | *Amphetamini sulfas (Phenaminum)* | Orally | 0.01 | 0.02 |
| 17. | *Apomorphini hydrochloridum* | Orally | 0.01 | 0.03 |
| 18. | *Aprofenum* | Orally | 0.03 | 0.1 |
| 19. | *Argenti nitras* | Orally | 0.03 | 0.1 |
| 20. | *Atropini sulfas* | Orally | 0.001 | 0.003 |
| 21. | *Barbamylum* | Orally | 0.3 | 0.6 |
| 22. | *Barbitalum* | Orally | 0.5 | 1.0 |
| 23. | *Barbitalum natricum* | Orally | 0.5 | 1.0 |
| 24. | *Bephenii hydroxynaphthoas (Naphthammonum)* | Orally | 5.0 | 5.0 |
| 25. | *Bendazolum (Dibazolum)* | Orally | 0.05 | 0.15 |
| 26. | *Benzobarbitalum (Benzonalum)* | Orally | 0.3 | 1.0 |
| 27. | *Betasinum* | Orally | 0.075 | 0.2 |
| 28. | *Bromisovalum* | Orally | 1.0 | 2.0 |
| 29. | *Carbacholum* | Orally | 0.001 | 0.003 |
| 30. | *Carbromalum* | Orally | 1.0 | 2.0 |
| 31. | *Chingaminum (Chloroquini phosphas)* | Orally | 0.5 | 1.5 |
| 32. | *Chiniofonum* | Orally | 1.0 | 3.0 |
| 33. | *Chloracizinum* | Orally | 0.05 | 0.15 |
| 34. | *Chlorali hydras* | Orally;rectally | 2.0 | 6.0 |
| 35. | *Chlorambucilum (Chlorbutinum)* | Orally | 0.015 | 0.015 |
| 36. | *Chloramphenicolum (Laevomycetinum)* | Orally | 1.0 | 4.0 |
| 37. | *Chloroformium* | Orally | 0.5 ml | 1 ml |
| 38. | *Chlorpromazini hydrochloridum (Aminasinum)* | Orally | 0.3 | 1.5 |
| 39. | *Chlorpropamidum* | Orally | 0.3 | 1.0 |
| 40. | *Chlortetracyclini hydrochloridum* | Orally | 0.5 | 2.0 |
| 41. | *Chlorotrianisenum* | Orally | 0.012 | 0.048 |
| 42. | *Cocaini hydrochloridum* | Orally | 0.03 | 0.03 |
| 43. | *Codeini phosphas* | Orally | 0.1 | 0.3 |
| 44. | *Codeinum* | Orally | 0.05 | 0.2 |
| 45. | *Coffeinum* | Orally | 0.3 | 1.0 |
| 46. | *Coffeinum – natrii benzoas* | Orally | 0.5 | 1.5 |
| 47. | *Cortisoni acetas* | Orally | 0.15 | 0.3 |
| 48. | *Cotarnini chloridum* | Orally | 0.1 | 0.3 |
| 49. | *Cupri sulfas* | Orally | *0.5 (to be used one-time as* emetic) | - |
| 50. | *Diaethylstilboestrolum* | Orally | 0.001 | 0.003 |
| 51. | *Dicolinum* | Orally | 0.3 | 1.0 |
| 52. | *Dicumarinum* | Orally | 0.1 | 0.3 |
| 53. | *Diethylcarbamazini citras (Ditrazini citras)* | Orally | 0.25 | 0.75 |
| 54. | *Digalen – neo* | Orally | 0.65 ml (20 drops) | 1.95 ml (60 drops) |
| 55. | *Digitoxinum* | Orally | 0.0005 | 0.001 |
| 56. | *Diiodthyrosinum* | Orally | 0.075 | 0.2 |
| 57. | *Diphenhydraminum (Dimedrolum)* | Orally | 0.1 | 0.25 |
| 58. | *Diphenyltropini hydrochloridum (Tropacinum)* | Orally | 0.03 | 0.1 |
| 59. | *Diprophyllinum* | Orally | 1.0 | 3.0 |
| 60. | *Ephedrini hydrochloridum* | Orally | 0.05 | 0.15 |
| 61. | *Erythromycinum* | Orally | 0.5 | 2.0 |
| 62. | *Ethisteronum (Praegninum)* | Orally | 0.02 | 0.06 |
| 63. | *Extractum Belladonnae siccum* | Orally | 0.1 | 0.3 |
| 64. | *Extractum Belladonnae spissum* | Orally | 0.05 | 0.15 |
| 65. | *Extractum Filicis maris spissum* | Orally | 8.0 (administer at one time) |   |
| 66. | *Extractum Opii siccum* | Orally | 0.05 | 0.15 |
| 67. | *Folium Belladonnae* | Orally | 0.2 | 0.6 |
| 68. | *Folium Digitalis* | Orally | 0.1 | 0.5 |
| 69. | *Folium Hyoscyami* | Orally | 0.4 | 1.2 |
| 70. | *Folium Stramonii* | Orally | 0.2 | 0.6 |
| 71. | *Ftivazidum (Phthivasidum)* | Orally | 1.0 | 2.0 |
| 72. | *Furazolidonum* | Orally | 0.2 | 0.8 |
| 73. | *Ganglefeni hydrochloridum (Gangleronum)* | Orally | 0.075 | 0.3 |
| 74. | *Herba Adonidis vernalis* | Orally | 1.0 | 5.0 |
| 75. | *Herba Convallariae* | Orally | 0.5 | 1.5 |
| 76. | *Herba Thermopsidis* | Orally | 0.1 | 0.3 |
| 77. | *Hexamethonii benzosulfonas (Benzohexonium)* | Orally | 0.3 | 0.9 |
| 78. | *Hexestrolum (Synoestrolum)* | Orally | 0.002 | 0.004 |
| 79. | *Hexobarbitalum* | Orally | 0.5 | 1.0 |
| 80. | *Homatropini hydrobromidum* | Orally | 0.001 | 0.003 |
| 81. | *Hydralazini hydrochloridum (Apressinum)* | Orally | 0.1 | 0.3 |
| 82. | *Hydrocodoni phosphas* | Orally | 0.02 | 0.06 |
| 83. | *Hyoscini hydrobromidum (Scopolamini hydrobromidum)* | Orally | 0.0005 | 0.0015 |
| 84. | *Imipramini hydrochloridum (Imizinum)* | Orally | 0.1 | 0.3 |
| 85. | *Isoniazidum* | Orally | 0.6 | 0.9 |
| 86. | *Kanamycini sulfas* | Orally | 1.0 | 4.0 |
| 87. | *Khellinum* | Orally | 0.04 | 0.12 |
| 88. | *Lanatosidum C (Celanidum)* | Orally | 0.0005 | 0.001 |
| 89. | *Lantosidum* | Orally | 0.5 ml (25 drops) | 1.5 ml (75 drops) |
| 90. | *Mebhydrolinum (Diazolinum)* | Orally | 0.3 | 0.6 |
| 91. | *Mepacrinum hydrochloridum (Acrichinum)* | Orally | 0.3 | 0.6 |
| 92. | *Meprobamatum (Meprotanum)* | Orally | 0.8 | 2.4 |
| 93. | *Mercaptopurinum* | Orally | 0.2 | 0.3 |
| 94. | *Mercazolylum* | Orally | 0.01 | 0.04 |
| 95. | *Metamizolum natricum (Analginum)* | Orally | 1.0 | 3.0 |
| 96. | *Methacinium iodide (Methacinum)* | Orally | 0.005 | 0.015 |
| 97. | *Methadonum (Phenadonum)* | Orally | 0.01 | 0.03 |
| 98. | *Methandriol (Methylandrostendiolum)* | Orally; under the tongue | 0.025 | 0.1 |
| 99. | *Methandrostenolonum* | Orally | 0.01 | 0.05 |
| 100. | *Methazidum* | Orally | 1.0 | 2.0 |
| 101. | *Methyltestosteronum* | Orally | 0.05 | 0.1 |
| 102. | *Methylthiouracilum* | Orally | 0.25 | 0.75 |
| 103. | *Morphini hydrochloridum* | Orally | 0.02 | 0.05 |
| 104. | *Myelosanum* | Orally | 0.006 | 0.01 |
| 105. | *Natrii nitras* | Orally | 0.3 | 1.0 |
| 106. | *Neostigmini methylsulfas (Proserinum)* | Orally | 0.015 | 0.05 |
| 107. | *Neriolinum* | Orally | 0.0002 | 0.0004 |
| 108. | *Nicethamidum (Cordiaminum)* | Orally |   | 2 ml |   | 6 ml |
| 109. | *Nitranolum* | Orally | 0.01 | 0.02 |
| 110. | *Nitrofuralum (Furacilinum)* | Orally | 0.1 | 0.5 |
| 111. | *Nitrofurantoinum (Furadoninum)* | Orally | 0.3 | 0.6 |
| 112. | *Omnoponum* | Orally | 0.03 | 0.1 |
| 113. | *Opium pulveratum* | Orally | 0.1 | 0.3 |
| 114. | *Oxytetracyclini dihydras* | Orally | 0.5 | 2.0 |
| 115. | *Oxytetracyclini hydrochloridum* | Orally | 0.5 | 2.0 |
| 116. | *Pachycarpini hydroiodidum* | Orally | 0.2 | 0.6 |
| 117. | *Papaverini hydrochloridum* | Orally | 0.2 | 0.6 |
| 118. | *Paracetamolum* | Orally | 0.5 | 1.5 |
| 119. | *Pempidini tosylas (Pirilenum)* | Orally | 0.01 | 0.03 |
| 120. | *Pentetrazolum (Corazolum)* | Orally | 0.2 | 0.5 |
| 121. | *Pentobarbitalum natricum (Aethamininalum – natrium)* | Orally | 0.3 | 0.6 |
| 122. | *Phenacetinum* | Orally | 0.5 | 1.5 |
| 123. | *Phenasonum (Antipyrinum)* | Orally | 1.0 | 3.0 |
| 124. | *Phenatinum* | Orally | 0.2 | 0.6 |
| 125. | *Phenylephrini hydrochloridum (Mesatonum)* | Orally | 0.03 | 0.15 |
| 126. | *Phenindionum (Phenylinum)* | Orally | 0.05 | 0.2 |
| 127. | *Phenobarbitalum* | Orally | 0.2 | 0.5 |
| 128. | *Phenylbutazonum (Butadionum)* | Orally | 0.2 | 0.6 |
| 129. | *Phthalylsulfathiazolum (Phthalazolum)* | Orally | 2.0 | 7.0 |
| 130. | *Plasmocidum* | Orally | 0.03 | 0.06 |
| 131. | *Platyphyllini hydrotartras* | Orally | 0.01 | 0.03 |
| 132. | *Prednisolonum* | Orally | 0.015 | 0.1 |
| 133. | *Prednisonum* | Orally | 0.015 | 0.1 |
| 134. | *Primidonum (Hexamidinum)* | Orally | 0.75 | 2.0 |
| 135. | *Procainamidi hydrochloridum (Novocainamidum)* | Orally | 1.0 | 4.0 |
| 136. | *Procaini hydrochloridum (Novocainum)* | Orally | 0.25 | 0.75 |
| 137. | *Proguanili hydrochloride (Bigumalum)* | Orally | 0.3 | 0.6 |
| 138. | *Promazini hydrochloridum (Propazinum)* | Orally | 0.25 | 2.0 |
| 139. | *Promeranum* | Orally | 0.036 | 0.144 |
| 140. | *Promethazini hydrochloridum (Diprazinum)* | Orally | 0.075 | 0.5 |
| 141. | *Quateronum* | Orally | 0.05 | 0.2 |
| 142. | *Qinocidum (Chinocidum)* | Orally | 0.03 | 0.03 |
| 143. | *Racemelphalanum (Sarcolysinum)* | Orally | 0.05 (1 time in 7 days) | - |
| 144. | *Reserpinum* | Orally | 0.002 | 0.01 |
| 145. | *Salsolini hydrochloridum* | Orally | 0.1 | 0.3 |
| 146. | *Santoninum* | Orally | 0.1 | 0.3 |
| 147. | *Secale cornutum* | Orally | 1.0 | 5.0 |
| 148. | *Securinini nitras* | Orally | 0.005 | 0.15 |
| 149. | *Solutio Iodi spirituosae 5 %* | Orally |  | 20 drop |  | 60 drop |
| 150. | *Solutio Iodi spirituosae 10 %* | Orally |  | 10 drops |  | 30 drops |
| 151. | *Solutio Lanatosidum C (Solutio Celanidi) 0.05 %* | Orally |  | 1 ml |  | 2 ml |
| 152. | *Solutio Neriolini 0.022 %* | Orally | 0.75 ml (37 drops) | 1.5 ml (75 drops) |
| 153. | *Sphaerophysini benzoas* | Orally | 0.05 | 0.1 |
| 154. | *Strychnini nitras* | Orally | 0.002 | 0.005 |
| 155. | *Sulfacarbamidum (Urosulfanum)* | Orally | 2.0 | 7.0 |
| 156. | *Sulfacetamidum natricum (Sulfacylum – natrium)* | Orally | 2.0 | 7.0 |
| 157. | *Sulfadimidinum (Sulfadimezinum)* | Orally | 2.0 | 7.0 |
| 158. | *Sulfaethidolum (Aethazolum)* | Orally | 2.0 | 7.0 |
| 159. | *Sulfaethidolum natricum (Aethazolum – natrium)* | Orally | 2.0 | 7.0 |
| 160. | *Sulfaguanidinum (Sulginum)* | Orally | 2.0 | 7.0 |
| 161. | *Sulfanilamidum (Streptocidum)* | Orally | 2.0 | 7.0 |
| 162. | *Sulfathiasolum (Norsulfazolum)* | Orally | 2.0 | 7.0 |
| 163. | *Sulfathiasolum – natricum (Norsulfazolum – natrium)* | Orally | 2.0 | 7.0 |
| 164. | *Tetracyclini hydrochloridum* | Orally | 0.5 | 2.0 |
| 165. | *Tetracyclinum* | Orally | 0.5 | 2.0 |
| 166. | *Thecodinum* | Orally | 0.01 | 0.03 |
| 167. | *Theobrominum* | Orally | 1.0 | 3.0 |
| 168. | *Theophyllinum* | Orally; rectally | 0.4 | 1.2 |
| 169. | *Trixexyphenidyli hydrochloridum (Thiphenum)* | Orally | 0.1 | 0.3 |
| 170. | *Thymolum* | Orally | 1.0 | 4.0 |
| 171. | *Thyreoidinum* | Orally | 0.3 | 1.0 |
| 172. | *Tinctura Belladonnae* | Orally | 0.5 ml (23 drops) | 1.5 ml (70 drops) |
| 173. | *Tinctura Opii benzoica* | Orally |   | 2 ml |   | 5 ml |
| 174. | *Tinctura Opii simplex* | Orally | 0.5 ml (22 drops) | 1.25 ml (55 drops) |
| 175. | *Tinctura Strophanthi* | Orally | 0.2 ml (10 drops) | 0.4 ml (20 drops) |
| 176. | *Tinctura Strychni* | Orally | 0.3 ml (15 drops) | 0.6 ml (30 drops) |
| 177. | *Tolbutamidum (Butamidum)* | Orally | 1.5 | 4.0 |
| 178. | *Trihexyphenidyli hydrochloridum (Cyclodolum)* | Orally | 0.01 | 0.02 |
| 179. | *Trimeperidini hydrochloridum (Promedolum)* | Orally | 0.05 | 0.2 |
| 180. | *Trimethinum* | Orally | 0.4 | 1.2 |
| 181. | *Vicasol (Vikasolum)* | Orally | 0.03 | 0.06 |

Minister for Health G. Bērziņš

**Annex 7**

Cabinet Regulation No. 304

18 April 2006

**Prescription Register**



|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | *(Receipt number)* |  |  | *(Name, address, phone number of the pharmacy)* |  | *(Receipt number)* |  | *Part to be attached to the medicinal product* |
|  | Patient |  |  | Patient | *(Receipt number)* |  |  |
|  | Prescription No. |  |  |  |  |  |
|  | Starting materials |  | **Price**(total) |  |  | Date and time of manufacture | Pharmaceutical form | Price |  |  |
|  | Packaging |  |  |  | oral solution | powder | eye drops |  | *(Receipt number)* |  | *Part to be attached to the prescription* |
|  | Correction amount |  |
|  | VAT |  |
|  | Date and time of dispensing |  |  |  | external solution | ointment | suppositories/pellets |  |  | Date/time of manufacture |  |
|  | Dispensed by: |  |  | Medicinal products are not to be dispensed without the receipt |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| *Part to be remained in the register* | *Receipt to be issued to a patient* |  |  |  |

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**Annex 8**

Cabinet Regulation No. 304

18 April 2006

**Information to Be Indicated on a Control Counterfoil**

1. Date.

2. The prescription number or the request number of the medical treatment institution;

3. The name and amount of starting materials.

4. Semi-finished products and concentrates used (if any used), the quantitative proportions thereof and the concentration.

5. Total weight. For powders, suppositories and pellets – also the weight of one dose and the number of doses.

6. Stabilising and isotonising agents (if any added) and the amount thereof if eye drops are being prepared.

7. Water absorption coefficients used in calculations if crude herbal medicinal plants are used in the preparation of medicinal products.

8. Coefficients for magnification of capacity of aqueous solutions used for calculations if the solution of substances is used in the preparation of medicinal products.

9. The given name, surname, signature of the pharmacist/pharmacist’s assistant.

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**Annex 9**

Cabinet Regulation No. 304

18 April 2006

**Permissible Deviations of the Total Mass or Volume of a Pharmaceutical Form and the Amount of Certain Substances**

1. Permissible deviations of the total mass, weighing out in doses

|  |  |  |
| --- | --- | --- |
| No. | Powder mass in grams | Permissible deviation in per cent |
| 1.1. | up to 0.1 |  | ± 15 |
| 1.2. | more than 0.1 to 0.2 |  | ± 10 |
| 1.3. | more than 0.2 to 0.3 |  | ± 7 |
| 1.4. | more than 0.3 to 0.5 |  | ± 5 |
| 1.5. | more than 0.5 to 0.8 |  | ± 4 |
| 1.6. | more than 0.8 to 1 |  | ± 3 |
| 1.7. | more than 1 to 2 |  | ± 4 |
| 1.8. | more than 2 to 5 |  | ± 3 |
| 1.9. | more than 5 to 10 |  | ± 2 |
| 1.10. | more than 10 |  | ± 1 |

2. Permissible deviations of the mass of certain components in powders and suppositories

|  |  |  |
| --- | --- | --- |
| No. | Amount prescribed in grams | Permissible deviation in per cent |
| 2.1. | from 0.01 to 0.02 |  | ± 20 |
| 2.2. | more than 0.02 to 0.05 |  | ± 15 |
| 2.3. | more than 0.05 to 0.2 |  | ± 10 |
| 2.4. | more than 0.2 to 0.3 |  | ± 8 |
| 2.5. | more than 0.3 to 0.5 |  | ± 6 |
| 2.6. | more than 0.5 to 1 |  | ± 5 |
| 2.7. | more than 1 to 2 |  | ± 4 |
| 2.8. | more than 2 to 5 |  | ± 3 |
| 2.9. | more than 5 to 10 |  | ± 2 |
| 2.10. | more than 10 |  | ± 1 |

3. Permissible deviations of the total volume in liquid pharmaceutical forms manufactured using the mass-volume method.

|  |  |  |
| --- | --- | --- |
| No. | Amount prescribed in millilitres | Permissible deviation in per cent |
| 3.1. | up to 10 |  | + 10 |
| 3.2. | more than 10 to 20 |  | + 8 |
| 3.3. | more than 20 to 50 |  | + 4 |
| 3.4. | more than 50 to 150 |  | + 3 |
| 3.5. | more than 150 to 200 |  | + 2 |
| 3.6. | more than 200 |  | + 1 |

4. Permissible deviations of the mass of certain components in liquid pharmaceutical forms manufactured using the mass-volume method.

|  |  |  |
| --- | --- | --- |
| No. | Amount prescribed in grams | Permissible deviation in per cent |
| 4.1. | from 0.01 to 0.02 |  | ± 20 |
| 4.2. | more than 0.02 to 0.1 |  | ± 15 |
| 4.3. | more than 0.1 to 0.2 |  | ± 10 |
| 4.4. | more than 0.2 to 0.5 |  | ± 8 |
| 4.5. | more than 0.5 to 0.8 |  | ± 7 |
| 4.6. | more than 0.8 to 1 |  | ± 6 |
| 4.7. | more than 1 to 2 |  | ± 5 |
| 4.8. | more than 2 to 5 |  | ± 4 |
| 4.9. | more than 5 |  | ± 3 |

5. Permissible deviations of the total volume in liquid pharmaceutical forms manufactured using the mass method.

|  |  |  |
| --- | --- | --- |
| No. | Amount prescribed in grams | Permissible deviation in per cent |
| 5.1. | up to 10 |  | + 10 |
| 5.2. | more than 10 to 20 |  | + 8 |
| 5.3. | more than 20 to 50 |  | + 5 |
| 5.4. | more than 50 to 150 |  | + 3 |
| 5.5. | more than 150 to 200 |  | + 2 |
| 5.6. | more than 200 |  | + 1 |

6. Permissible deviations of the mass of certain components in liquid pharmaceutical forms manufactured using the mass method.

|  |  |  |
| --- | --- | --- |
| No. | Amount prescribed in grams | Permissible deviation in per cent |
| 6.1. | up to 0.1 |  | ± 20 |
| 6.2. | more than 0.1 to 0.2 |  | ± 15 |
| 6.3. | more than 0.2 to 0.3 |  | ± 12 |
| 6.4. | more than 0.3 to 0.5 |  | ± 10 |
| 6.5. | more than 0.5 to 0.8 |  | ± 8 |
| 6.6. | more than 0.8 to 1 |  | ± 7 |
| 6.7. | more than 1 to 2 |  | ± 6 |
| 6.8. | more than 2 to 10 |  | ± 5 |

7. Permissible deviations of the total mass for ointments

|  |  |  |
| --- | --- | --- |
| No. | Amount prescribed in grams | Permissible deviation in per cent |
| 7.1. | up to 5 |  | + 15 |
| 7.2. | more than 5 to 10 |  | + 10 |
| 7.3. | more than 10 to 20 |  | + 8 |
| 7.4. | more than 20 to 30 |  | + 7 |
| 7.5. | more than 30 to 50 |  | + 5 |

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