LAW ON THE MEDICINAL PRODUCTS IN HUMAN MEDICINE

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Chapter One

GENERAL PROVISIONS

Section I
General provisions

Article 1. This law shall regulate the terms and procedures for:

1. authorisation for use or registration of medicinal products designated for the human medicine, which are industrially manufactured or the manufacturing method of which includes industrial process;

2. authorisation of manufacturing and import of medicinal products and active substances;

3. approval and conduct of clinical trials;

4. wholesale of and retail trade in medicinal products;

5. parallel import of medicinal products;

6. advertising of medicinal products;

7. follow-up of the safety of the medicinal products released on the market;

8. classification of the method of prescribing and dispensing medicinal products;

9. control of the manufacture and import, wholesale and retail trade, conduct of clinical trials, advertising, and the system for the follow-up of the safety the medicinal products released on the market;

10. pricing of medicinal products;

11. development of positive drug list.

Article 2. The purpose of this law is to establish conditions for enduring the release on the market of medicinal products, which comply with the requirements relating to quality, safety, and efficiency.

Article 3. (1) Medicinal product is any substance or combination of substances, which:

1. are intended for treatment or prophylactic of diseases in humans, or

2. are administered with the aim of recovery, correction, or modification of physiological functions in humans by means of pharmacological, metabolic, or immunological action or are used for diagnostic purposes.

(2) Substance is any matter, the origin or which could be:

1. human (human blood, human blood products, and others);

2. animal (microorganisms, animal organs, extracts, secretions, toxins, blood products, and others.);

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3. vegetal (microorganisms, plants and parts thereof, plant extracts, secretions, and others.);

4. chemical (elements, natural chemical materials, synthetic and semisynthetic substances, and others).

Article 4. Where a product meets simultaneously the characteristics of both a medicinal product and another product regulated by other law, the provisions of this law shall apply.

Article 5. Medicinal products shall be classified according to the anatomic-therapeutic-chemical classification in accordance with the requirements of the World Health Organisation (WHO).

Article 6. This law shall not be applicable to:

1. hermetically closed radionuclides;

2. blood, plasma, or blood cells derived by a method including an industrial process.

Article 7. (1) Only the manufacture of, import, wholesale and retail trade in, advertising of and treatment, prophylaxis, and diagnosis with medicinal products, which have received marketing authorisation, shall be permitted under terms of:

1. this law or

2. Regulation (EC) 726/2004 of the European Parliament and the Council.

(2) The import of, trade in, treatment, prophylaxis and diagnosis with medicinal products beyond their expiry date shall be prohibited.

(3) Possession of a marketing authorisation or certificate of use, manufacture, and clinical trials of medicinal products issued in accordance with this law shall not constitute ground for discharge according to the legislation in force.

Article 8. Marketing authorisation according to this law shall not be required for:

1. medicinal product prepared according to magisterial recipe in a pharmacy;

2. medicinal product prepared according to pharmacopoeia recipe in a pharmacy;

3. intermediate products designated for industrial processing by a person who has received authorisation for manufacture under the terms of this law;

4. active and auxiliary substances;

5. medicinal products in the course of development and/or test;

6. medicinal products designated for export.

Article 9. (1) The treatment of a specific patient a medicinal product, which has not been authorised under the terms of chapter three, can be applied according to a special procedure for therapeutic establishment for hospital care under the terms and procedures as set out in an ordinance issued by the minister of health.

(2) The manager of the healthcare establishment shall be responsible for the treatment according to paragraph 1.

Article 10. (1) The Minister of health can authorise for certain period of time treatment with a medicinal product which has not been authorised according to chapter three, by an order on the basis of reasoned proposal from chief state health inspector coordinated with the director Bulgarian Drug Agency (BDA) wherever there is a declared epidemic in the country caused by pathogenic microorganisms or toxins or there is suspected or confirmed dissemination of chemical agents or nuclear radiation and there is no suitable medicinal product authorised for use.

(2) In the cases under paragraph 1, the marketing authorisation holders, manufacturers, and medical specialists shall not bear civil or administrative and penal responsibility for the consequences of the use in an unauthorised indication of a medicinal product or of a medicinal product, which has not been authorised according to chapter three.

(3) Paragraph 2 does not exclude the responsibility for defective products according to the Law for the Protection of the Consumers

Article 11. (1) The Minister of health can, due to reasons relating to the protection of the health of the population, instruct by way of order the executive director of the BDA to authorise the use of a medicinal product, which has not been authorised for use on the territory of the Republic of Bulgaria and for which no application for issuing of an authorisation has been submitted but which has been authorised in another Member State.

(2) In the cases under paragraph 1, the director of BDA, or his authorised representative shall:

1. inform the holder of the marketing authorisation for the medicinal product on the initiation of a procedure for the authorisation of the medicinal product for use;

2. register the person referred to in point 1 as a holder of the issued authorisation;

3. demand from the regulatory body of the Member State that has issued the marketing authorisation a copy of the assessment report and a copy of the marketing authorisation.

(3) The Bulgarian Drug Agency shall be obliged to ensure compliance of the label, patient information leaflet, classification, advertising, and follow-up of the safety of the medicinal product released on the market according to paragraph 1 with the requirements of this law.

(4) The Executive Director of BDA shall inform the European Commission about the authorisation issued according to paragraph 1, the name and address of the authorisation holder, as well as about the date of termination of the validity thereof.

Article 12. (1) The official pharmacopoeia of the Republic of Bulgaria shall be the European Pharmacopoeia

(2) The official pharmacopoeia may be supplemented with the requirements of the Bulgarian pharmacopoeia.

(3) The Minister of health shall determine by way of order the dates of entry into effect of the current edition of the official pharmacopoeia and the annexes thereof.

(4) The order according to paragraph 3 shall be promulgated in the State gazette and published on the internet site of BDA.

Article 13. (1) The monographs of the European Pharmacopoeia shall be obligatory for all substances, preparations, and pharmaceutical forms contained therein. In the cases where there is no monographs in the European Pharmacopoeia, the requirements of the current editions of the pharmacopoeias of the Member States, the U.S.A, and Japan provided that these are in compliance with the general rules of the European Pharmacopoeia.

(2) Where the specification contained in a monograph of the European Pharmacopoeia or other national pharmacopoeia is insufficient to ensure the quality of the substance or pharmaceutical form, the Bulgarian Drug Agency can require supplementation of the specification by the applicant/marketing authorisation holder.

Chapter Two

MANAGING AND FINANCING BODIES

Section I
Managing bodies

Article 14. (1) The medicinal product policy in the Republic of Bulgaria is part of the State health policy and is implemented by the Minister of Health.

(2) The Minister of health shall:

1. be the national coordinator for the problems of medicinal product;

2. take part in international bodies and organizations carrying out activities in the domain of the medicinal products;

3. Issue approvals for retail trade with medicinal products in pharmacy and close pharmacies;

4. Carry out other activities set out by a law.

When activities according paragraph 2, point 3 carried out, the Ministry of Health collect taxes in amount, determined in tariff according to Article 21, paragraph 2.

Article 15. (1) Pharmacopoeia Committee shall be established with the Minister of health as a consulting body on issues relating to the current pharmacopoeia.

(2) The Minister of health shall, on the grounds of a proposal of the Executive Director of the BDA determine by an order the composition of the Pharmacopoeia Committee and the expert groups thereto and shall approve the regulation relating to their activity.

(3) The activity of the Pharmacopoeia Committee shall be financed by the budget of the Ministry of Health.

Article 16. (1) Higher Council of Pharmacy shall be established to the minister of health as a consulting body on issues relating to pharmacy. It shall be composed by five representatives appointed by the Minister of Health, five representatives from Bulgarian Pharmaceutical Union, two representatives from National Health Insurance Fund (NHIF) and one representative from Faculty of pharmacy of the high medicinal schools. The Minister of Health is a chairman of the council without right of vote.

(2) The Higher Council of Pharmacy is consultative body, which discuss and provide statements for:

1. Basic approaches and priorities in the pharmaceutical area;

2. Ethical problems of the pharmacy;

3. Projects for normative acts, related with the pharmacy;

4. The scientific priorities in the area of pharmacy;

5. Programs for organization of social educational campaign in the area of medicinal products.

(3) The Higher Council of Pharmacy reviews the applications for retail trade with medicinal product and makes motivated proposal to the Minister of Health for issuing approval or refusal, and also for deprivation of issued approvals.

(4) The organization and the activity of the Higher Council of Pharmacy are settled with ordinance issued by the Minister of Health, after proposal of Higher Council of Pharmacy.

Article 17. (1) The Bulgarian Drug Agency shall be a specialized body at the minister of health for the surveillance on the quality, safety, and efficacy of the medicinal products.

(2) The Bulgarian Drug Agency shall be a legal entity budget financed with registered office in the city of Sofia and shall act as an authorising officer by way of subdelegation to the Minister of Health.

(3) The Bulgarian Drug Agency shall be managed and represented by an Executive Director who shall be appointed under the terms of the Law on the Administration.

(4) The structure, functions, and work organisation of the Bulgarian Drug Agency shall be regulated by statutes adopted by the Council of Ministers.

(5) The Bulgarian Drug Agency shall:

1. issue manufacture authorisation for medicinal products;

2. issue marketing authorisations and registration certificated for medicinal products;

3. issue authorisations for wholesale of medicinal products;

4. issue authorisations for parallel import of medicinal products;

5. issue registration certificates for drugstores;

6. issue authorisations to conduct clinical trials of medicinal products;

7. carry out assessment of the quality, efficacy, safety of medicinal products in relation with their marketing authorisations;

8. issue authorizations for the advertising of medicinal products;

9. exert control on the manufacture, import, storage, wholesale and retail trade, clinical trials, safety, and advertising of medicinal products;

10. carry out laboratory analysis in case of doubt of deviation in the quality, efficacy, and safety of the medicinal products and shall undertake the measures provided by law;

11. organize a pharmacovigillance system and undertake the corresponding measures;

12. issue certificates according to the certification system of the World Health Organisation;

13. Issue Good Manufacturing Practice certificates;

14. coordinate investment projects for the construction of new and/or refurbishing of existing sites relating to the manufacture of medicinal products in accordance with the rules of Good Manufacturing Practice;

15. execute the functions of national coordinator and consulting body on the issues relating to the quality, efficacy, and safety of medicinal products;

16. carry out consulting, scientific, information, and publishing activity in the domain of the medicinal sector;

17. coordinate and participate in activities relating to the European Pharmacopoeia and the development of the Bulgarian Pharmacopoeia;

18. take part in activities in the field of the medicinal products relating to the work of the European Medicines Agency, the European Directorate of the Quality of the Medicinal Products and Healthcare, of international bodies and organizations, as well as relating to the fulfilment of international treaties in which Bulgaria is a party to;

19. carry out other activities provided by a law.

(6) The Bulgarian Drug Agency coordinates its activity with the regional inspectorates for the prevention and control of public health in the field of the control on the medicinal products.

Section II
Registers

Article 18. The Ministry of Health shall keep a register of the issued authorizations for opening pharmacies.

Article 19. (1) The Bulgarian Drug Agency shall keep registers of:

1. manufacturers of medicinal products on the territory of the Republic of Bulgaria and qualified persons according to Article 148, point 2;

2. importers of medicinal products on the territory of the Republic of Bulgaria and qualified persons according to Article 161, paragraph 2, point 1;

3. authorised/registered medicinal products on the territory of the Republic of Bulgaria;

4. wholesalers of medicinal products on the territory of the Republic of Bulgaria;

5. issued certificates of registered drugstores;

6. authorised clinical trials;

7. issued authorisations for parallel import.

(2) The data of the registers according to paragraph 1, points 1 to 5 and point 7 shall be published on the internet site of the Bulgarian Drug Agency.

(3) The Bulgarian Drug Agency shall maintain systems for electronic data exchange with the regulatory bodies of other Member States, European Commission, and the European Medicines Agency.

Section III
Financing

Article 20. (1) The activity of the Bulgarian Drug Agency is financed from the budget funds and its own activity.

(2) Budget funds shall be ensured by a subsidy from the state budget through the budget of the Ministry of Health.

Article 21. (1) The Bulgarian Drug Agency shall be the administrator of the revenues of its own activity, namely:

1. chemico-pharmaceutical examinations;

2. laboratory analyses and tests;

3. assessment of documentation and issue of authorizations, certificates, and other documents set forth in this law;

4. evaluation by the renewal, variation and cease of marketing authorization approval and certificate for registration of medicinal product;

5. maintenance of marketing authorizations of medicinal products;

6. fines and property sanctions imposed by penal ordinances issued for infringements of this law;

7. consulting, publishing, and research activities in the field of the drug sector;

8. coordination of investment projects for the construction of new and/or refurbishing of existing sites relating to the manufacture of medicinal products;

9. conduct of inspections in connection with assessment of compliance of the manufacturing conditions with the requirements of Good Manufacturing Practice;

10 other sources.

(2) During the execution of the activities according to paragraph 1, points 1 – 5, points 7 – 9 the Bulgarian Drug Agency shall collect fees to the amounts as defined in a tariff adopted by the Council of Ministers.

Article 22. (1) The funds according to Article 21 shall be spent for:

1. control activity of the BDA;

2. Payment of the activities according to Article 21, paragraph 1, т. 1 и 2, when The BDA is assigned their execution of another persons by contract;

3. acquisition of fixed assets of the Bulgarian Drug Agency and for the maintenance and repair thereof;

4. establishment and maintenance and update of the registers according to Article 19, paragraph 1;

5. maintenance of systems for electronic data exchange with the regulatory bodies of the other Member States, with the European Commission, with and the European Medicines Agency;

6. information and publishing activities relating to the quality, efficacy, and safety of the medicinal products;

7. provision of the activity of the specialized commissions according to Article 47, Par. 1 and 2 and the council according to Article 251, paragraph 3;

8. carry out of programmes for training employees of the BDA;

9. participations in international and national inter-laboratory tests;

10. supplementary material incentives of the employees of the BDA to the extent of up to 40 percent of the funds according to Article 21, paragraph 1, points 1-8 under conditions and order as defined by internal rules of the executive director of the Bulgarian Drug Agency.

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(2) The funds according to Article 14, paragraph 2 shall be spent for:

1. activities of the Higher Council of Pharmacy;

2. activities of the Pharmacopoeia Committee;

3. activities of the Commission on Medicinal Product Prices, the Commission on the Positive Drug List, and the Transparency Commission ;

4. carry out of programmes for training the employees of the Ministry of Health in the field of medicinal product policy;

5. supplementary material incentives of the employees of the Ministry of Health to the extent of up to 40 percent of the funds according to Article 14, paragraph 3 under conditions and order as defined by internal rules of the Minister of Health.

Chapter Three

PLACING MEDICINAL PRODUCTS ON THE MARKET

Section I
General provisions

Article 23. (1) An industrially manufactured medicinal product or a medicinal product obtained by a method involving an industrial process may only be placed on the market after a marketing authorization or a registration certificate has been issued under the terms of:

1. this law or

2. Regulation (EC) 726/2004 of the European Parliament and the Council.

(2) A marketing authorization within the meaning of paragraph 1 shall also be required for a radionuclide generator, radionuclide precursor, or a kit.

(3) Types of procedures according to paragraph 1 shall be:

1. centralised procedure;

2. mutual recognition /decentralised procedure;

3. national procedure.

Article 24. (1) Marketing authorisation shall not be required for radiopharmaceuticals prepared immediately before use from authorized radionuclide generators, radionuclide precursors, or kits in accordance with the manufacturer's instructions.

(2) The products according to paragraph 1 shall be prepared by qualified persons I laboratories or institutes authorized for such activity under the terms of the Law on the Safe Use of Nuclear Energy.

(3) The preparation, use, and administration of the products according to paragraph 1 shall be performed in compliance with the nuclear medicine standard.

Article 25. (1) The criteria for the determination of a medicinal product designated for the treatment, prophylaxis, or diagnostics of rare diseases are laid down in Regulation (EC) 141/2000 of the European Parliament and the Council.

(2) The conditions and order for granting of a marketing authorisation of the medicinal products according to paragraph 1 are laid own in (EC) № 726/2004 of the European Parliament and the Council.

Article 26. (1) A marketing authorisation of a medicinal product, a registration certificate for the authorization of a homeopathic medicinal product according to Article 35, or a registration certificate for the authorization of a traditional herbal medicinal product according to Article 37 on the territory of the Republic of Bulgaria shall be issued by the executive director BDA to a natural or legal person established on the territory of a Member State or a state member of the European Economic Area.

(2) Where the person according to paragraph 1 is not established on the territory of the Republic of Bulgaria, it shall designate a representative.

(3) The marketing authorization holder takes responsibility for the medicinal products placed on the territory of the Republic of Bulgaria. The designation of a person according to paragraph 2 shall not release the marketing authorization holder from responsibility according to the acting legislation in Republic of Bulgaria.

Section II
Requirements relating to the documentation for granting a marketing authorisation

Article 27. (1) For granting a marketing authorisation of a medicinal product, the person according to Article 26, paragraph 1, shall submit to the BDA a formal application accompanied by a dossier in the format of the Common Technical Document, which shall contain:

1. name and address of management and/or permanent address of the applicant according to Article 26, paragraph 2; where the applicant is a person other than the manufacturer(s) – address of the manufacture sties;

2. name of the medicinal product;

3. qualitative and quantitative particulars of the medicinal product, including its international non-proprietary name (INN) recommended by the WHO, where an INN for the medicinal product exists, or the relevant chemical name;

4. therapeutic indications, contraindications and adverse drug reactions;

5. posology, pharmaceutical form, method and route of administration and expected shelf-life;

6. precautions and safety measures during storage of the medicinal product, its administration to patients and for the disposal of waste products together with an indication of potential risks for the environment;

7. description of the method of manufacture;

8. description of the control methods employed by the manufacturer;

9. assessment of the potential risks presented by the medicinal product for the environment for every individual case and measures for the limitation thereof;

10. results of:

а) pharmaceutical (physico-chemical, biological or microbiological) tests;

б) preclinical (toxicological and pharmacological) tests;

в) clinical trials;

11. declaration that the ethic principles of the Good Manufacturing Practice have been complied with in the clinical trials conducted outside the territory of the Member States;

12. description of the pharmacovigilance system, which is to be implemented and, where appropriate, description of the risk management system;

13 data of the person according to Article 186, paragraph 1 – name, address, and professional qualification;

14. summary of product characteristics according to Article 34;

15. mock-up of the immediate and outer packaging of the product and a proposed package leaflet in compliance with the requirements of chapter six;

16. copy of the manufacturing authorisation issued by the regulatory authority of the country where manufacture is performed accompanied by a Good Manufacturing Practice certificate or a certificate evidencing that the manufacture of the medicinal product and the active substances contained in its composition has been performed in compliance with standards, which are at least equivalent to the standards of the Good Manufacturing Practice;

17. copy of a document evidencing that the medicinal product is designated for treatment, prophylaxis, or diagnostics of rare diseases accompanied by a copy of the opinion of the European Medicines Agency;

18. copies of all marketing authorizations issued in other Member States or in a third state of the medicinal product applied for marketing authorisation;

19. list of the Member States where an application for marketing authorisation the medicinal product has been submitted;

20. copy of the summary of product characteristics proposed by the person according to Article 26, paragraph 1, or a copy of the summary of product characteristics approved by a regulatory authority of a Member State/ states members of the European Economic Area, which has already issued a marketing authorisation;

21. copy of a refusal for a marketing authorisation in a Member State or a third state accompanied by motives; information for temporary suspension or termination of the effect of the marketing authorisation;

22. copy of the proposed package leaflet accompanied by a summary of the results of the assessment of the level of comprehensibility of the contents of the package leaflet by a target patient group selected by the applicant or a copy of a leaflet approved by a regulatory authority in a Member State, which has already issued a marketing authorisation;

23. document of paid fee in amounts up in the tariff according to Article 21, paragraph 2.

(2) The documents according to paragraph 1, point 18, relating to the Member States, and point 19, respectively, shall only be submitted in the procedures according to section VII.

(3) To radionuclide generators, the following documents shall be added to the data according to paragraph 1:

1. description of the system together with a detailed description of its components, which may affect the composition or quality of the daughter radionuclides;

2. qualitative and quantitative particulars of the eluate or the sublimate.

(4) The documents and data from pharmaceutical tests, preclinical and clinical trials shall be accompanied by summarized reports prepared by experts with the required technical and professional qualification. To the reports a curricula vitae report of the experts shall be applied.

(5) The dossier of the medicinal product shall be submitted in the Bulgarian and/or English language.

Article 28. (1) The person according to Article 26, paragraph 1, insofar as he does not infringe industrial and commercial property rights, shall not submit to the BDA the data according to Article 27, paragraph 1, point 10, letters “b” and “c” provided that he can prove that the medicinal product indicated in the application is generic of a reference medicinal product, which is or has been authorized to market for not less than 8 years in a Member State or in a state member of the European Economic Area.

(2) The marketing authorization holder of a generic product according to paragraph 1 may not place it to market until 10 years from the initial marketing authorisation of the reference medicinal product have elapsed.

(3) Under observance of the conditions of paragraphs 1 and 2, the person according to Article 26, paragraph 1, may submit to the BDA an application for marketing authorisation of a medicinal product, which is generic of a reference medicinal product, even where the reference product has never had marketing authorization on the territory of the Republic of Bulgaria.

(4) In the cases according to paragraph 3, the person according to Article 26, paragraph 1, shall indicate in the application according to Article 27, paragraph 1, the Member State where the reference product is or has been authorised to market.

(5) In the cases according to paragraph 3, the BDA shall request from the regulatory authority of the Member State indicated in the application according to Article 27, paragraph 1, a

confirmation of the information according to paragraph 4, the qualitative and quantitative composition of the reference product and, if necessary, additional documentation.

(6) At the request of a regulatory authority of a Member State where the application for a medicinal product generic to a referent medicinal product, which is or has been authorized to market on the territory of the Republic of Bulgaria, is submitted, the BDA shall submit the requested information according to paragraph 5 within one month from the request date.

(7) The ten-year period according to paragraph 2 may be extended by maximum one year at the request of the marketing authorization holder of the reference medicinal product provided that during the first 8 years from the issue of the marketing authorisation of the reference medicinal product its marketing authorization holder has received authorisation for a new therapeutic indication the significant clinical advantages of which versus the existing therapeutic opportunities are scientifically well-grounded.

Article 29. (1) The person according to Article 26, paragraph 1, shall submit to the BDA the results of the required preclinical and/or clinical trials in the cases where the medicinal product indicated in the application:

1. cannot be defined as generic or

2. the bioavailability tests do not prove bioequivalence, or

3. there is a change in the active substance(s), therapeutic indications, pharmaceutical form, and/or posology compared with the reference medicinal product, or

4. is offered in dosage units, which are different compared with the reference medicinal product.

(2) Where a biological medicinal product indicated in the application as similar to a reference biological medicinal product does not comply with the conditions to be determined as a generic medicinal product due to different method of manufacture or different starting materials compared with the reference product, or for other reasons, the applicant shall submit to the BDA the results of the required preclinical and/or clinical trials associated with these conditions.

(3) In the cases according to paragraphs 1 and 2 the documentation as laid down in the regulation according to Article 42 shall also be submitted**.**

Article 30. (1) The person according to Article 26, paragraph 1, insofar as he does not infringe the industrial and commercial property, shall not submit to the BDA the data according to Article 27, paragraph 1, point 10, letters "b" and "c" provided that he can prove that the conditions laid down in the regulation according to Article 42 to the effect that the active substance included in the composition of the medicinal product applied for marketing authorisation has a well-established use in the medical practice and possesses acknowledged efficacy and acceptable safety level. In these cases, the results from the tests and tests may be replaced by the relevant scientific publications.

(2) The person according to paragraph 1 shall submit the results from the required preclinical and clinical trials in case that the medicinal product containing active substances with well-established use, which have not been used for therapeutic use in the proposed combination. In this case, the documentation relating to each active substance shall not be submitted.

(3) Where an active substance within the meaning of paragraph 1 has a proven new therapeutic indication on the basis of significant preclinical or clinical data associated with the new indication, the next applicant may not refer to the data for the new indication of the active substance more than once in a year.

Article 31. In case, when medicinal product containing active substances used in the composition of authorised medicinal products but which are not used in the proposed

combination for therapeutic purposes, the person according to Article 26, paragraph 1, shall submit the results of the preclinical trials and clinical trials associated with this combination. In this case the applicant shall not submit documentation relating to the safety and efficacy of each separate active substance**.**

Article 32. The marketing authorisation holder of a medicinal product may authorise the use of the pharmaceutical, preclinical and clinical documentation contained in the dossier of the medicinal product for the assessment of subsequent applications for medicinal products with the same qualitative and quantitative composition with respect to the active substances and with the same pharmaceutical form.

Article 33. Conducting the necessary studies and tests for the purpose of preparing the documentation for marketing authorisation and the subsequent practical requirements in connection with the authorization to market of medicinal products according to Article 28 and Article 29 shall not be regarded as breach of patent rights or to supplementary protection certificates of medicinal products.

Article 34. (1) The summary of product characteristics shall contain the following information:

1. name of the medicinal product, quantity of the active substance in a dose unit, and pharmaceutical form;

2. qualitative and quantitative composition in terms of the active substances and constituents of the excipient, the information of which is essential for proper administration of the medicinal product. The usual common name or chemical description shall be used;

3. pharmaceutical form;

4. clinical particulars:

a) therapeutic indications,

b) posology and method of administration for adults and, where necessary, for children,

c) contra-indications,

d) special warnings and precautions for use and, in the case of immunological medicinal products, any special precautions to be taken by persons handling such products and administering them to patients, together with any precautions to be taken by the patient,

e) interaction with other medicinal products and other forms of interactions,

f) use during pregnancy and lactation,

g) effects on ability to drive and to use machines,

h) undesirable effects,

i) overdose (symptoms, antidotes, emergency measures).

5. pharmacological properties:

a) pharmacodynamic properties,

b) pharmacokinetic properties,

c) preclinical safety data.

6. pharmaceutical particulars:

a) list of excipients,

b) major incompatibilities,

c) shelf life, where necessary after reconstitution of the medicinal product or where the immediate packaging is opened for the first time,

d) special precautions for storage,

e) nature and contents of container,

f) special precautions for disposal of unused medicinal product or waste materials from such medicinal product.

7. marketing authorisation holder.

8. registration number.

9. date of the first marketing authorisation or renewal of the marketing authorisation.

10. date of a variation in the summary of product characteristics.

11. for radiopharmaceuticals, full details of internal radiation dosimetry.

12. for radiopharmaceuticals, detailed instructions for extemporaneous preparation and quality control and, where appropriate, maximum storage time during which any intermediate preparation such as an eluate or the ready-to-use pharmaceutical will conform to its specifications.

(2) The summary of product characteristics of medicinal products according to Articles 28-33, those parts of the summary of product characteristics of the reference medicinal product referring to indications or dosage forms which were still covered by patent law at the time when a generic medicine was marketed shall not be included.

(3) The requirements relating to the form and content of the summary of product characteristics shall be laid down in the regulation according to Article 42.

Section III
Specific requirements applicable to homeopathic medicinal products

Article 35. (1) Certificate for the registration of a homeopathic medicinal product shall be issued according to a simplified procedure provided that it complies with the following conditions:

1. they are administered orally or externally;

2. no specific therapeutic indications appear on the labelling of the medicinal product or in any information relating thereto;

3. there is a sufficient degree of dilution to guarantee the safety of the medicinal product; in particular, the medicinal product may not contain either more than one part per 10 000 of the mother tincture or more than 1/100th of the smallest dose used in allopathy with regard to active substances whose presence in an allopathic medicinal product results in the obligation to submit a doctor's prescription.

(2) For granting a registration certificate of a homeopathic medicinal product the person according to Article 26, paragraph 1, shall submit to the BDA a formal application, which may cover a series of medicinal products derived from the same homeopathic stock or stocks.

(3) The following documentation shall be included in the application according to paragraph 2 in order to demonstrate the pharmaceutical quality and the batch-t-batch homogeneity of the products concerned:

1. scientific name or other name given in a pharmacopoeia of the homeopathic stock or stocks, together with a statement of the various routes of administration, pharmaceutical forms, and degree of dilution to be registered;

2. dossier describing how the homeopathic stock or stocks is/are obtained and controlled, and
justifying its/their homeopathic use, on the basis of an adequate bibliography;

3. manufacturing and control file for each pharmaceutical form and a description of the method of dilution and potentiation;

4. manufacturing authorisation accompanied by a Good Manufacturing Practice certificate or by a certificate evidencing that the product is manufactured under conditions equivalent to the requirements of the Good Manufacturing Practice;

5. copies of any registrations or authorisations obtained for the same medicinal product in other Member States;

6. one or more mock-ups of the outer packaging and the immediate packaging of the medicinal products to be registered;

7. data concerning the stability of the medicinal product.

(4) The requirements relating to the data according to paragraph 3 shall be laid down in the regulation according to Article 42.

Article 36. (1) Homeopathic medicinal products other than those referred to in Article 35, paragraph 1, the provisions of Articles 27 – 32 shall apply.

(2) For the homeopathic medicinal products according to paragraph 1 the person according to Article 26, paragraph 1, shall not submit results of preclinical and clinical trials provided that it can be proven by bibliographical data from scientific literature that the homeopathic use of the medicinal product or homeopathic stocks involved in its composition have an established safety.

(3) In the cases according to paragraph 2 the following shall be proven from the bibliographical data:

1. the homeopathic character of the uses raw materials and their traditional use in the indication applied for;

2. the innoxiousness of the homeopathic medicinal product with respect to the degree of dilution of each component.

Section IV
Specific provisions applicable to traditional herbal medicinal products

Article 37. (1) Registration certificate for a traditional herbal according to a simplified procedure provided that the product complies with the following conditions:

1. the product has indications exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment;

2. the product is exclusively administered in accordance with a specified strength and posology;

3. the product is administered orally, by inhalation, or is designated for external use;

4. the period for traditional use according to Article 38, paragraph 1, point 5, has elapsed;

5. the data on the traditional use of the medicinal product are sufficient; in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-standing use and experience.

(2) The BDA may apply the procedure according to paragraph 1 to a herbal medicinal product containing vitamins or minerals for the safety of which there is well documented evidence shall not prevent the product from being eligible for registration in accordance with paragraph 1, provided that the action of the vitamins or minerals is ancillary to that of the herbal active ingredients regarding the specified claimed indication(s).

Article 38. (1) For granting a registration certificate for a traditional herbal product the person according to Article 26, paragraph 1, shall submit to the BDA an application accompanied by the following documentation:

1. the data according to Article 27, paragraph 1, points 1 – 9 and point 10, letter “a”;

2. summary of product characteristics without the data according to Article 34, paragraph 1, point 4**;**

3. in case of a herbal medicinal product according to Article 37, paragraph 2, or of a combined herbal medicinal product – the information according to Article 37, paragraph 1, point 5 for the combination; where the individual active substances of the combined product are not sufficiently known, data on the traditional use of each shall be provided;

4. a copy of the marketing authorisation or registration certificate of the herbal medicinal product granted by a Member State or a third country and/or a copy of a refusal accompanied by the motives of the decision;

5. bibliographical or expert evidence to the effect that the medicinal product in question or a corresponding product has been in medicinal use throughout a period of at least 30 years preceding the date of the application including at least 15 years within a Member State or country of the European Economic Area preceding the date the application;

6. bibliographical evidence of the safety the product accompanied by an expert report for the product accompanied by an expert report;

7. a copy of the manufacturing authorisation accompanied by a Good Manufacturing Practice certificate or by a certificate evidencing that the product is manufactured under conditions equivalent to the requirements of the Good Manufacturing Practice.

(2) The BDA may request additional information from the applicant for the assessment of the safety of the medicinal product according to paragraph 1.

(3) The BDA may request an opinion of the Committee for Herbal Medicinal Products at the European Medicines Agency relating to the adequacy of the data according to paragraph 1, point 5, by submitting the necessary parts of the dossier of medicinal product.

(4) The data submitted according to paragraph 1, point 5 shall also be valid in the cases where throughout the period of 30 years of use in the medical practice:

1. the medicinal product, which is similar to the product which is applied for registration, has been marketed without authorisation or registration or

2. where the number of the components or the strength of the medicinal product, which is applied for registration, is decreased.

Article 39. (1) Where the product has been used in the Community for less than 15 years, but is otherwise eligible for simplified registration Article 37, paragraph 1, the BDA shall submit the documentation according to Article 38, paragraph 1, to the Committee on Herbal Medicinal Products for opinion.

(2) The BDA shall make the final decision following the establishment of the monograph of the Committee according to paragraph 1 on the compliance or the product with the criteria for registration for traditional use.

(3) In the cases according to paragraph 1 the term according to Article 44 shall cease to run.

Article 40. The BDA may request from the applicant for herbal medicinal product to submit the documentation according to Articles 27 - 32 or according to Article 35.

Article 41. (1) The BDA shall publish on its internet site a list of the herbal substances, preparations, or combinations thereof used in the traditional herbal medicinal products established by the Committee on Herbal Medicinal Products of the European Evaluation Agency. The list shall contain therapeutic indications, strength, posology and method of administration as well as other information, which is necessary for the safe use of the herbal substance as a traditional medicinal product.

(2) Where the product proposed in the application for registration for traditional use contains herbal substance, preparation, or combination of products included in the list according to paragraph 1, the applicant shall not submit the data according to Article 38, paragraph 1, points 4 - 6.

(3) Where the herbal substance, preparation, or combination thereof are excluded from the list according to paragraph 1, the holder of the registration certificate of a herbal medicinal product must submit to the BDA the full documentation according to Article 38 within three months from the amendment.

(4) In case the holder of the registration certificate of the herbal medicinal product does not fulfil the obligation according to paragraph 3, the BDA shall cancel the registration certificate of the product.

Section V
Procedure for granting marketing authorisation of medicinal products and registration of homeopathic and traditional herbal products

Article 42. The requirements relating to the dossier data and documentation according to Articles 27 - 32, Article 35, paragraph 3, Article 36, paragraph 2, and Article 38 shall be laid dawn in a regulation of the minister of health.

Article 43. (1) Within 30 of the submission date of the documentation according to Articles 27-32, Article 35, paragraph 3, or according to Article 38, the BDA shall review the completeness of the parts of the dossier accompanying the application and their compliance with the requirements for granting a the marketing authorisation or the registration certificate according to this law.

(2) Where no incompleteness or discrepancies in the documentation according to paragraph 1 are established, the BDA shall, within the term according to paragraph 1 above, notify the applicant in writing that the documentation is valid. This notification shall state the date from which the time limit according to Article 44 shall start to run.

(3) Where incompleteness and/or discrepancies in the documentation according to paragraph 1 are established, the BDA shall notify the applicant in writing to submit additional information and/or present an oral or written explanation of the established incompleteness and discrepancies within 14 days of the notification date.

(4) Where the requirements according to paragraph 3 have not been satisfied within the said term, the BDA shall notify the applicant in writing that the application is invalid. In such case the BDA shall return the submitted documentation in 14 days period and shall refund 75 percent of the fee paid by the applicant.

(5) Where the requirements according to paragraph 3 have been satisfied within the said term, the BDA shall notify the applicant in writing that the documentation is valid stating in the notification the date from which the term according to Article 44 shall start to run.

Article 44. The procedure for granting marketing authorisation or registration certificate of a medicinal product shall start from the date indicated in the notification according to Article 43, paragraph 2, respectively Article 43, paragraph 5, and shall end within 210 days.

Article 45. (1) Where in the BDA has been submitted an application for marketing authorisation or registration of a medicinal product for which, according to Article 27, paragraph 1, point 18, there is information of a marketing authorization granted in a Member State, the BDA shall notify the applicant in writing to implement the procedure according to Article 74.

(2) Where in the BDA has been submitted an application for marketing authorisation or registration of a medicinal product for which, according to Article 27, paragraph 1, point 19,

there is information that the dossier of the same medicinal product is in a procedure of assessment in a Member State, the BDA shall not review the documentation according to Articles 27-32 or Article 35, paragraph 3, or according to Article 38 and shall notify the applicant in writing to implement the procedure according to Article 75.

(3) For the implementation of the provisions of paragraph 1 and 2, a medicinal product shall be deemed as the same as authorised in another Member State, or as a product in a procedure of assessment of the dossier in another Member State where both medicinal products:

1. have the same qualitative and quantitative composition with respect t the active substance(s) and are offered in the same pharmaceutical form, whereas admissible shall be differences in the excipients provided that this shall not affect the safety and efficacy, and where

2. belong to the same company or the application for the medicinal products is submitted by the same company or group of companies, or where the application for the medicinal products is submitted by persons who have concluded a license or other agreement or conduct joint activities relating to the placing on the market of the respective medicinal product in different Member States.

Article 46. (1) For the assessment of the documentation the BDA shall:

1. may conduct tests of the final product, intermediate product, or the starting materials of the medicinal product or forward these for tests in a laboratory in a Member State belonging to the system of official medicines control laboratories in order to establish whether the control methods of analysis used by the manufacturer and described in the dossier comply with the requirements;

2. confirm, following inspection on the spot or by documents, whether the manufacturers of medicinal products from third states conduct the manufacture in compliance with the data set out in Article 27, paragraph 1, point 7, and/or conduct the control in compliance with the methods set out in Article 27, paragraph 1, point 8;

3. inspect the manufacturing site indicated in the application where the manufacturer(s) has, by way of exception, assigned to another manufacturer to conduct certain stages of the manufacture or control of the medicinal product.

(2) Where the BDA conducts an inspection on the spot of a manufacturing site, the term according to Article 44 shall cease to run until the establishment of a report of the results of the inspection.

(3) In the cases according to paragraph 1, points 2 and 3, the manufacturers shall pay a fee in amount, determined in the tariff according to Article 21, paragraph 2.

Article 47. (1) To the executive director of the BDA with the statute of consulting authorities shall be established following specialized committees

1. Committee for medicinal products;

2. Committee for immunological medicinal products;

3. Committee for homeopathic medicinal products;

4. Committee for herbal medicinal products;

5. Committee for radiopharmaceuticals.

(2) In case of necessity, the executive director of the BDA may also establish specialized committees other than those mentioned in paragraph 1.

(3) The specialized committees shall involve medical and other specialists with scientific achievements and practical experience in the respective fields of application of the medicinal products.

(4) External specialists with scientific achievements and practical experience in the field of a specific group of medicinal products may be involved in the standing staff of the committees.

(5) The executive director of the BDA shall appoint by an order the composition of the committees for a period of three years, the amount of their remuneration and shall approve a regulation on the conditions and order of their work.

(6) Not later than 30 January of each year, the executive director of the BDA shall approve lists of the experts outside the composition of the committees according to paragraph 1 after receiving the approval of the minister of health.

(7) The executive director of the BDA may ahead of term dismiss a member of a specialized committee on his own request, in case of failure to fulfil his obligations for a period of more than three months, or in case of unconscious conduct of his functions.

(8) The composition of the committees and the list of experts according to paragraph 6 shall be published on the internet site of the BDA.

Article 48. (1) The members of the specialized committees according to Article 47, paragraph 1, and the experts according to Article 47, paragraph 4, shall sign a declaration to the effect of their obligation:

1. not to disclose data and circumstances, which have become known to them during or on the occasion of the conduct of their activities;

2. not to be involved in activities associated with the manufacture of or wholesale or retail trade in medicinal products.

(2) In case the persons according to paragraph 1 have been involved in the stages or preparation of the documentation necessary for the marketing authorization of a medicinal product, they shall not participate in the sessions of the respective specialized committee according to Article 47.

(3) The persons according to paragraph 1 shall not vote during making of a decision on issues in which they or members of their families have commercial, financial, or other interests.

Article 49. (1) Within 200 days from the receipt of a valid documentation, the BDA, jointly with the respective committee according to Article 47, shall assess the quality, safety, and efficacy of the medicinal product and shall establish an assessment report, which shall be submitted to the executive director of the Agency. The assessment report shall be updated upon receipt of new information relating to the quality, safety and efficacy of the product.

(2) Where a medicinal product contains genetically modified organisms, the BDA shall submit to the Ministry of Environment and Waters the necessary documentation of the dossier of the medicinal product and request an opinion with respect to the potential risk to the environment established within 60 days. The sixty-day period shall be within the frames of the period according to paragraph 1.

(3) In the cases of radiopharmaceuticals, the BDA shall submit the necessary documentation of the dossier of the medicinal product to the Nuclear Regulatory Agency request an opinion with respect to the quality and safety of the product established within 60 days. The sixty-day period shall be within the frames of the period according to paragraph 1.

(4) Where the Ministry of Environment and the Nuclear Regulatory Agency do not pass a judgment within the terms according to paragraphs 2 and 3, it shall be presumed that their opinion is positive.

Article 50. (1) Where the BDA establishes incompliance of the dossier with the requirements for granting marketing authorisation or registration certificate according to this

law, it shall notify the applicant in writing to submit additional information associated with the documentation according to Articles 27-32 or according to Article 35, paragraph 3, or according to Article 38, and or to present an oral or written explanation of the established incompleteness and discrepancies within 180 days of the notification date.

(2) In the cases according to paragraph 1, the term according to Article 44 shall cease to run as from the notification date until the presentation of the requested information.

(3) The executive director of the BDA shall terminate the procedure for granting a marketing authorisation or authorisation for registration of a medicinal product where:

1. the applicant has not submitted the information according to paragraph 1 within the required time limit;

2. the persons according to Article 26, paragraph 1, request its termination in writing.

Article 51. Within 10 days of the establishment of the assessment report according to Article 49, paragraph 1, the executive director of the BDA shall issue a marketing authorisation/registration certificate of the medicinal product or make a motivated refusal.

Article 52. (1) Within 5 days of granting, the marketing authorisation/registration certificate shall be inscribed in the register according to Article 19, paragraph 1, point 3, which shall contain:

1. registration number;

2. number and date of the marketing authorisation/registration certificate of the medicinal product;

3. name of the medicinal product;

4. international non-proprietary name of any active substance;

5. name and address of the holder of the marketing authorization/registration certificate;

6. date of variation of the marketing authorisation/registration certificate;

7. date of termination of the marketing authorisation/registration certificate;

8. other data.

(2) The marketing authorisation/registration certificate of the medicinal product shall be delivered to the person according to Article 26, paragraph 1, and shall enter into effect as from the date of its inscription in the register according to Article 19, paragraph 1, point 3.

Article 53. (1) The BDA shall publish on its internet site data according to Article 52 for the marketing authorisation of the medicinal product granted and the approved summary of product characteristics within 14 days of the granting thereof.

(2) On the grounds of the assessment report according to Article 49, paragraph 1, the BDA shall establish a public assessment report including the motives of the decision taken without the data representing commercial secret. The assessment report shall be published on the internet site of the BDA.

Article 54. (1) The holder of a marketing authorization/registration certificate of a medicinal product shall notify the BDA in writing about the date on which the medicinal product is to be placed on the market.

(2) The holder of a marketing authorization/registration certificate of a medicinal product shall notify the BDA in writing about any discontinuation of the sales of the medicinal product irrespective temporary or permanent.

(3) In case of a planned discontinuation of the sales of the medicinal product, the holder of a marketing authorization/registration certificate of a medicinal product shall notify the BDA in writing at least two months in advance.

(4) In case of discontinuation of the sales of a medicinal product as a result of unforeseen circumstances, the holder of a marketing authorization/registration certificate of a medicinal product shall notify the BDA in writing within 24 of the establishment of the circumstances.

Article 55. (1) The marketing authorisation/registration certificate of a medicinal product shall be issued by the executive director of the BDA for a period of 5 years.

(2) Upon expiration of the period according to paragraph 1, the marketing authorisation/registration certificate of the medicinal product may be renewed by the BDA on the basis of an assessment of the benefit/risk ratio.

(3) In the case according to paragraph 2, the holder of a marketing authorisation/registration certificate shall submit to the BDA renewal application accompanied by a summarised dossier relating to the quality, safety, and efficacy the medicinal product including the variations thereof effected during the validity period according to paragraph 1 within 6 months prior to the expiration of the period.

(4) The marketing authorisation/registration certificate shall become timeless upon its renewal.

(5) In the presence of well-grounded reasons associated with the safety of the product, the BDA may request the holder of a marketing authorization/registration certificate to submit a renewal application under the terms of paragraph 3 for another 5 years.

(6) Upon expiration of the term of the marketing authorisation, the medicinal product may be sold until the quantities available in this country are exhausted but for not more than one year of the expiration of the marketing authorisation.

(7) The executive director of The BDA shall revoke by an order the marketing authorisation of a medicinal product provided that:

1. the holder has not placed the medicinal product on the market within three years from the date of granting the marketing authorisation or

2. the sales of the medicinal product have been discontinued for a period of 3 consecutive years after its placing on the Bulgarian market.

(8) The order according to paragraph 7 shall be subject to appeal under the terms of the Administrative procedure code.

(9) By way of exception and in the interest of the public health, the provision of paragraph 7 may not be applied provided that the marketing authorization holder of the medicinal product shall indicate well-grounded reasons. In these cases the executive director of the BDA shall motivate his decision.

(10) The holder of a marketing authorisation shall annually pay a fee as laid down in the tariff according to Article 21, paragraph 2, for the maintenance of the granted marketing authorisation.

Article 56. (1) By way of exception, upon indicating objective reasons and presentation of relevant evidence, the executive director of the BDA may grant a conditional marketing authorisation after consultation with the applicant.

(2) The type and scope of the conditions according to paragraph 1 and the period for the implementation thereof shall be determined in annexes to the granted marketing authorisation/registration certificate.

(3) The marketing authorisation in the cases according to paragraph 1 shall be granted for a period of one year and shall be renewed for any consecutive year on the basis of an assessment of the BDA of the satisfaction of the conditions according to paragraph 2.

(4) The conditions according to paragraph 2 and the periods for the implementation thereof shall be published on the internet site of the BDA.

(5) The executive director of the BDA shall revoke the marketing authorisation provided that the conditions under which the authorization has been granted have not been satisfied within the terms according to paragraph 2.

Article 57. (1) The executive director of The BDA shall refuse to grant a marketing authorisation or registration certificate of a medicinal product where, after assessment of the dossier according to Articles 27 – 32, it shall be established that:

1. the benefit/risk ratio is unfavourable or

2. the efficacy of the medicinal product has not been convincingly defended by he applicant, or

3. the qualitative and quantitative composition of the medicinal product does not comply with those described in the dossier.

(2) The executive director of The BDA shall refuse to grant a marketing authorisation/registration certificate of medicinal product where certain data in the dossier do not comply with the requirements of Articles 27 - 32.

(3) The executive director of The BDA shall refuse registration of a traditional herbal medicinal product where, after assessment of the documentation, it shall be established that the product does not comply with the conditions according to Article 37, paragraph 1, the data in the dossier do not comply with Article 38, or:

1. the qualitative and quantitative composition does not comply with those described in the dossier;

2. the medicinal product can be noxious at correct use;

3. the data for the traditional use are insufficient, especially where the pharmacological properties or the efficacy are not proven on the basis long-standing use and the experience acquired;

4. the pharmaceutical quality of the medicinal product is insufficiently grounded.

Article 58. The marketing authorization holder takes the responsibility for the completeness and authenticity of the data in the dossier.

Article 59. (1) The refusal of the executive director of the BDA to grant a marketing authorisation/registration certificate of a medicinal product may be appealed under the terms of the Administrative procedure code.

(2) The refusal of the executive director of the BDA and the motives thereof shall be published on the internet site of the Agency.

Section VI
Variations in a granted marketing authorisation

Article 60. (1) The marketing authorisation holder of a medicinal product shall be obliged to immediately notify the BDA about any change in the conditions under which the marketing authorization has been granted.

(2) Variations may be minor – type IA and type IB, or major – type II.

(3) The criteria according to which the variations are classified as type IA or type IB shall be paid down in the regulation according to Article 42.

(4) Any variation, which is not type IA or type IB, shall be major variations type II.

Article 61. (1) In case of variations type IA or type IB type II the person according to Article 26, paragraph 1 shall submit to the BDA an application accompanied by:

1. documentation associated with the variations as laid down in the regulation according to Article 42;

2. a document for paid fee as laid down in the tariff according to Article 21, paragraph 2.

(2) The application according to paragraph 1 shall also include a proposal of the date wherefrom the variations are to come into effect.

(3) The marketing authorization holder of a medicinal product shall submit a separate application for any variation type IA or type IB or type II.

(4) Where the marketing authorization holder of a medicinal product makes more than one variation in the granted marketing authorisation, he shall submit a separate application for each variation, indicating data about the type of variations for which the other applications are submitted.

(5) Where the variation applied for leads to subsequent interrelated variations of the same type, the marketing authorization holder of the medicinal product shall submit a single common application indicating the relationship between the basic variation and related variations.

(6) Where the variation type IB applied for leads to subsequent interrelated variations type IA or type IB, the marketing authorization holder of the medicinal product shall submit a single common application type IB indicating the relationship between the basic and related variations.

(7) Where the variation leads to change in the data contained in the summary of product characteristics, the packaging, and/or package leaflet, these changes shall be regarded as a part of the variation applied for and no separate application shall be submitted accordingly.

Article 62. (1) The executive director of the BDA shall approve the variations type IA within 14 days from the submission of the application provided that the requirements of Article 60, paragraph 3, and Article 61 are complied with.

(2) If the requirements of Articles 60 and 61 have not been complied with, the BDA shall notify the applicant that the application is invalid and the variations are not accepted within the term according to paragraph 1.

Article 63. (1) The executive director of the BDA shall approve the variations type IB within 30 days from the submission of the application stating the date of coming into force of the said variation.

(2) Where the BDA establishes discrepancies between the submitted documentation and the requirements according to Article 61, paragraph 1, point 1, it shall notify the marketing authorization holder.

(3) The marketing authorization holder shall amend or supplement the documentation within 30 days from the date of receipt of the notification. In this case the term according to paragraph 1 shall cease to run.

(4) Where the marketing authorization holder of the medicinal product fails to submit the requested information within the term according to paragraph 3, the executive director of the

BDA shall terminate the procedure and shall notify the marketing authorization holder accordingly.

Article 64. (1) The BDA shall establish an assessment report within 60 days of the date of submission of a valid application for variation type II.

(2) The term according to paragraph 1 may be:

1. decreased in cases of emergency, which are associated with the safe use of the medicinal product or

2. extended up to 120 days in case of a variation amending or supplementing a therapeutic indication.

(3) Where the BDA establishes incompatibilities between the submitted documentation and the requirements of Article 61, paragraph 1, point 1, it shall notify the marketing authorization holder and shall set out a term for the provision of the additional information.

(4) In the cases according to paragraph 3 the term according to paragraph 1 shall cease to run until provision of additional information.

(5) The executive director of the BDA shall approve the variations in the marketing authorisation and grant a variation authorisation or make a motivated refusal on the basis of the assessment report. This authorisation shall also state the date wherefrom these variations shall come into force.

(6) The refusal, pursuant to paragraph 5 of the executive director shall be subject to appeal under the terms of the Administrative procedure code.

Article 65. (1) Where the marketing authorization holder has established a risk for the health from the use of the medicinal product, he shall undertake urgent limiting measures and shall immediately notify the BDA in writing.

(2) The BDA shall pass a judgment regarding the measures within 24 hours of the notification.

(3) Where the BDA has not passed a judgment within the term according to paragraph 2, it shall be presumed that the measures have been approved.

(4) Where the BDA has established that there is a risk for the health of the population from the use of medicinal product, it shall order the marketing authorization holder to immediately undertake limiting measures.

(5) In the cases according to paragraphs 1 and 4, the marketing authorization holder of the medicinal product shall coordinate the method and term of implementation of the undertaken measures with the BDA.

(6) Marketing authorization holder of the medicinal product shall submit to the executive director of The BDA a variation application under the terms Article 64 not later than 15 from the date undertaking the measures.

Article 66. (1) The holder of the marketing authorisation of a medicinal product shall submit an application for enlargement of the scope of the granted marketing authorisation in case of:

1. a variation in the quality of the active substance indicated in the dossier, which does not essentially change the safety and efficacy characteristics of the medicinal product, and the changed substance is not defined as new:

a) substitution of the medicinal substance(s) with another salt/complex of esters/derivatives (with the same therapeutic part);

b) substitution with another isomer, another mixture of isomers, or a mixture with an isolated isomer;

c) substitution of a biological active substance or of a biotechnological product with a substance or a product with slightly changed molecular structure; modification of the vector used for obtaining the antigenic/starting material including a new primary cell bank of a different source;

d) a new ligand or binding mechanism in case of radiopharmaceuticals;

e) a change of the extracting solvent or in the ratio medicinal herbal substance/herbal preparation;

2. a change in the bioavailability;

3. a change in the pharmacokinetics as a change in the release rate;

4. a change or addition of a new quantity/activity of the active substance;

5. a change or addition of a new pharmaceutical form;

6. a change or addition of a new method of administration – in case of parenteral use it shall be necessary to make a distinction between intraarterial, intravenous, intramuscular, subcutaneous, or other methods of administration.

(2) The application according to paragraph 1 shall be accompanied by the documentation according to Article 27, paragraph 1, point 10, associated with variations according to paragraph 1.

(3) The requirements to the documentation according to paragraph 2 shall be laid down in the regulation according to Article 42.

(4) The name of the medicinal product in the granted authorization for enlargement of the scope of the initial marketing authorisation shall not be changed.

(5) The granting of an authorization for enlargement of the scope of a granted marketing authorisation of a medicinal product shall be performed under the conditions and under the terms of Articles 49 - 51.

Article 67. (1) The marketing authorization holder of a medicinal product shall submit an application for granting a new marketing authorisation in case of:

1. addition or deletion of one or more active substances including antigenic components in case of vaccines;

2. change in the quality of the active substance indicated in the dossier, which essentially changes the safety and efficacy characteristics of the medicinal product, and the changed substance is defined as a new one;

3. addition of a new or change in an existing therapeutic, prophylactic, or diagnostic indication in another therapeutic field.

(2) The application shall be accompanied by the documentation laid down in the regulation according to Article 42.

(3) The procedure according to Articles 49 – 51 shall be applied in the cases according to paragraph 1.

Article 68. (1) The holder of the marketing authorisation of a medicinal product shall be obliged to immediately notify the BDA about:

1. any new information, which may affect the benefit/risk ratio and necessitate variation in the data according to Article 27 - 32 and in the summary of product characteristics;

2. any ban or limitation imposed by regulatory authorities of other states where the medicinal product is sold as well as the reasons standing behind those measures.

(2) The marketing authorization holder shall be obliged to submit to the BDA upon request the following:

1. data in support of the positive benefit/risk ratio of the medicinal product;

2. data associated with the sales volume of the medicinal product and data derived from the issued medical prescriptions for the product, if any available.

Article 69. (1) The marketing authorisation holder of a vaccine or immunological medicinal product designated for immunization shall be obliged to submit to the BDA the following prior to the placing of any batch of the product on the market:

1. a sample of the finished product and/or a sample of the bulk/not finalised product;

2. protocols of the manufacturing and quality control;

3. document for paid fee as paid down in the tariff according to Article 21, paragraph 2.

(2) The marketing authorization holder of new immunological medicinal products or immunological medicinal products manufactured by new or altered technologies or by technologies, which are new for a given manufacturer, shall fulfil the obligations according to paragraph 1 for a defined period set out in the marketing authorisation.

(3) Within 60 days from the date of submission of the full set of documents, the BDA shall perform an assessment of the manufacturing and quality control protocols of live vaccines, immunological, and new immunological medicinal products and tests of the provided samples in an accredited laboratory in order to establish whether the medicinal products according to paragraphs 1 and 2 are manufactured in compliance with the approved specifications.

(4) In case of a positive result from the tests, the BDA shall issue a batch release certificate.

(5) The conditions and order, as well as the requirements to the documentation for granting a batch release certificate for the products according to paragraph 1 и 2 shall be laid down in the regulation of the minister of health.

(6) Where the assessment and tests according to paragraph 3 of the respective batch of medicinal products have been conducted in an official laboratory for control of medicinal products in another Member State, the marketing authorization holder shall submit to the BDA the medicinal products batch release certificate issued by the regulatory bogy of the Member State.

(7) In the cases according to paragraph 6 the BDA shall not conduct the activities according to paragraphs 3 and 4.

Article 70. (1) Prior to the placement on the market of each batch of the product the marketing authorisation of a medicinal product obtained from human blood or human plasma shall submit to the BDA the following:

1. a sample of the finished product and/or a sample of the bulk/ unfinished product;

2. manufacturing and quality control protocols;

3. document for paid fee as laid down in the tariff according to Article 21, paragraph 2.

(2) Within 60 days of the submission of the full set of documents, the BDA shall perform an assessment of the manufacturing and control protocols of the medicinal product obtained from human blood or human plasma and tests of the submitted samples in an accredited laboratory in order to establish whether the medicinal product according to paragraph 1 is manufactured in compliance with the approved specifications.

(3) In case of a positive result from the tests, the BDA shall issue a batch release certificate.

(4) The conditions and order, as well as the requirements to the documentation for granting a batch release certificate for the products according to paragraph 1 shall be laid down in the regulation according to Article 69, paragraph 5.

(5) Where the assessment and tests according to paragraph 2 of the respective batch of medicinal products have been conducted in an official laboratory for control of medicinal products in another Member State, the marketing authorization holder shall submit to the BDA the medicinal products batch release certificate issued by the regulatory authority of the Member State for the respective batch of the medicinal product.

(6) In the cases according to paragraph 6 the BDA shall not conduct the activities according to paragraphs 2 and 3.

Article 71. (1) The marketing authorisation holder shall be obliged to maintain a system for blocking and recall of medicinal products, which do not comply with the requirements relating to quality, safety, and efficacy.

(2) The marketing authorisation holder shall be obliged to block and recall of medicinal products, which do not comply with the requirements relating to quality, safety, and efficacy under the terms in the regulation pursuant to Article 274, paragraph 1.

Article 72. (1) The marketing authorisation holder of the medicinal product shall be obliged to update the data according to Article 27, paragraph 1, points 7 and 8 in compliance with the changes in the commonly accepted methods as a result of science and technology progress.

(2) The changes according to paragraph 1 shall be approved by the executive director of BDA under the terms of this section.

Article 73. (1) The marketing authorization holder may assign the rights over the marketing authorisation of a medicinal product to another legal person or to unions, which are not legal persons established on the territory of the Member States.

(2) The marketing authorization holder shall submit to the BDA an application appending the documentation laid down in the regulation according to Article 42 indicating a proposal for the date of assignment.

(3) In case of establishing incompleteness in the documentation according to paragraph 2, the BDA shall notify the marketing authorization holder in writing to, within 30 days, submit the necessary additional information. The term according to paragraph 5 shall cease to run as from the notification date until submission of the requested information.

(4) if the marketing authorization holder does not supplement the documentation within the term according to paragraph 3, the procedure of assignment of the marketing authorisation of the medicinal product shall be terminated.

(5) Within 30 days from the date of submission of the application according to paragraph 2, the executive director of the BDA shall issue an authorisation for variation for the transfer. In the variation approval of the assignment stating explicitly the date of assignment of the marketing authorisation is pointed out.

(6) The holder of the marketing authorisation shall wholly assume the rights and obligations of the former marketing authorisation holder.

(7) By the transfer of the marketing authorisation of the medicinal product pursuant to the order of paragraph 1-6 the time limit shall remain unchanged.

Section VII
Mutual recognition procedure and decentralized procedure

Article 74. (1) Where the person according to Article 26, paragraph 1, has a granted marketing authorisation in another Member State for the same product within the meaning of Article 45, paragraph 3, for which this person has submitted an application for marketing authorisation to the BDA, this person shall submit a request to the regulatory authority of the state indicated in the application, hereinafter referred to as "Reference Member State", to establish an assessment report or update the existing one.

(2) Together with the application, the person according to paragraph 1 shall submit to the BDA a dossier identical to the one submitted in the reference Member State and in the other Member States indicated in the application, hereinafter referred to as "Concerned Member States".

(3) The BDA and the applicant shall officially receive the assessment report together by the approved summary of product characteristics and the approved packaging mock-up and package leaflet from the regulatory authority of the Reference Member State according to paragraph 1.

(4) The BDA shall review the documents according to paragraph 3 and inform the reference Member State for the decision taken in writing within 90 days from the date of receipt thereof.

(5) Within 30 days of the receipt of a notification for the accomplishment of the procedure from the part of the Reference Member State, the executive director of the BDA shall issue a marketing authorisation of the medicinal product for the territory of the Republic of Bulgaria with the approved summary of product characteristics, packaging mock-up, and package leaflet.

Article 75. (1) Where the person according to Article 26, paragraph 1 submits simultaneously to the BDA and in other Member States an application for marketing authorisation of a medicinal product for which there is a granted marketing authorisation on the territory of a Member State, this person shall indicate in the application the regulatory authority of the Member State, hereinafter referred to as "reference member state", which shall establish a draft assessment report, a draft summary of product characteristics and packaging mock-up and package leaflet.

(2) Together with the application the person according to paragraph 1 shall submit to the BDA a dossier identical to the one submitted in all other Member States indicated in the application, hereinafter referred to as "states concerned".

(3) The BDA and the applicant shall officially receive from the regulatory authority of the Reference Member State the draft assessment report, draft summary of product characteristics and draft packaging mock-up and packaging leaflet.

(4) The BDA shall review the documents according to paragraph 3 and inform the Reference Member State for the decision taken in writing within 90 days from the date of receipt thereof.

(5) Within 30 days of the receipt of a notification for the accomplishment of the procedure from the part of the Reference Member State, the executive director of the BDA shall issue a marketing authorisation of the medicinal product for the territory of the Republic of Bulgaria with the approved summary of product characteristics, packaging mock-up, and patient leaflet.

Article 76. (1) Where the Republic of Bulgaria is a Reference Member State according to Article 74, the BDA shall:

1. forward the assessment report accompanied by the approved summary of product characteristics and the approved packaging mock-up and package leaflet within 90 days from the submission of a valid documentation;

2. close the procedure and notify the applicant and the Concerned Member States provided that all Concerned Member States have approved it.

(2) Within 30 days of the closure of the procedure according to paragraph 1, point 2, the executive director of the BDA shall issue a marketing authorisation of the medicinal product for the territory of the Republic of Bulgaria with the approved summary of product characteristics, packaging mock-up, and package leaflet.

(3) Where The Republic of Bulgaria is a reference Member State according to Article 75, the BDA shall:

1. submit to the regulatory authorities of the Concerned Member States and the applicant the draft assessment report, draft summary of product characteristics, and draft packaging mock-up and packaging leaflet within 120 days from the submission date of a valid documentation;

2. close the procedure and notify the applicant and the Concerned Member States provided that all Concerned Member States have approved it.

(4) Within 30 days of the closure of the procedure according to paragraph 3, point 2, the executive director of the BDA shall issue a marketing authorisation of the medicinal product for the territory of the Republic of Bulgaria with the approved summary of product characteristics, packaging mock-up, and package leaflet.

Article 77. (1) Where the BDA disapproves the submitted documentation according to Article 74, paragraph 4 or according to Article 75, paragraph 4, due to considerations of potential serious risk for the population health, it shall establish a detailed report with motives to the Referent Member State, the other Concerned Member States, and the applicant.

(2) Disputable issues according to paragraph 1 shall be considered by the Coordination Group to the European Medicines Agency. The applicant may present his position for consideration in writing or by word of mouth.

(3) The BDA shall participate in the sessions of the Coordination Group according to paragraph 2 until the closure of the procedure by the Reference Member State.

(4) The executive director of the BDA shall issue a marketing authorization of the medicinal product with the approved summary of product characteristics, packaging mock-up, and package leaflet within 30 days from the receipt of a notification for the closure of the procedure by the Reference Member State.

Article 78. (1) Where the Member States do not reach agreement before the Coordination Group, pursuant to Article 22, paragraph 2, the disputable issues shall be considered by the Committee for Medicinal Products for Human Medicine to the European Medicines Agency according to an arbitrage procedure. A copy of the documentation shall be forwarded to the applicant.

(2) The applicant shall submit to the European Medicines Agency the dossier of the medicinal product and the summary of product characteristics.

(3) In the cases according to paragraph 1, provided that the BDA has approved the assessment report, draft summary of product characteristics and packaging mock-up and package leaflet submitted by the Reference Member State, the executive director of the BDA may, upon a request of the applicant, grant a marketing authorisation of the medicinal product prior to the completion of the arbitrage procedure according to paragraph 1.

(4) After the accomplishment of the arbitrage procedure, the executive director of the BDA shall put the granted marketing authorisation according to paragraph 3 into effect in compliance with the decision of the European Commission.

Article 79. (1) Where the regulatory authorities of one or several Member States have made different decisions with respect to the marketing authorisation of the same medicinal product or with respect to its temporary suspension or revocation, the BDA or the applicant/marketing authorization holder may refer the issue to the Committee on Medicinal products in Human Medicine to the European Medicines Agency for application of the arbitrage procedure. The Applicant or the marketing authorisation holder may apply the question to the Committee for Human Medicinal Products at the European Evaluation Agency for applying arbitration procedure upon its evaluation.

(2) Where the use of the product causes a threat to public health, the BDA or the applicant or marketing authorisation holder may refer the issue relating to the granting of a marketing authorisation of a definite medicinal product, its temporary suspension, cancellation of the authorization validity or variation in connection with information according to chapter VIII to the committee according to paragraph 1 for an arbitrage procedure.

(3) In the cases according to paragraph 1 and 2, the BDA or the applicant/marketing authorization holder of the medicinal product shall submit to the European Medicines Agency the whole available information on the respective issue.

(4) Depending on the decision of the European Commission after the accomplishment of the arbitrage procedure, the BDA shall, within 30 days of receipt of the notification:

1. grant or terminate the marketing authorisation or

2. request variations in the granted authorisation in order to achieve compliance with the decision of the European Commission.

(5) The BDA shall notify the European Commission and the European Medicines Agency for the issued deed according to paragraph 4.

Article 80. The conditions and order for effecting variations in authorisations granted according to shall be settled according to Regulation (EC) 1084/2003 of the European Commission.

Chapter Four

CLINICAL TRIALS

Section I
General provisions

Article 81. Clinical trials of medicinal products in human subjects can be conducted:

1. to reveal and confirm clinical, pharmacological, or pharmacodynamic effects of one or more study medicinal products;

2. to determine the adverse reactions to one or more study medicinal products;

3. to investigate the absorption, distribution, metabolism, and excretion of one or more study medicinal products and/or to establish their safety and/or efficacy.

Article 82. (1) Clinical trials in human subjects shall be conducted with observation of the basic principles for the protection of human rights and human dignity in any medico-biological study according to the Declaration of Helsinki.

(2) Any clinical test of medicinal products in human subjects including bioavailability and bioequivalence shall be planned, conducted, and reported in compliance with the principles of Good Clinical Practice and in accordance with the requirements of this law.

(3) The rules of Good Clinical Practice shall be laid down in a regulation issued by the minister of health.

Article 83. (1) The rights, safety, and health of the subjects in the clinical test shall be placed above the interests of science and society.

(2) The available preclinical and/or clinical data about the study medicinal product shall be sufficient to substantiate the conduct of a clinical test.

Article 84. (1) The clinical test shall be scientifically substantiated and clearly described in detail in the study protocol.

(2) During the development of the documentation and the conduct of the clinical test of a medicinal product, the contracting authority and the researcher shall take into account any available guidelines published by the European Commission and the European Medicines Agency, and the scientific committees thereto.

Article 85. (1) Any clinical test of a medicinal product in human subjects shall be conducted with observation of the required quality assurance procedures in any aspect of the clinical test.

(2) The whole information from a clinical test shall be recorded and kept in a manner ensuring its accurate reporting, interpretation, and confirmation with protection of the personal data of the subjects.

Article 86. (1) All persons conducting clinical trials shall possess the respective qualification, training, and experience to perform the study related tasks in compliance with rules for Good Clinical Practice.

(2) A clinical test of a medicinal product shall be conducted under the leadership of a medical doctor or a doctor of dental medicine with acknowledged medical specialty in the respective field and shall be familiar with the available preclinical and/or clinical data about the product and the study risks and procedures.

(3) During a clinical test, responsible for the medical care delivered to a study subject and for the medical decisions taken shall be a medical doctor or a doctor of dental medicine with adequate qualification.

Article 87. (1) A clinical test can only be conducted in hospital healthcare establishments, dispensaries and diagnostic-consulting centres that have received positive accreditation assessment of their overall activity and the activities performed in functionally differentiated structures of the healthcare establishment related with the clinical test in accordance with the Law on Healthcare Establishments.

(2) A clinical test can only be conducted in healthcare establishments which shall have an ethics committee established and inscribed in the register of the BDA in accordance with Article 103.

(3) The manager of the healthcare establishment, in which a clinical test of a medicinal product is to be conducted, shall give his/her consent as to the participation of the principal researcher in the study, as well as to the conduct of the study.

Article 88. (1) A clinical test in human subjects shall be conducted with:

1. medicinal products unauthorised for use in the Republic of Bulgaria;

2. medicinal products authorised for use in the Republic of Bulgaria where these are studied for an unauthorised indication, pharmaceutical form different from the authorised one, in a so far unstudied patient group, or for obtaining additional data.

(2) Medicinal products authorised for use in the Republic of Bulgaria within the meaning of paragraph 1 above shall be medicinal products that have received marketing authorisation under the terms of this law or under the terms of Regulation 726/2004 (EC) of the European Parliament and the Council.

Article 89. (1) A clinical test in human subjects shall be conducted with medicinal products, which are manufactured, maintained, and stored in compliance with the rules for Good Manufacturing Practice for medicinal products under development and research.

(2) The rules for Good Manufacturing Practice for medicinal products under development and research shall be laid down in the regulation according to Article 152.

(3) A medicinal product can be proposed for a clinical test where pharmacological and toxicological studies have been conducted in accordance with the requirements for Good Laboratory Practice.

Article 90. The clinical test can be started and conducted provided that:

1. the anticipated therapeutic benefits for the study subjects, for current and future patients and the benefits for the healthcare justify the foreseen risks;

2. the physical and mental immunity of the study subjects, their right of immunity of their private life and the right of personal data protection have been guaranteed pursuant to the Law on the Protection of Personal Data;

3. insurance or indemnity for covering researcher or contracting authority liability has been provided.

Article 91. The contracting authority and the principal researcher shall make insurance covering their liability for property or non-property damages to the study subjects caused in or on the occasion of the conduct of the clinical test.

Article 92. (1) The contracting authority shall be responsible in case of injury of the health or death caused by or in the occasion of the conduct of the clinical test where the clinical test has been conducted in compliance with the requirements and procedures of the study protocol as approved by the ethics committee.

(2) The principal researcher shall be responsible in case of injury of the health or death caused by or in the occasion of the conduct of the clinical test where the clinical test has not been conducted in compliance with the requirements and procedures of the study protocol as approved by the ethics committee.

Article 93. (1) Contracting authority of a clinical test shall be a person established on the territory of a Member State.

(2) Contracting authority and researcher can be the same person.

Article 94. The contracting authority shall gratuitously provide the study medicinal product(s) and any device required for the administration thereof.

Article 95. (1) The contracting authority shall develop the labelling of the study medicinal product in compliance with the rules for Good Manufacturing Practice for medicinal products under development and research.

(2) The requirements relating to the data on the packaging of medicinal products for a clinical test shall be determined by the regulation according to Article 170.

Article 96. (1) A clinical test with medicinal products shall only be allowed in a person who has:

1. been informed in a preliminary conversation with a physician member of the study team about the purposes, risks and inconveniences of the study and about the conditions in which it is to be conducted;

2. been informed about his/her right to withdraw from the study at any time without this having any negative consequences for him/her;

3. personally given written informed consent to participate having been familiarized of the essence, importance, consequences, and eventual risks of the clinical test.

(2) Where the person cannot write, the informed consent to participate in the clinical test shall be given by word of mouth in the presence of at least one independent witness who shall certify in writing that this subject has expressed informed consent to participate in the clinical test in person.

(3) The informed consent according to paragraph 1, point 3, and paragraph 2 can only be given by a capable person who understands the essence, importance, scope, consequences, and eventual risks of the clinical test. Informed consent to participate in a clinical test can be withdrawn at any time.

(4) The informed consent according to paragraph 1, point 3, of an incapable major person shall be given by his/her legal representative. The consent of the legal representative must represent the supposed will of the subject and can be withdrawn at any time without negative consequences for the subject.

(5) In the cases according to Article 162, paragraph 3 of the Law on Health, informed consent shall be given by the person appointed by the court.

(6) An incapable person shall be given information about the clinical test, eventual risks, and benefits in accordance with his/her capability to understand.

(7) The explicit will of an incapable major person to refuse to participate in or to withdraw from the clinical test at any time must be taken into consideration by the researcher or, in case of necessity, by the principal researcher.

Article 97. (1) A clinical test in a minor person shall be conducted after obtaining written informed consent by both subject's parents or guardians with observation of Article 96, paragraphs 1 and 3.

(2) Parents' or guardians' consent must represent the supposed will of the minor person and can be withdrawn at any time without negative consequences for the minor person.

(3) The express will of the minor person to participate or to at any time withdraw from the clinical test must be taken into consideration by the researcher or, in case of necessity, by the principal researcher.

(4) A clinical test in a minor person shall be conducted after obtaining written informed consent by both parents and the guardian in compliance of Article 96, paragraphs 1 and 3. Where one of the parents is unknown, deceased, or deprived of parental rights or such rights have not been delegated in case of divorce, the written informed consent shall be given by the parent who is exercising the parental rights.

(5) Minor's, parents' and guardian's' consent can be withdrawn at any time without negative consequences for the minor person.

(6) The express will of the minor person to at any time withdraw from the clinical test must be taken into consideration by the researcher or, in case of necessity, by the principal researcher.

(7) The minor or underage person shall be provided information about the clinical test and for the eventual risks and benefits in a manner understandable for that person by a physician with experience with minor or underage persons.

Article 98. Informed consent to participate in a clinical test shall not be required if immediate decision is imperative to save the patient's life or if at that moment it cannot be obtained. Decision shall be taken by at least two physicians who are not part of the study team.

Article 99. (1) In the course of the clinical test the study subject shall receive additional information by a person independent from the contracting authority upon request.

(2) The written information provided to the subjects in a clinical test of a medicinal product shall contain contact details of an independent person for additional information.

Section II
Clinical trials in vulnerable patient groups

Article 100. A clinical test in minor or underage persons can be undertaken provided that:

1. the study protocol has been approved by the respective ethics committee after discussion of the clinical, moral, and psycho-social aspects of childhood age in which at least two paediatricians have participated;

2. there is an anticipated direct benefit of the clinical test for the patient group, which is to be included;

3. the study is directly associated with the clinical condition from which the minor or underage person is suffering;

4. the study medicinal product is designated for the diagnosis, treatment, or prophylaxis of diseases, which are specific for minor or underage persons;

5. the study is designated to be conducted in minor or underage persons;

6. the study purpose is to check data obtained in clinical trials in persons who are capable of giving informed consent or of data obtained by other research methods;

7. the results obtained from clinical trials in adults and the interpretation thereof cannot be considered also valid for minor or underage persons;

8. the study is planned in a manner that pain, inconvenience, fear, and other disease-associated foreseeable risks are minimized and the risk threshold and physical pain degree have been determined in advance and shall be incessantly controlled throughout the clinical test;

9. the study has been planned and shall be conducted in compliance with the guidelines of the European Medicines Agency;

10. no financial or other incentives shall be given except compensations.

Article 101. (1) Clinical trials in the persons according to Article 96, paragraphs 4 and 5, who are not capable of giving informed consent, shall be conducted in compliance with the requirements of Article 90.

(2) Except for the requirements of paragraph 1, inclusion of major persons who are not capable of giving informed consent in clinical trials is permitted provided that:

1. the respective ethics committee with the participation of a specialist competent in the respective disease or in the patient group has approved the study protocol after discussion of the clinical, moral, and psycho-social aspects relating to the respective disease and patient group;

2. it can be anticipated that taking the medicinal product subject to research would result in benefits, which overweigh the risks or the risks are fully eliminated;

3. the study purpose is to check data obtained from clinical trials in persons who are capable of giving informed consent or of data obtained through other research methods;

4. the study is directly associated with a disease, which is life-threatening or resulting in disability, from which the major person who is not capable of giving informed consent is suffering;

5. the clinical trials are planned in such manner that pain, inconvenience, fear, and the other foreseeable risks associated with the disease are minimized and the risk threshold and physical pain degree have been determined in advance and shall be incessantly controlled throughout the clinical test;

6. no financial or other incentives shall be given except compensations.

Article 102. No clinical test with a medicinal product can be conducted in pregnant women or breastfeeding mothers except if the medicinal product is required for their treatment or cannot be tested in other patient groups.

Section III
Ethics committee

Article 103. (1) Ethics Committee for multicentre clinical trials shall be established to the minister of health the composition of which shall be determined by an order.

(2) Ethics committees shall be established at the healthcare establishments where clinical trials are to be conducted the composition of which shall be determined by an order of the manager of the healthcare establishment.

(3) The BDA shall maintain and keep a register of ethics committees.

(4) The register of healthcare establishments where ethics committees have been established shall be published on the internet site of the BDA.

Article 104. (1) The committees according to Article 103 paragraphs 1 and 2 shall be composed of 7 to 12 persons with qualification and experience to review and assess the scientific, medical, and ethic aspects of the proposed clinical test.

(2) The committees according to paragraph 1 shall include at least two persons of non-medical education, representatives of both genders, who are financially and administratively independent of the healthcare establishment where the clinical test is to be conducted.

(3) The committees according to paragraph 1 can involve external specialists for the needs of their work.

(4) In clinical trials in minor or underage persons the respective ethics committee at the healthcare establishment can involve external experts in order to facilitate its work.

Article 105. (1) The mandate of the ethics committee members shall have duration of 4 years.

(2) One half of the composition of the ethics committees shall be renewed every 2 years.

(3) A member of an ethics committee cannot be appointed in the same committee for more than two consecutive mandates.

Article 106. (1) The ethics committees according to Article 103, paragraphs 1 and 2, shall draw written standard operating procedures in compliance with the rules for Good Clinical Practice, which shall determine the conditions and order for their work within one month from its establishment.

(2) The standard operating procedures of the ethics committees shall be approved by the executive director of the BDA.

(3) The sessions of the ethics committees shall be held in camera. In case of necessity, the chairman of the ethics committee can invite the contracting authority or the principal researcher to participate.

(4) only members of ethics committees who do not participate in a particular clinical test and are administratively and financially independent of the contracting authority and the principal researcher can vote and participate in the discussion.

(5) To certify the circumstances according to paragraph 4, the members of the ethics committees shall sign declarations for conflict of interests.

Article 107. (1) Central Ethics Committee shall be established to the Council of Ministers.

(2) The Central Ethics Committee shall consist of 9 members, representatives of both genders and shall obligatorily include medical doctors, doctors of dental medicine, a psychologist, a theologian, and a lawyer.

(3) The composition of the committee shall be determined by a decision of the Council of Ministers according to a proposal of the minister of health for a period of 4 years.

(4) The Central Ethics Committee shall provide opinions on deontological and ethics issues in the field of clinical trials where it is approached by the ethics committees according to Article 103, paragraphs 1 and 2, the BDA, or by contracting authorities.

(5) The Central Ethics Committee shall carry out the methodical guidance with respect to the ethics committees according to Article 103, paragraphs 1 and 2.

(6) The sessions of the Central Ethics Committee shall be held in camera. In case of necessity, the chairman of the Central Ethics Committee can invite the contracting authority or the principal researcher to participate.

(7) The Council of Ministers, according to a proposal of the minister of health, shall determine the conditions and order for the work of the Central Ethics Committee by a regulation.

Article 108. (1) A member of the Central Ethics Committee cannot be appointed in the same committee for more than two consecutive mandates. The duration of a mandate shall be 4 years.

(2) Half of the composition of the Central Ethics Committee shall be renewed every 2 years.

Section IV
Authorisation to conduct a clinical test

Article 109. A clinical test can be started provided that the following conditions have been met:

1. the respective ethics committee has given a positive opinion and

2. the executive director of BDA has issued a written authorisation for the conduct thereof where one of the study medicinal products is either:

a) a medicinal product for gene therapy;

b) a medicinal product for somato-cellular therapy;

c) a medicinal product, which contains genetically modified organisms;

d) a high technology medicinal product described in the Annex to Regulation (EC) 726/2004 of the European Parliament and the Council;

e) a medicinal product, which contains biological substance(s) of human or animal origin or contains biological components of human or animal origin or the manufacturing process of which involves such components, or

3. the contracting authority has not been notified by the BDA in writing that the clinical test cannot be conducted within the time limit as set out by the law; for medicinal products outside those according to 2.

Article 110. (1) For obtaining opinion, the principal researcher or the coordinating researcher shall submit to the respective ethics committee according to Article 103 the following documentation:

1. administrative documentation;

2. subject information;

3. documentation about the study protocol;

4. documentation about the study medicinal product(s);

5. documentation about the technical requirements and about the staff;

6. data about the financing and administrative organization of the clinical test.

(2) The content, form, and requirements to the documentation according to paragraph 1 shall be determined in the regulation according to Article 82, paragraph 3.

Article 111. (1) The ethics committee shall establish an opinion taking into consideration the following:

1. importance of the clinical test;

2. positive assessment of the ratio between the anticipated benefits and risks according to Article 90, paragraph 1, and the motivation of the conclusions;

3. protocol of the clinical test;

4. to what extent the principal researcher and the study team are adequate for the conduct of the clinical test;

5. researcher's brochure;

6. availability of the required equipment and its adequate quality;

7. compliance and completeness of the written information, which is to be given, as well as the procedure for obtaining informed consent and the validity of the clinical test in human subjects incapable of giving informed consent in the cases according to Articles 100 and 101;

8. provided indemnity or recovery in case of injury or death, which could result from the clinical test;

9. insurance covering researcher or contracting authority liability;

10. where necessary, the conditions and order for remuneration or indemnification of study researchers and subjects and the elements of the contract between the contracting authority and the healthcare establishment;

11. conditions and order for subject recruitment.

(2) The ethics committee shall:

1. give positive opinion;

2.. refuse in a motivated manner, or

3. request amendment of a part of the documentation as a condition for obtaining a positive opinion.

Article 112. (1) Within 60 days from the submission of an application, the ethics committee shall pass resolution with an opinion, which shall be sent to the applicant and the BDA.

(2) Where the clinical test involves a medicinal product for gene therapy or somato-cellular therapy or a medicinal product containing genetically modified organisms, the time limit according to paragraph 1 shall be extended by 30 days.

(3) Where for the review of a clinical test involving a medicinal product for gene therapy or somato-0-cellular therapy or a medicinal product containing genetically modified organisms it shall be imperative to consult a specially established for the purpose expert committee by an order to the director of the BDA, the time limit for drawing an opinion shall be 180 days.

Article 113. (1) During assessment of the documentation, the ethics committee can once request additional written documentation from the applicant. The time limits according to Article 112 shall cease to run until submission of the requested documentation.

(2) The review procedure of the study shall be terminated if the applicant should not submit the additional documentation required by the committee within 30 days of the receipt of the request for additional information.

Article 114. (1) Where the clinical test is to be conducted in more than one centre on the territory of the Republic of Bulgaria, the application shall be submitted to the ethics committee for multicentre tests according to Article 103, paragraph 1.

(2) Where the clinical test is to be conducted in only one centre on the territory of the Republic of Bulgaria, the application can be submitted to the ethics committee according to Article 103, paragraph 1 or 2 at applicant's discretion.

(3) The opinion of the ethics committee according to Article 103, paragraph 1, shall be valid for all centres on the territory of the Republic of Bulgaria.

Article 115. (1) Where the opinion of the respective ethics committee according to Article 103 is negative, the applicant can appeal before the Central Ethics Committee within 90 days of the date of notification.

(2) Where the negative opinion of the respective ethics committee according to Article 103 is established without taking into consideration the opinion of the expert commission according to Article 112, paragraph 3, the contracting authority can, within 14 days of the date of notification, request in writing that the committee revise its opinion.

(3) The expert committee according to Article 112, paragraph 3, shall, within 60 days of the date of receipt of a written application of the applicant, pass a resolution on the negative opinion of the respective committee and can either challenge or support it, wherefore it shall notify the ethics committee in writing. The ethics committee shall take final decision and send it to the applicant.

(4) Where the expert commission according to Article 112, paragraph 3, supports the negative opinion, the contracting authority can, within 14 days of the date of notification, appeal against the decision before the Central Ethics Committee.

(5) The opinion of the Central Ethics Committee shall be final and binding on the respective ethics committee.

Article 116. (1) The applicant shall submit to the BDA an application after the pattern for the conduct of the clinical test.

(2) Where the applicant for the clinical test is not the contracting authority, the application shall be accompanied by documentation certifying that the person has been empowered by the contracting authority.

(3) Where the contracting authority has not been registered as a natural person or legal entity on the territory of Bulgaria, the application shall be accompanied by a document evidencing the data of his empowered representative on the territory of the Republic of Bulgaria.

(4) The following documents shall be appended to the application:

1. administrative documentation;

2. subject information;

3. documentation about the study protocol;

4. documentation about the study medicinal product(s);

5. documentation about the technical requirements and about the staff;

6. data about the financing and administrative organization of the clinical test.

(5) The content, form, and requirements to the documentation according to paragraph 1 shall be determined in the regulation according to Article 82, paragraph 3.

Article 117. (1) During assessment of the documentation, the BDA can once request additional written documentation from the applicant.

(2) The time limits according to Articles 118, 119, and 120 shall cease to run until submission of the requested documentation.

Article 118. (1) Within 60 days of the date of submission of an application for a clinical test of medicinal products according to Article 109, point 3, the BDA shall notify the applicant that:

1. the clinical test can be conducted on the territory of the Republic of Bulgaria or

2. the clinical test cannot be conducted indicating the reasons therefore.

(2) In the cases according to paragraph 1, point 2, the contracting authority can submit to the BDA an application amended in accordance with the motives set out or submit the required information in accordance with the requirements of the BDA within 30 days.

(3) Within 30 days of the submission of the amended application according to paragraph 2 or the additional information, the BDA shall notify the applicant in writing that:

1. the clinical test can be conducted on the territory of the Republic of Bulgaria or

2. that it refuses the conduct of the clinical test stating the reasons therefore.

(4) The refusal according to paragraph 3, point 2, shall be subject to appeal under the terms of the Administrative Procedure Code.

(5) The clinical test can be started provided that within the time limit according to paragraph 1 the BDA has not issued a notification with motives of disapproval of the clinical test.

(6) Provided that the applicant does not submit an application according to paragraph 2 within the stipulated time limit, the procedure shall be terminated and the clinical test shall no be conducted.

Article 119. (1) Within 60 days of the date of submission of an application for a clinical test with the medicinal products according to Article 109, point 2,, the executive director of the BDA shall:

1. issue authorisation for the conduct of the clinical test, or

2. issue a motivated refusal.

(2) The refusal according to paragraph 1, point 2, shall be subject to appeal under the terms of the Administrative procedure code.

Article 120. (1) In case of medicinal products according to Article 109, point 2, letters „a" - „c" the time limit according to Article 119, paragraph 1, for the issue of authorisation by the BDA for the conduct of a clinical test can be extended by 30 days.

(2) Provided that the BDA should consult the expert commission according to Article 112, paragraph 3, which is to assess the safety of the medicinal products according to paragraph 1, the extended time limit according to paragraph 1 can be extended by another 90 days.

Article 121. The executive director of the BDA shall refuse to issue authorisation for the conduct of a clinical test of medicinal products for gene therapy where there is a risk of modifying the genome of the reproductive cells of a study subject.

Article 122. (1) In case of a multicentre clinical test in the Republic of Bulgaria and in a third state, the BDA shall request the contracting authority to submit a declaration that he shall provide access to representatives of the BDA for inspection aimed at the establishment of compliance with the requirements and principles of Good Clinical Practice and Good Manufacturing Practice.

(2) Provided that the contracting authority should not submit the declaration according to paragraph 1, the BDA shall not review the submitted application.

Article 123. The contracting authority shall declare that the documentation submitted to the BDA and the ethics committee contains the same information.

Article 124. (1) The procedures in the ethics committee and in the BDA can be carried out simultaneously or consecutively at the discretion of the contracting authority.

(2) The time limit for documentation review according to Article 118, paragraph 1, shall not cease to run in case of lack of decision of the ethics committee.

Article 125. The clinical test shall be conducted in compliance with the study protocol, which has received positive opinion of the respective ethics committee according to Article 103 and under the conditions set out in the submitted documentation.

Section V
Amendments

Article 126. (1) The contracting authority can at any time make amendments in the study protocol different from the essential amendments according to Article 127, paragraph 2.

(2) In the cases according to paragraph 1 the contracting authority shall keep the documentation relating to the amendments and shall provide it to the BDA and the ethics committee upon request.

Article 127. (1) Amendment in the conduct of a clinical test can be required by the BDA wherever necessary to guarantee the safety of the subjects, the scientific value of the clinical test, and/or the observation of the rules for Good Clinical Practice.

(2) Essential amendment in the conduct of the clinical test shall be any amendment in the study protocol and/or in the information and the documentation according to Articles 110 and 116, which can affect:

1. the safety or the physical and mental immunity of the study subjects;
2. the scientific value of the clinical test;
3. the conduct or the organization of the clinical test;

4. the quality or the safety of any study medicinal products.

Article 128. (1) The contracting authority can also implement planned study essential protocol and documentation amendments according to Articles 110 and 116 wherever:

1. the ethics committee has given a written positive opinion;

2. the executive director of the BDA has issued a written authorisation as to clinical trials with medicinal products according to Article 109, point 2, or

3. the contracting authority has not been notified by the BDA about refusal of the proposed amendment in the clinical test with medicinal products according to Article 109, point 3.

(2) The provision of paragraph 1 shall not apply to changes in an approved protocol, which are imperative to protect the subjects from immediate threat in case of occurrence or new information associated with the conduct of the clinical test or the development of the study medicinal product.

(3) In the cases according to paragraph 2, the contracting authority shall immediately notify the ethics committee according to paragraph 1, point 1, and the BDA about the available new information, the measures taken, and the applied changes in the protocol.

Article 129. (1) While planning essential amendments to the clinical test and the documentation according to Articles 110 and 116, the applicant shall submit a formal written application to the BDA and the respective ethics committee.

(2) The application shall be accompanied by documentation, which is necessary for grounding the amendments and certifies that after the implementation of the amendment the assessment of the benefit/risk ratio according to Article 90, paragraph 1, shall remain unchanged.

(3) The requirements relating to the application and the documentation for the amendment shall be determined in the regulation according to Article 82, paragraph 3.

Article 130. (1) Within 35 days of receipt of an application for amendment, the ethics committee shall notify the contracting authority of its decision by issuing:

1. positive opinion on the requested amendment or

2. motivated refusal of the amendments in the clinical test.

(2) Within 35 days of the date of receipt of an application with positive opinion of the ethics committee, the BDA shall:

1 approve the amendments in a clinical test of medicinal products according to Article 109, point 2, or

2. disapprove the amendments with explicit motivation.

(3) Provided that within 35 days of the submission of the documentation for amendments in clinical trials of medicinal products according to Article 109, point 3, the applicant does not receive notification for disapproval of the amendment, the proposed amendments can be implemented.

Article 131. (1) In the cases according to Article 130, paragraph 2, point 2, the contracting authority can submit alteration of the proposed amendments consistent with the motives not later than 14 days prior to the implementation of the amendments.

(2) Within 14 days of the date of receipt of the amended documentation according to paragraph 1, the BDA shall issue and amendment of its authorisation for the clinical test of medicinal products according to Article 109, point 2, or shall issue a refusal, which shall not be subject to appeal.

(3) The refusal according to paragraph 2 shall not be subject to appeal.

Section VI
Cessation of the clinical test

Article 132. (1) The contracting authority or the researcher can undertake urgent measures to protect the study subjects from suddenly occurred risks for their safety and health.

(2) In the cases according to paragraph 1 the contracting authority shall immediately notify the BDA and the respective ethics committee about the undertaken actions and the reasons, which have raised these.

Article 133. (1) Where the clinical test is to be conducted under conditions different from those determined at the issue of the authorisation or there is information vitiating the scientific validity of the clinical test or the safety of the study subjects, the BDA can temporarily stop the conduct of the test or put a ban on it.

(2) The ban can be imposed for a specific centre or for all centres in a multicentre clinical test on the territory of the Republic of Bulgaria.

(3) In case of termination of the clinical test in all centres on the territory of the Republic of Bulgaria, the BDA shall, prior to undertaking actions according to paragraph 1, notify the contracting authority and the principal researcher or the coordinating researcher in writing.

(4) Within 7 days of the receipt of the notification the contracting authority and/or the principal researcher can express an opinion on the undertaken measures by the BDA.

(5) The provision of paragraph 3 shall not apply provided that there is an immediate threat for the health and safety of the study subjects.

Article 134. In the cases according to Article 133, paragraph 1, the BDA shall immediately notify the respective ethics committee, the regulatory bodies of the Member States, the European Medicines Agency, and the European Commission about the undertaken measures and the reasons therefore.

Section VII
Pharmacovigilance

Article 135. (1) The principal researcher shall immediately report in writing or by word of mouth any serious adverse event that has occurred in the course of the clinical test in a study subject at the centre he is responsible for.

(2) A detailed written report shall be submitted after the report according to paragraph 1.

(3) At the notification according to paragraph 1 and in the report according to paragraph 2 the study subject shall be identified by a unique code number as defined in the study protocol.

(4) The provisions of paragraphs 1 and 2 shall not apply provided that the protocol of the clinical test or the researcher's brochure explicitly states that there is no requirement for an urgent report of a specific serious adverse event.

(5) The researcher shall report to the contracting authority any adverse events or laboratory aberrations, which are defined in the study protocol as critical with respect to safety, within the timelines and format as required by the protocol.

Article 136. Where the outcome of an adverse event during the conduct of a clinical test is death, the researcher shall be obliged to submit to the contracting authority and the ethics committees any information requested additionally.

Article 137. The contracting authority shall keep detailed records of any serious adverse events provided to him by the researchers and shall present these upon request to the BDA or the regulatory bodies of the Member States where the clinical test is conducted in case of multicentre clinical test.

Article 138. (1) The contracting authority shall notify the BDA, the regulatory bodies of all Member States where the clinical test is conducted in case of a multicentre test, and the respective ethics committee of any suspected serious adverse drug reaction occurring in the course of the clinical test, which has resulted in death or has been life-threatening not later than 7 days of receipt of information thereof.

(2) The contracting authority shall provide the bodies according to paragraph 1 with additional information on the case within 8 days of the date of the notification sent.

(3) The contracting authority shall notify the bodies according to paragraph 1 of any other suspected unexpected serious drug reactions occurring in the course of the clinical test, which are different from those set out in paragraph 1, not later than 15 days from the date of receipt of the information for their occurrence.

Article 139. (1) The contracting authority can fulfil his obligations according to Article 138, paragraphs 1 and 3, by entering his reports in the European adverse drug reactions database.

(2) Where the clinical test is also conducted in countries outside the Member States and the European Economic Area, the contracting authority shall enter his reports of suspected unexpected serious adverse drug reactions in the European adverse drug reactions database.

(3) The format and content of the reports for adverse drug reactions shall be determined by the regulation according to Article 191, paragraph 1.

(4) The contracting authority shall inform the researchers conducting a clinical test with medicinal product about any suspected unexpected serious adverse drug reaction associated with the study medicinal product irrespective of its origin.

Article 140. (1) The contracting authority shall submit to the BDA and the respective ethics committee a list of all suspected serious adverse drug reactions occurring during the past period and a report about the safety of the study subjects once yearly.

(2) The format and content of the reports for adverse drug reactions shall be determined by the regulation according to Article 191.

Article 141. (1) The BDA shall document any information about suspected unexpected serious adverse drug reactions of the study medicinal products provided under the terms of Article 138, paragraphs 1 and 3.

(2) The BDA shall immediately enter the information according to paragraph 1 in the European adverse drug reactions database.

Section VIII
Notification of clinical test closure

Article 142. (1) The contracting authority shall notify in writing the BDA and the respective ethics committee of the closure of the clinical test on the territory of the Republic of Bulgaria.

(2) The notification shall be submitted within 90 days of the closure of the clinical test in a format as defined by the regulation according to Article 82, paragraph 3.

(3) Provided that nothing is otherwise stipulated in the protocol as approved by the respective ethics committee, the last subject visit shall be considered as end of study.

(4) Where the study is prematurely terminated, the contracting authority shall notify the BDA and the respective ethics committee within 15 days of taking such decision providing the reasons thereof.

Article 143. The contracting authority shall submit a final report of the clinical test to the BDA and the respective ethics committee.

Article 144. (1) The BDA shall enter data of any clinical test conducted on the territory of the Republic of Bulgaria in the European clinical trials database: application submitted, ethics committee decision, authorisation, essential amendments, end of study, and data of any audit conducted.

(2) Upon request by another Member State, the European Medicines Agency or the European Commission, the BDA shall provide additional information besides that entered in the European clinical trials database.

(3) During the fulfilment of its obligations according to paragraph 1, the BDA shall observe the published guidelines of the European Commission.

Section IX
Non-interventional study

Article 145. (1) A non-interventional study shall be conducted with medicinal products authorised for use in the Republic of Bulgaria where these are studied to obtain additional information about the product prescribed in the usual manner in compliance with the conditions determined in the marketing authorisation.

(2) The contracting authority shall submit to the respective ethics committee and the BDA documentation for the conduct of a non-interventional study as set out in the regulation according to Article 82, paragraph 3.

(3) A non-interventional study can be started provided that the candidate shall not receive an explicit refusal by the director of the BDA within one month of the date of submission of an application and the documents according to paragraph 22 with the BDA.

Chapter Five

AUTHORISATION FOR MANUFACTURING AND IMPORT OF MEDICINAL PRODUCTS

Section I
Manufacture

Article 146. (1) Within the meaning of this law manufacture of all types of medicinal products, active substances used as starting materials, and medicinal products intended for clinical trials can only be performed on the territory of the Republic of Bulgaria by natural or legal persons registered as traders on the territory of a Member State which have received manufacturing authorisation issued by the director of the BDA.

(2) Manufacturing authorisation shall also be required in the cases where the products according to paragraph 1 are intended for export only.

(3) Manufacturing authorisation shall also be required for persons who perform simultaneously of separately one of the following activities: packaging, retail packaging, repackaging, labelling of medicinal products, and medicinal products intended for clinical trials.

(4) Manufacturing authorisation shall also be required for persons who perform simultaneously or separately one of the following activities: complete or partial manufacture of active substances intended for the manufacture of medicinal products and various processes of packaging, retail packaging, repackaging, and re-labelling of active substances.

(5) No manufacturing authorisation shall be required where the processes of retail packaging, mixing, or packaging are performed according to magisterial or pharmacopoeia recipe in a pharmacy.

Article 147. The BDA shall send copies of the issued manufacturing authorisations according to Article 146 to the European Medicines Agency to be entered in the European Union database.

Article 148. To obtain manufacturing authorisation the person according to Article 146 must possess:

1. personnel with adequate qualification depending on the specificity of the manufactured types of medicinal products and pharmaceutical forms;
2. always at least one qualified person, who correspond to the condition of Article 159 at any time;
3. manufacturing, control, and storage facilities for the medicinal products equipped with the required technical equipment and control laboratories.

Article 149. The managers of manufacture and quality control of medicinal products in the manufacturing enterprises shall be:

1. persons with educational qualification master's degree in pharmacy, chemistry, or biology and at least two-year practical experience in the pharmaceutical manufacture;
2. for the manufacture of radiopharmaceuticals or medicinal products subjected to ionizing radiation – persons who comply with the requirements according to point 1 and have an additionally recognized specialty in radiobiology or radiochemistry.
3. for the manufacture of immunological medicinal products including vaccines, toxins, sera, biotechnological products, and medicinal products obtained from human plasma or human blood – persons with recognized speciality in medical haematology, medical microbiology, virology, or immunology.

Article 150. (1) The person according to Article 146 shall submit to the BDA a formal application as approved by the director of the Agency.

(2) Together with the application according to paragraph 1 the applicant shall also submit:

1. diploma, document for acquired speciality, document for length of service, certificate of clean court record, and employment contract for the persons according to Article 148, point 2, and Article 149;

2. copies of contracts of assignment of the manufacture and/or control of the products ordered for manufacture – in the cases according to Article 151;

3. actual certificate for entry in the trade register, respectively document for actual court registration;

4. list of the medicinal products, forms, and active substances, which will be manufactured;

5. schemes of the premises for the manufacture, control, and storage and a dossier of the manufacturing capacity;

6. assessment of the environmental impact during the manufacture of the medicinal products for the cases stipulated in the Law on the Protection of the Environment;

7. authorisation by the Nuclear Regulatory Agency where the application concerns manufacture of radiopharmaceuticals or medicinal products subjected to ionized radiation during their manufacture;

8. authorisation for the use of the premises for manufacture, control, and storage issued according to order of the Law on the Organization of the Territory or another substituting document;

9. conclusion of the regional inspectorate for the preservation and control of the environment after on the spot inspection;

10. document for paid fee, in amount determined in the tariff to Article 21, paragraph 2.

(3) For the manufacturing of narcotic substances and pharmaceutical forms containing such substances, the requirements of the Law on the Control of Narcotic Substances and Precursors shall be observed.

Article 151. Where some aspects of the stages of manufacture or control tests within the manufacturing process shall be carried in another site of the territory of Bulgaria or abroad under contract, the persons according to Article 146 shall be obliged to indicate the location of that site and a copy of the contract determining the responsibilities of the parties thereto with respect to the observation of the requirements of the Good Manufacturing Practice for medicinal products the obligations of the qualified person according to Article 148, point 2.

Article 152. The conditions for the issue of a manufacturing authorisation and the principles for the Good Manufacturing Practice for all types of medicinal products, medicinal products for clinical trials, and active substances shall be arranged by a regulation of the minister of health.

Article 153. (1) Upon receipt of an application according to Article 150, the BDA shall assess the submitted documentation and shall conduct inspection on the spot of the location of the sites for manufacture, control, and storage including the cases according to Article 151 to determine the compliance between the submitted documentation and the conditions for manufacture, control, and storage of the starting manufacturing materials and the finished medicinal products and their compliance with the requirements of the Good Manufacturing Practice.

(2) The expenses for the conduct of an on the spot inspection according to paragraph 1 shall be carried out at the expenses of the applicant.

(3) For conducting of on the spot inspection according to paragraph 1 the applicant shall pay a fee of the amount as laid down in the tariff under Article 21, paragraph 2.

Article 154. (1) Where the BDA finds omissions in the documentation submitted and/or inconsistencies between the content of the submitted documentation and the condition of

the site or the requirements for the qualification of the personnel, it shall notify the applicant in writing and give written instructions.

(2) In the cases according to paragraph 1 the time limit under Article 155, paragraph 1 shall cease to run until rendering the site or documentation in compliance with the requirements.

Article 155. (1) Within 90 days of the date of submission of the application according to Article 150, the executive director of the BDA shall:

1. issue manufacturing authorisation or

2. state it reasoned refusal.

(2) Manufacturing authorisation shall only be issued for medicinal products and forms, active substances, medicinal products intended for clinical trials, indicated in the application and for the premises where manufacture, control, and storage shall be carried out**.**

(3) The deeds according to paragraph 1 shall be delivered to the applicant.

(4) The manufacturing authorisation shall be timeless.

(5) The refusal according to paragraph 1, point 2, shall be subject to appeal according to order of the Administrative procedure code.

Article 156. (1) The manufacturing authorisation holder shall submit an application in case of change of:

1. the person according to Article 148, point 2;

2. the persons according to Article 149;

3. the manufacturing equipment;

4. the location or reorganisation of some of the sites for manufacture, control, and storage;

5. the manufacturing operations;

6. the manufactured active substances, medicinal products, and forms;

7. the court registration.

(2) the application according to paragraph 1 shall be accompanied by documents associated with the change, which as laid down in the regulation according to Article 152.

(3) The manufacturing authorisation shall be cancelled provided that its holder terminates his activity and he shall be obliged to notify the BDA accordingly.

Article 157. (1) When issuing the authorisation allowing the change, the provisions of Article 150 and 151 shall apply, whereas the time limit for issuing shall be:

1. 14 days - in the cases under Article 156, paragraph 1, points 1, 2 and 7 – up to 14 days;

2. 90 days in the cases under Article 156, paragraph 1, points 3**, 4, 5 and 6**

(2) Where the changes according to Article 156, paragraph 1, points 3, 4, 5 and 6 cannot be assessed according to documents, the BDA shall conduct on the spot inspection. In such cases the term according to paragraph 1, point 2, shall cease to run until the accomplishment of the inspection.

(3) The expenses for the conduct of the inspection on the spot according to paragraph 2 shall be for the account of the applicant.

(4) For the conduct of an inspection on the spot according to paragraph 2, the applicant shall pay a fee to the amount as laid down in the tariff according to Article 21, paragraph 2.

Article 158. (1) The BDA shall keep a register according to Article 19, paragraph 1, point 1, of the issued manufacturing authorisations, which shall contain:

1. number and date of the manufacturing authorisation;

2. name, place of business, and address of administration of the person who has been granted manufacturing authorisation;

3. address of the premises for the manufacture, control, and storage of the medicinal product;

4. the active substances, medicinal products, and forms for which the authorisation has been granted;

5. name of the person according to Article 148, point 2;

6. names of the persons according to Article 149;

7. date of deletion from the register of the manufacturing authorisation and the reason therefore.

(2) The data from the register of the issued manufacturing authorisations shall be published on the internet site of the BDA.

(3) Upon request of the European Commission or another regulatory body of a Member State, the BDA shall provide information for an issued manufacturing authorisation.

Article 159. (1) The manufacturing authorisation holder shall employ on a labour contract at least one qualified person according to Article 148, point 2, who shall be constantly at his disposal.

(2) The qualified person according to paragraph 1 must meet the following requirements:

1. to be a master of medicine, pharmacy, chemistry, biotechnology, or biology;

2. to have at least two-year practical experience in the pharmaceutical manufacture and in conducting qualitative and/or quantitative analysis of medicinal products and active substances;

(3) Where the manufacturing authorisation holder of a medicinal product complies with the requirements according to paragraph 2, he can perform the obligation of the qualified person.

(4) The qualified person shall issue a certificate for the release of each batch evidencing that the batch of the medicinal product has been manufactured and controlled in compliance with the requirements of the manufacturing authorisation according to order of this law.

(5) The qualified person shall issue a certificate of release each batch certifying that the batch of the medicinal product intended for clinical trials has been manufactured and controlled in compliance with the requirements for Good Manufacturing Practice, with the manufacturing dossier of the product, and the information submitted according to Article 110, paragraph 1, point 4.

(6) The qualified person shall keep a register of the issued release certificates for each batch of a medicinal product.

(7) The data from the register according to paragraph 6 shall be kept at least 5 years after the last entry and shall be provided to the control bodies upon request.

(8) In case of constitution of an administrative-penal procedure for violations committed during the execution of the obligations of the qualified person, the BDA shall order the manufacturing authorisation holder to temporarily dismiss the qualified person from the position.

(9) The criteria and requirements relating to the qualification and training of the persons according to Article 148, point 2, shall be laid down in the regulation according to Article 152.

Article 160. (1) The manufacturing authorisation holder shall:

1. ensure the performance of the manufacturing operations in compliance with the requirements of the Good Manufacturing Practice and in compliance with the information according to Article 27, paragraph 1, points 7 and 8 approved from the BDA, and in the cases of medicinal products for clinical trials – in compliance with the information according to Article 110, paragraph 1, point 4 submitted to the agency by the contracting authority.

2. use as starting materials only active substances, which have been manufactured in compliance with the requirements of the Good Manufacturing Practice;

3. ensure on a permanent basis qualified personnel for the production and control according to the requirements the regulation according to Article 152;

4. only dispose of medicinal products, which have marketing authorisation, respectively with medicinal products intended for clinical trials in compliance with the requirements of this law;

5. notify the control bodies about any change according to Article 156 in advance;

6. immediately notify the control bodies in case of substitution of the qualified person according to Article 148, point 2;

7. ensure access of the control bodies to the premises and the documentation at any time;

8. ensures to the qualified person according to Article 148, point 2 the required condition to fulfil his obligations.

(2) The manufacturing authorisation holder shall keep the samples of and the documentation for the manufactured medicinal products, active substances, and medicinal products intended for clinical trials under the conditions and under the terms laid down in the regulation according to Article 152.

(3) In case of a medicinal product intended for clinical trials, the manufacturing authorisation holder shall guarantee that all manufacturing operations shall be carried out in compliance with the information submitted by the contracting authority to the BDA in accordance with the regulation according to Article 82, paragraph 3.

(4) The documentation for any deal made shall be kept for 5 years and shall contain the date, description of the medicinal product, quantity delivered, consignee's name and address, and batch number.

(5) The manufacturing authorisation holder shall ensure and maintain a system for blocking and recall of medicinal products, which have shown discrepancies with the requirements relating to quality.

(6) The manufacturing authorisation holder shall be obliged to block and recall the medicinal products, which have shown discrepancies with the requirements relating to quality, efficacy, and safety under the terms of the regulation according to Article 274, paragraph 1.

(7) The manufacturing authorisation holder shall be obliged to update the manufacturing methods in compliance with the development of new technologies and the development of medicinal products for tests.

Section II

Import of medicinal products and active substances

Article 161. (1) Import on the territory of the Republic of Bulgaria from third country of medicinal products, active substances used as starting materials, and medicinal products intended for clinical trials from a third country within the meaning of this law can only be carried out by natural or legal persons registered as traders according to the legislation of the Member State who has been granted import authorisation issued by the executive director of the BDA.

(2) To obtain import authorisation, the person according to paragraph 1 must:

1. at any time dispose of at least one qualified person who meets the requirements of Article 159, paragraphs 2 and 9;

2. dispose of a quality control laboratory in compliance with the requirements of the regulation according to Article 152 and premises for the storage of the medicinal products, active substances and exipients and medicinal products for clinical trials having the required technical equipment in compliance with the requirements of the regulation according to Article 198.

Article 162. (1) To obtain import authorisation, the person according to Article 161, paragraph 1, shall submit to the BDA a formal application as approved by the executive director of the agency.

(2) The following documents shall be annexed to the application according to paragraph 1:

1. certificate of actual court registration, document for actual court registration respectively;

2. list of the active substances, the medicinal products and forms, which are to be imported;

3. copy of the manufacturing authorisation issued by the regulatory body of the exporting country;

4. documents certifying the circumstances according to Article 159, paragraphs 1 and 2 for the qualified person;

5. data about the address of the laboratory on the territory of the Republic of Bulgaria for the conduct of complete quantitative and qualitative analysis at least of the active substances and of any other tests and checks required to prove the quality of any imported batch of a medicinal product in compliance with the requirements of the marketing authorisation under the terms of this law and the address of the storage premises;

6. a contract, where the responsibilities of the parties are determined there to with respect to the observation of the principles of the Good Manufacturing Practice by the assignee and the method according to which the qualified person according to Article 161, paragraph 2, point 1, shall fulfil its obligations in the cases where the person according to Article 161, paragraph 1, does not have a laboratory of his own;

7. document for paid fee to the amount as laid down in the tariff according to Article 21, paragraph 2.

(3) Where the manufacturing facilities are situated in a third country with which the European Community has a signed agreement for mutual recognition of Good Manufacturing Practice certificates, the persons according to Article 161, paragraph 1 shall annex to the application the address of any facility manufacturing medicinal products, active substances, or medicinal products intended for clinical trials, name, place of business and address of management of the person who has been granted manufacturing authorisation, certificate evidencing compliance of he manufacturing, control, and storage conditions with standards,

which equivalent to the standards approved with the requirements pf the Good Manufacturing Practice, and the name of the qualified person.

(4) In the cases different from 3, the BDA shall perform, if necessary, on the spot inspection to determine the compliance of the documentation with the manufacturing, control, and storage of the medicinal products in the country, exporter. Provided that compliance with the Good Manufacturing Practice has been established, the BDA shall issue a certificate.

(5) The expenses for the conduct of an inspection on the spot according to paragraph 4 shall be for the account of the importer.

(6) For conduction an inspection on the spot according to paragraph 4 the applicant shall pay a fee to the amount as laid down in the tariff according to Article 21, paragraph 2.

Article 163. (1) The qualified person according to Article 161, paragraph 2, point 1, shall issue a certificate of release for each batch evidencing that the batch of a medicinal product imported from a third country has been subjected to complete quantitative and qualitative analysis, at least of the active substances, and all required tests and checks for compliance with the requirements for issuing a marketing authorisation under the terms of this law have been performed prior to the introduction to the market on the territory of, irrespective whether the product has been manufactured in another Member State or not.

(2) Where the batch of a medicinal product imported from a third country has been subjected to the analyses according to paragraph 1 in another Member State and is accompanied y a certificate of batch release signed by another qualified person, no conduct of control tests on the territory of the Republic of Bulgaria shall be required.

(3) Where the batch of a medicinal product imported from a third country with which the European Community has signed an agreement for mutual recognition of Good Manufacturing Practice certificates, the qualified person shall issue a certificate of batch release based in the documents accompanying the batch without obligation to perform control tests on the territory of the Republic of Bulgaria.

(4) The qualified person according to paragraph 1, shall issue a certificate of release for each imported batch certifying that the batch of the medicinal product on the territory of the Republic of Bulgaria intended for a clinical test has been manufactured and controlled in compliance with standards, which are equivalent to the Good Manufacturing Practice and with the manufacturing dossier of the product and that all required quality analyses and tests in accordance with the information submitted by the contracting authority to the BDA according to the regulation Article 82, paragraph 3, have been performed**.**

(5) The qualified person according to Article 161, paragraph 2, point 1, shall issue a certificate of release for each batch of a medicinal product used as a comparator in a clinical test conducted on the territory of the Republic of Bulgaria, which is to be imported from a third country and is not accompanied by a document evidencing that the product has been manufactured and controlled in compliance with standards equivalent to the Good Manufacturing Practice including where this medicinal product has an issued marketing authorisation.

(6) No conduct of control tests on the territory of the Republic of Bulgaria shall be required where the requirements according to paragraphs 4 or 5 have been fulfilled in another Member State or a country of the European Economic Area and a medicinal product intended for clinical trials is accompanied by a certificate of batch release signed by another qualified person.

(7) The qualified person according to paragraph 1 shall keep the documentation for any imported batch of a medicinal product at least 5 years and shall provide it to the control bodies upon request.

(8) The import authorisation holder shall ensure and maintain a system for blocking and recall of medicinal products, which have shown discrepancies with the quality requirements.

(9) The import authorisation holder shall be obliged to block and recall medicinal products, which have shown discrepancies with the requirements of safety, and efficacy according to the regulation according to Article 274, paragraph 1.

(10) The provisions of Article 160, paragraph 1, points 4, 5, and 7, shall also be applied with respect of import authorisation holders.

(11) The import authorisation holder shall ensure to the qualified person according to Article 161, paragraph 2, point 1, the required condition for the fulfilment of his obligations and shall immediately notify the control bodies of his substitution.

(12) In case of constitution of an administrative-penal procedure for violations committed during the execution of the obligations of the qualified person, the BDA shall order the import authorisation holder to temporarily dismiss the qualified person from the position.

Article 164. (1) The executive director of the BDA shall issue an import authorisation within 30 days of the date of submission of the application according to Article 162 or make a motivated refusal.

(2) The refusal according to paragraph 1 shall be subject to appeal under the terms of the Administrative procedure code.

(3) The import authorisation shall only be issued for the medicinal products, forms thereof, active substances, medicinal products intended for clinical trials indicated in the application and for the premises where control and storage are to be carried out**.**

(4) The import authorisation is timeless.

Article 165. (1) The import authorisation holder of a third country shall submit to the BDA in case of change of:

1. the person according to Article 161, paragraph 2, point 1;

2. the active substances, medicinal products, and forms he has been issued the import authorisation for;

3. address of the laboratory according to Article 161, paragraph 2, point 2;

4. trader's court registration.

(2) Documents associated with the change defined in the regulation according to Article 152 shall be annexed to the application according to paragraph 1.

Article 166. (1) The provisions of Article 164 shall be applied at the issue of the authorisation allowing the changes, whereas the terms for the issue thereof are:

1. in the cases according to Article 165, paragraph 1, point 1, 2, and 4 – up to 14 days;

2. in the cases according to Article 165, paragraph 1, point 3 – up to 30 days.

(2) Where the change according to Article 165, paragraph 1, point 3, cannot be assessed by documents, the BDA shall conduct inspections on the spot. In these cases the term according to paragraph 1, point 2, shall cease to run until the accomplishment of the inspection.

(3) The expenses for the conduct of the inspection on the spot according to paragraph 2 shall be for the account of the account of the applicant.

(4) For the conduct of the inspection on the spot according to paragraph 2 the applicant shall pay a fee to the amount as laid down on the tariff according to Article 21, paragraph 2.

Article 167. (1) The BDA shall keep a register according to Article 19, paragraph 1, point 2, of the issued import authorisations, which shall contain:

1. number and date of the import authorisation;

2. name, place of business and address of management of the person, who has been granted import authorisation;

3. address of the premises for the control and storage of the medicinal products;

4. active substances, medicinal products, and forms for which the authorisation has been obtained;

5. name of the person according to Article 161, paragraph 2, point 1;

6. date of deletion of the import authorisation from the register and reason thereof.

(2) Data from the register shall be published on the internet site of the BDA.

Chapter Six

PACKAGING AND LEAFLETS OF MEDICINAL PRODUCTS

Article 168 (1) Medicinal product packaging consists of primary and/or secondary packaging and patient information leaflet.

(2) The secondary packaging of medicinal products containing substances listed in Annex № 2 to Art. 3, paragraph 2 of the Law on the Control of Narcotic Substances and Precursors shall be marked diagonally with two red strips and the secondary packaging of medicinal products containing substances listed in Annex № 3 to Art. 3, paragraph 2 of the Law on the Control of Narcotic Substances and Precursors – with two blue strips. The packaging shall obligatorily contain a notice that the medicinal product shall only be dispensed by special medical prescription.

(3) The secondary packaging and the medicinal product leaflet can contain symbols or pictograms the designation of which is to illustrate the information contained so that it could be easier understood by the patient.

(4) The secondary packaging and the transport container with medicinal products containing radionuclides must be marked according to the requirements for safe transportation of radioactive materials of the International Atomic Energy Agency.

(5) Where a medicinal product is to be authorised for use on the territory of the Republic of Bulgaria, a marking for separate collection and recycling according to the Law on Waste Management and the acts for the application thereof shall be placed in its secondary packaging.

(6) Where a medicinal product is to be authorised for use, its name on the secondary packaging, pharmaceutical form, and content of active substance in a single dose shall also be printed in the Braille's alphabet.

(7) The requirements of paragraph 6 are not applied for vaccines and medicinal products in hospital's packages.

Article 169. (1) The information of the packaging and the medicinal product leaflet must be in full compliance with the data in the summary of product characteristics approved by the BDA upon the issue of the marketing authorisation and must comply with the requirements set out in the regulation according to Article 170.

(2) The information on the packaging and leaflet can be in several languages but one of these must obligatorily be Bulgarian language. The content of the information in various languages must be identical.

(3) The name of the medicinal product shall obligatorily be written in the Bulgarian language and the international non-proprietary name of the medicinal substance shall be written according to the Anatomic-Chemical-Therapeutic Classification of the WHO. The name and address of the marketing authorisation holder can be written in Latin.

(4) The information of the packaging and leaflet must be in a language comprehensible for the patient and must be readable and indelible.

Article170. The requirements relating to the packaging and leaflets of medicinal products shall be determined by a regulation of the minister of health.

Chapter Seven

CLASSIFICATION OF MEDICINAL PRODUCTS

Article 171. (1) Depending on the method of dispensing, the medicinal products shall be classified as follows:

1. medicinal products dispensed on medical prescription;

2. medicinal products dispensed without medical prescription.

(2) The dispensing regime of a medicinal product shall be determined by the BDA in the marketing authorisation/registration certificate.

(3) The person according to Article 26, paragraph 1, shall indicate the dispensing regime of a medicinal product in the application for marketing authorisation/registration certificate, variation of the marketing authorisation or its renewal.

Article 172. The medicinal products according to Article 171, paragraph 1, point 1, shall be divided in the following categories:

1. medicinal products with restricted medical prescription intended only for use in certain specialized fields;

2. medicinal products subject to special medical prescription;

3. medicinal products for multiple or single dispensing on the same medical prescription.

Article173. Medicinal products, which meet the following requirements, shall be dispensed on medical prescription:

1. medicinal products, which can represent a direct or indirect danger for human health even at correct use if administered without medical observation;

2. medicinal products, which are frequently and very widely administered in a wrong manner and as a result of that can represent a threat for the people's health;

3. medicinal products containing substances the activity and/or adverse drug reactions of which require subsequent additional study;

4. medicinal products, which are usually prescribed by a physician for potential administration.

Article 174. Medicinal products shall be subject to special medical prescription wherever these meet one of the following conditions:

1. contain narcotic substances within the meaning of the Law on the Control of Narcotic Substances and Precursors in admissible for use quantities;

2. in case of incorrect use can cause significant risk of misuse, lead to drug addiction, or be used for illegal purposes;

3. contain new medicinal substances the characteristics of which are not sufficiently known and therefore these can be assigned to the group of medicinal products according to point 2.

Article 175. Medicinal products shall be subject to limited medical prescription wherever these meet one of the following conditions:

1. are limited to administration in hospital conditions only due to limited experience with their use or in the interest of public health;

2. are intended for treatment of pathological conditions, which can only be diagnosed in therapeutic establishments, irrespective that their administration and follow-up in the course of treatment can be carried out in other healthcare establishments;

3. are intended for treatment of out-patients but their use can cause serious adverse drug reactions, which can require specialist prescribing and monitoring in the course of treatment.

Article 176. (1) The BDA can refuse to approve the dispensing regime of a medicinal product requested by the applicant according to Article 26, paragraph 1, on the grounds of assessment of:

1. the maximum single dose, maximum daily dose, quantity of the active substance in one dose unit, pharmaceutical form, specific appearance of the primary product packaging, and/or

2. other specific conditions of use.

(2) The BDA can refuse to indicate the exact category of a medicinal product according to Article 172 but pursuant to the criteria according to Article 174 and Article 175 shall determine whether a medicinal product shall be classified as a product dispensed only on medical prescription.

Article 177. Medicinal products, which do not meet the requirements according to Articles 173, 174, and 175 and the criteria laid down in the regulation according to Article 178, shall be dispensed without medical prescription.

Article 178. The criteria for classification of medicinal products and the requirements to the documentation for changing the classification shall be determines by a regulation of the minister of health.

Article 179. (1) The BDA shall draw and publish on its internet site a list of the medicinal products, which shall be dispensed on the territory of the Republic of Bulgaria on medical prescription.

(2) The list according to paragraph 1 shall be updated annually.

Article 180. Should new data of a medicinal product, which has a marketing authorisation/registration certificate issued, become available, the BDA shall reconsider and if necessary change the classification in accordance with the requirements of Article 173 and the criteria laid down in the regulation according to Article 178.

Article 181. In the cases where a change in the classification of a given medicinal product is authorised on the grounds of significant preclinical and clinical trials, next applicants or marketing authorisation holders cannot refer within one year of the date of authorisation of the change issued by a regulatory body of a member country when submitting an application for a change in the classification of the same substance.

Article 182. Annually the BDA shall notify the European commission and the regulatory bodies of the other Member States of changes occurred in the list according to Article 179.

Chapter Eight

PHARMACOVIGILANCE

Article 183. Medical specialists shall be obliged to immediately report to the marketing authorisation holder and to **t**he BDA any suspected serious or unexpected adverse drug reaction irrespective whether the medicinal product is used in compliance with the approved summary of product characteristics or not.

Article 184. (1) The BDA shall organise and maintain a system to monitor the safety of the medicinal products placed on the market.

(2) The system according to paragraph 1 shall have the purpose of registering all reports of adverse drug reactions received from the authorised medicinal products including information about misuse and use, which is not in compliance with the summary of product characteristics approved by the BDA, scientific analysis if the collected data, and undertaking appropriate measures as to the decrease the risk laid down in this law.

(3) The BDA shall provide electronically the information collected by this system about suspected serious adverse drug reactions observed on the territory of the Republic of Bulgaria to the regulatory bodies of the other Member States and to the European Agency for entering in the data base established under the terms of Regulation (EC) 726/2004 of the European Parliament and the Council within not more than 15 days of its receipt.

(4) The BDA shall provide the reports of suspected serious adverse drug reactions observed on the territory of the Republic of Bulgaria to the marketing authorisation holder of the respective product within 15 of the date of receipt of the report.

(5) The BDA shall publish the pharmacovigilance guidelines issued by the European Commission and the European Medicines Agency on its internet site.

Article 185. The marketing authorisation holder shall be obliged to organize and maintain a system for monitoring and assessment of the safety of the medicinal products, by which he shall guarantee his responsibility for the products launched on the Bulgarian market and his readiness to undertake immediate action in case of necessity.

Article 186. (1) The marketing authorisation holder shall appoint a pharmacovigilance qualified person established on the territory of a Member State.

(2) The data of the person according to paragraph 1: name, professional biography, address, telephone, and fax shall be submitted to the BDA together with the application for marketing authorisation.

(3) The marketing authorisation holder shall notify the BDA at any change in the data according to paragraph 2.

Article 187. The qualified person according to Article 186 shall be responsible for:

1. documenting and analysis of all reports of suspected adverse drug reactions, which have become known to the marketing authorisation holder according to Article 188;
2. submission to the BDA of the expedited adverse drug reaction reports and the periodic updated safety reports according to Article 189 и 190;
3. immediate provision upon request by the BDA of additional information necessary to assess the benefit/risk ratio associated with the use of a medicinal product, about the sales or prescribing including data of this medicinal product;

4. provision to the BDA of any new information irrespective of its source, which can have relationship with the assessment of the benefit/risk ratio associated with the use of a medicinal product including information from postmarketing product safety studies.

Article 188. (1) In fulfilment of his obligations according to Article 185, the marketing authorisation holder shall be obliged to document all reports of suspected adverse drug reactions observed on the territory of the European Union or third countries.

(2) The reports according to paragraph 1 must be accessible for review, check-up, and assessment in at least one person according to Article 186, paragraph 1.

Article 189. The marketing authorisation holder shall submit to the BDA a report within 15 days of the date of receipt of an adverse drug reaction in the following cases:

1. by reports by medical specialists of a suspected serious adverse drug reaction observed on the territory of the Republic of Bulgaria ;

2. by other reports of suspected serious adverse drug reactions observed on the territory of the Republic of Bulgaria**,** which meet the criteria laid down in the regulation according to Article 191, paragraph 1, and for which he has been informed of;

3. by reports of suspected serious and of unexpected adverse drug reactions, as well as any case of suspected transmission of infectious agents through medical products observed in third countries in compliance with the requirements of the regulation according to Article 191, paragraph 1;

4. by reports of suspected serious adverse drug reactions observed in the other Member States in the cases according to Article 76.

Article 190. (1) Besides the cases according to Article 189 and where there are no other requirements imposed as a condition for marketing authorisation, the marketing authorisation holder shall be obliged to provide to the BDA periodic updated safety reports, which shall contain all reports of adverse drug reactions and assessment of the benefit/risk ratio associated with the use of a medicinal product immediately upon request by the BDA or every 6 months of the date of the marketing authorisation until the date launch on the market according to Article 54, paragraph 1.

(2) Where there are no other requirements imposed as a condition for marketing authorisation, the marketing authorisation holder shall be obliged to provide to the BDA periodic updated safety reports, which shall contain assessment of the benefit/risk ration associated with the use of a medicinal product immediately upon request by the agency or:

1. every 6 months during the first two years of the launch date of a medicinal product on the market;

2. once yearly during the next two years;

3. once in three years after the fourth year of the launch date of the medicinal product on the market.

(3) After obtaining marketing authorisation, its holder can request an alteration of the terms according to paragraphs 1 and 2 for submission of periodic updated safety reports under the terms of this law.

Article 191. (1) The requirements to the collection, confirmation, and provision of the information for adverse drug reactions and to the content and form of the reports according to Articles and 190 shall be laid down in a regulation of the minister of health.

(2) At fulfilment of his obligations according to this chapter the marketing authorisation holders shall comply with the guidelines issued by the European Medicines Agency and the European Commission and shall use the internationally adopted medical terminology.

Article 192. (1) The marketing authorisation holder cannot provide information to the public associated with the safety data of an authorised medicinal product without prior coordination with the BDA.

(2) The information according to paragraph 1 must be objective and not misleading.

Article 193. (1) In the cases where as a result of the assessment of the safety data the BDA may judge that the marketing authorisation must be temporarily stopped, bereaved, or amended, it shall inform the holder, the other Member States, and the European Medicines Agency accordingly with the aim of obtaining an official opinion of the respective committee at the European Commission.

(2) Wherever it is necessary to undertake urgent measures for the protection of public health, the BDA can temporarily stop the marketing authorisation of a medicinal product notifying the European Medicines Agency, the European Commission, and the other Member States within one working day.

(3) The BDA shall be obliged to implement the temporary and/or final measures recommended by a decision of the European Commission.

Article 194. The provisions of this chapter shall not apply to homeopathic medicinal products according to Article 35.

Chapter Nine

WHOLESALE AND PARALLEL IMPORT OF MEDICINAL PRODUCTS

Section I
Wholesale of medicinal products

Article 195. (1) Wholesale of medicinal products can perform natural and legal persons registered as traders pursuant to the national legislation of a Member State and possessing authorisation for such activity issued by a regulatory body of the respective Member State.

(2) Where the person according to paragraph 1 is in possession of warehouse premises on the territory of the Republic of Bulgaria, he can perform wholesale of medicinal products after receipt of authorisation from the executive director of the BDA.

Article 196. (1) Manufacturer of medicinal products within the meaning of this law can only perform wholesale of the medicinal products, which he has an issued manufacturing authorisation for.

(2) Importer of medicinal products within the meaning of this law can only perform wholesale of the medicinal products, which he has an issued import authorisation for.

Article 197. The persons according to Article 195 shall dispose of:

1. suitable premises, equipment and outfits, and transport vehicles ensuring correct storage, distribution, and transportation of the medicinal products in compliance with the requirements of the Good Distribution Practice;

2. personnel and responsible master-pharmacist with at least two years length of service in his speciality and whose obligations shall be laid down in the regulation according to Article 198.

Article 198. The principles and requirements of the Good Distribution Practice shall be laid down in a regulation of the minister of health.

Article 199. (1) The persons according to Article 195, paragraph 2, shall submit to the BDA:

1. application containing name, place of business and address of management of the trader; address and description of the premises and equipment for the storage of the medicinal products;

2. actual certificate of actual court registration;

3. name, certificate of clean court record, diploma for higher education and length of service for the responsible master - pharmacist according to Article 197, point 2, and a copy of his/her employment contract;

4. authorisation for use of the premises for storage according to Article 197, point 1, issued under the terms of the Law on the Organization of the Territory or other substituting document;

5. investment project for the premises according to Article 197, point 1, approved under the terms of the Law on the Organization of the Territory;

6. document certifying the legal grounds for the use of the premises;

7. conclusion of the Regional Inspectorate for the Preservation and Control of Public Health after inspection on the spot evidencing that the health requirements in the whole sale premises according to the regulation according to Article 198.

8. document for paid fee as laid down in the tariff Article 21, paragraph 2.

(2) The persons according to Article 195, paragraph 1, shall submit to the BDA an application accompanied by the following documents:

1. copy of the wholesale authorisation issued by a regulatory body of a Member State;

2. name and address of the contact person on the territory of the Republic of Bulgaria;

3. address of the premises for the storage of the medicinal products on the territory of the Member State.

(3) In case of wholesale of narcotic substances, as well as pharmaceutical forms containing such substances, the requirements of the Law on the Control of Narcotic Substances and Precursors shall also be applied

.

(4) In case of wholesale of radiopharmaceuticals, an opinion of the Nuclear Regulatory Agency shall also be submitted.

Article 200. The BDA shall assess the documentation the documentation and conduct an inspection on the spot of the sites mentioned in the application to certify their compliance with the requirements of the Good Distribution Practice.

Article 201. (1) Provided that the BDA establishes omissions in the submitted documentation, it shall notify the applicant in writing.

(2) In the cases according to paragraph 1 the term according to Article 202, paragraph 1, shall cease to run.

Article 202. (1) In a period of 90 days of the date of submission of the application according to Article 199, paragraph 1, the executive director of the BDA shall issue a wholesale authorisation or make a motivated refusal.

(2) The refusal according to paragraph 1 shall be subject to appeal under the terms of the Administrative procedure code.

Article 2 In a period of 15 days of the date of submission of the documentation according to Article 199, paragraph 2, the executive director of the BDA shall issue a registration certificate for wholesale on the territory of the Republic of Bulgaria to the person according to Article 195, paragraph 1.

Article 204. (1) The wholesale authorisation for medicinal products shall be timeless.

(2) The authorisation according to Article 202 or the certificate according to Article 203 shall be cancelled provided that its holder requests so from the executive director of the BDA in writing.

(3) The person according to Article 195 shall be obliged to notify the BDA in writing within 7 days of the termination of its activities relating the wholesale of medicinal products. In such cases, the executive director of the BDA shall cancel the issued authorisations/certificates for wholesale of medicinal products.

Article 205. (1) The BDA shall keep a register of the issued authorisations for wholesale of medicinal products according to Article 202, paragraph 1, which shall contain:

1. authorisation number and date;

2. name, place of business and address of management of the person who has received the authorisation;

3. address of the premises for the storage of the medicinal products;

4. the data of the respective master - pharmacist according to Article 197, point 2;

5. list of the medicinal products containing narcotic substances, radiopharmaceuticals, immunological medicinal products, and medicinal products obtained from human plasma and human blood;

6. date of deletion of the authorisation from the register and reason therefore;

7. remarks relating to the inscribed circumstances.

(2) The BDA shall keep a register of the issued certificates according to Article 203 for wholesale of medicinal products, which shall contain:

1. certificate number and date;

2. number of the authorisation for wholesale of medicinal products and the issuing body;

3. name, place of business and address of management of the person who has received the certificate;

4. data for the person according to Article 199, paragraph 2, т. 2;

5. date of deletion of the certificate from the register and reason therefore;

6. remarks relating to the inscribed circumstances.

(3) Data from the register shall be published on the internet site of the BDA.

Article 206. (1) In case of change of the circumstances associated with the issued wholesale authorisation, its holder shall summit to the BDA an application under the terms of Article 199 and append the documentation associated with the change.

(2) The change authorisation shall be issued under the conditions and under the terms of Article 200-202. In case of change of the premises for storage, the term according to Article 202 shall apply and for the other cases the term shall be 14 days.

Article 207. (1) The wholesale authorisation holder who conducts his activity on the territory of the Republic of Bulgaria shall be obliged to:

1. at any time ensure access of the control bodies to the premises for storage of the medicinal products;

2. only trade in medicinal products authorised to the order of this law;

3. trade in medicinal products, whose packaging and leaflets of which are in compliance with the issued marketing authorisation and under the terms of this law and the expiry term of which has not elapsed;

4. only supply medicinal products from manufacturers, importers, and wholesalers of medicinal products who have received authorisation to perform such activity under the terms of this law;

5. supply medicinal products to other wholesale authorisation holders, pharmacies, and drugstores, opened under the terms of this law;

6. supply medicinal products to physicians and physicians in dental medicine where a settlement has no pharmacy under the conditions and order laid down in a regulation of the minister of health;

7. maintain a system for covering the movement of the received and delivered medicinal products, which shall contain:

а) date of receipt and delivery;

б) name of the medicinal product;

в) batch number and number of the batch release certificate issued by the qualified person according to Article 148, point 2 or the qualified person according to Article 161, paragraph 2, point 1, respectively, and number of the batch release certificate issued by the BDA in the cases according to Articles 69 and 70;

г) received or delivered quantity;

д) name and address of the person whom the medicinal product has been received from or delivered to;

8. keep purchase/sale documentation for all medicinal products;

9. observe the requirements of the Good Distribution Practice laid down in the regulation according to Article 198.

(2) The documentation according to paragraph 1, points 7 and 8 shall be kept for at least 5 years and shall be provided to the control bodies upon request.

Article 208. The obligations according to Article 207, paragraph 1, points 2-9, and paragraph 2 shall also apply to the wholesalers according to Article 203, as well as to the importers and manufacturers trading in medicinal products manufactured by them.

Article 209. The requirements of the special provisions of other laws shall also apply to the wholesale of medicinal products containing narcotic substances or obtained from blood, or immunological products, or radiopharmaceuticals.

Article 210. (1) The manufacturers, importers, and wholesalers of medicinal products can provide samples of authorised medicinal products to:

1. physicians and physicians in dental medicine;

2. higher medical schools and medical colleges;

3. other manufacturers and wholesalers of medicinal products.

(2) In the cases according to paragraph 1, the packaging of the medicinal products shall bear an inscription "Sample".

(3) The persons according to paragraph 1, point 1, maid be supplied not more than two pieces of the same pharmaceutical form of a medicinal product in one calendar year in the smallest existing pack of a manufacturer, and the higher medical schools and medical colleges – only in quantities required for the purposes of the education.

(4) The manufacturers, importers, and wholesalers of medicinal products shall keep record of all persons whom they have delivered samples to, about the type, quantity, and time of delivery and shall provide this data to the control bodies upon request.

Article 211. (1) The wholesalers must have a system for blocking and recall of medicinal products, which have shown discrepancies with the requirements relating to quality, safety, and efficacy.

(2) The holder of approval for wholesale is duty to freeze and draw out medicinal product, which showed discrepancies with the requirement for quality, safety and efficacy based on the order, determined in the regulation according Art 274, paragraph 1..

Article 212. (1) The executive director of the BDA shall notify the European Commission, the regulatory bodies of the other Member States, and the European Medicines Agency for the issued wholesale authorisations, temporarily stopped, or bereaved authorisations and the reasons therefore.

(2) Where the executive director of the BDA has established that the person according to Article 195, paragraph 1, does not fulfil its obligations according to Article 207, paragraph 1, points 2-9, he shall notify the regulatory body of the Member State, which has issued the wholesale authorisation, as well as the European Commission.

(3) Where the regulatory body according to paragraph 2 has temporarily stopped or bereaved the wholesale authorisation of the person according to Article 195, paragraph 1, it shall notify the executive director of the BDA and the European Commission.

Section II
Parallel import of medicinal products

Article 213. Parallel import of medicinal products on the territory of the Republic or Bulgaria can be performed by a natural or legal person registered according to the Commercial Law, the legislation of a Member State, or the legislation of a state party to the Agreement on the European Economic Area after receipt of a parallel import authorisation issued by the executive director of the BDA.

Article 214. (1) A medicinal product authorised for use in another Member State, can be imported on the territory of the Republic of Bulgaria, provided that it is identical or similar to a medicinal product authorised for use in the Republic of Bulgaria under the terms of this law.

(2) Within the meaning of paragraph 1 a medicinal product is identical or similar provided that:

1. it has identical qualitative and quantitative composition with respect to the active substance(s), is supplied in the same pharmaceutical form, the same primary packaging, under the same name, with the same graphic design of the packaging, or where

2. the medicinal product authorised for use in the Republic or Bulgaria and the product, which is to be imported parallel, have been manufactured by different manufacturers with which the marketing authorisation holder has concluded license agreements or another contract for the manufacture thereof.

Article 215. (1) To obtain authorisation to perform parallel import on the territory of the Republic of Bulgaria, the person according to Article 213, paragraph 1 shall submit to the executive director of BDA an application stating the Member State from which the parallel import is to be effected from.

(2) The following data and documents shall be appended to the application:

1. name, pharmaceutical form, quantity of the active substance in a dose unit of the medicinal product authorised for use in the Republic of Bulgaria;

2. name, pharmaceutical form, quantity of the active substance in a dose unit of the medicinal product intended for parallel import;

3. name of the marketing authorisation holder and the manufacturer if a person different from the marketing authorisation holder;

4. number of the marketing authorisation of the medicinal product in the Republic of Bulgaria and number of the marketing authorisation of the medicinal product in the Member State where the parallel import is to be effected from;

5. declaration for establishment of circumstances pursuant 217, issue 1;

6. copy of the patient information leaflet and a sample of the medicinal product in the form in which it is sold in the Member State where the parallel import is to be effected from, translation of the patient information leaflet in the Bulgarian language accompanied by a declaration that the translation is in compliance with the original of the leaflet;

7. proposal for patient information leaflet of the parallel imported medicinal product accompanied by a declaration that the content of the leaflet is identical with the content of the medicinal product authorised in the Republic of Bulgaria except for the following data:

a) name and address of management of the person effecting the parallel import;

b) name of manufacturer where it is different for both products;

c) stability period where it is different for both products;

d) excipients where these are different in both products;

8. in case of repackaging:

а) sample of the parallel import product;

б) copy of the contract between the person carrying out parallel import and the persons performing partial manufacturing activity – packaging, labelling;

в) certificate of Good Manufacturing Practice where the repackaging processes are performed outside the territory of the Republic of Bulgaria;

г) where repackaging is performed by the person according to Article 213, paragraph 1, copy of the manufacturing authorisation issued by the regulatory body of the Member State where repackaging is to be performed;

9. document for paid fee, in the amount as laid down in the tariff according to Article 21, paragraph 2.

(3) Where there are differences (in the composition of the excipients or other) between the parallel imported medicinal product and the product authorised for use on the territory of the Republic of Bulgaria, the person according to paragraph 1 shall submit evidence that these do not affect the therapeutic qualities of the parallel imported medicinal product.

(4) In the cases according to paragraph 3 the person according to paragraph 1 shall point out the differences on the packaging and in the patient information leaflet of the parallel imported medicinal product.

(5) Where the person according to Article 213, paragraph 1, is repackaging and/or labelling the medicinal product in the Bulgarian language on the territory of the Republic of Bulgaria, it must possess a manufacturing authorisation issued by the executive director of the BDA.

(6) The parallel imported product shall be used according to the conditions of the issued marketing authorisation for the use of the medicinal product on the territory of the Republic of Bulgaria.

Article 216. (1) The authorisation for parallel import on the territory of the Republic of Bulgaria shall be issued within 45 days of the date of submission of the documentation to the BDA.

(2) Where the BDA shall request additional documentation from the applicant, the term according to paragraph 1 shall cease to run until receipt of the requested information.

(3) Where the BDA shall require information relating to the issue of the marketing authorisation of the imported medicinal product from the regulatory body of the Member State where the parallel import is to be effected from, the term according to paragraph 1 shall be extended by 45 days.

(4) If the BDA does not receive the requested documentation within the term according to paragraph 3, the procedure for the issue of a parallel import authorisation for the territory of the Republic of Bulgaria shall be terminated.

(5) The issued parallel import authorisations for the territory of the Republic of Bulgaria shall be published on the internet site of the BDA.

(6) The parallel import authorisation shall be valid for 5 years. New authorisation shall be issued under the terms of Article 215.

(7) The parallel import authorisation shall not be automatically cancelled where the marketing authorisation holder of the medicinal product launched on the market on the territory of the Republic of Bulgaria would withdraw it for reasons, which are not associated with a threat for the health of the population.

Article 217. The parallel import authorisation holder shall be obliged to:

1. notify the marketing authorisation holder of the medicinal product launched on the territory of the Republic of Bulgaria of his intention to effect parallel import and provide a sample of the parallel imported medicinal product upon request;

2. keep the following information for 5 years: name and address of the person whom the parallel imported medicinal product is to be delivered to, date of delivery, delivered quantity, and batch number;

3. submit in BDA:

a) actualized patient's leaflet of parallel imported product according with the variations in issued marketing authorisation of the approved medicinal product in Republic of Bulgaria;

b) declaration that the content of the leaflet according to letter "a" shall be identical with the content of the product leaflet, approved in Republic of Bulgaria except of the data according to Article 215, paragraph 2, point 8, letters "a" – "g";

4. document and report to the marketing authorisation holder and the BDA all reports of adverse drug reactions of the imported medicinal product.

Chapter Ten

RETAIL TRADE IN MEDICINAL PRODUCTS

Article 218. Retail trade in medicinal products can only be conducted by pharmacies and drugstores under the terms of this law except for the cases according to Article 232, paragraph 2.

Article 219. (1) Pharmacy is a health establishment conducting the following activities: storage, preparation, packaging, control, giving out consultations, dispensing medicinal products, medical devices authorised in Republic of Bulgaria on or without medical prescription, as well as food additives, cosmetic, and sanitary-hygienic articles according to a list determined by the minister of health.

(2) The structure, order, and organization of work in the pharmacies, the nomenclature of the medicinal products, as well as the list according to paragraph 1 shall be laid down in a regulation of the minister of health.

(3) Pharmacies shall offer food supplements without registering under the terms of the Law on Foods.

Article 220. (1) The activities according to Article 219, paragraph 1, shall be conducted by a master - pharmacist.

(2) The master - pharmacy shall be obliged to fulfil a given medical prescription including pharmaceutical forms prepared according to magisterial and pharmacopoeia recipe under the terms laid down in the regulation according to Article 221.

(3) The assistant pharmacist can fulfil all activities according to Article 219, paragraph 1 in the presence and under the control of master - pharmacist, excluding: release of medicinal product with prescription, control and consultancy.

Article 221. The minister of health shall determine in a regulation the medical specialists who can issue prescriptions, the order for prescribing of medicinal products, the term for fulfilment, as well as the cases and order where the master - pharmacist can refuse to fulfil a medical prescription or make a change therein.

Article 222. (1) Entitled to carry out retail with medicinal product, to retail trade with medicinal products shall have a master of pharmacy registered (sole trader or company with limited distribution) according to the Commercial Law, the legislation of a Member State, or the legislation of a state party to the Agreement on the European Economic Area. In the scope of activities of the trader is written only fulfilment of retail trade with medicinal products.

(2) A person obtaining Master in pharmacy who has been granted approval for retail trade with medicinal products according to paragraph 1 is manager of the pharmacy and he/she obligatory works in it.

(3) Entitled to retail trade with medicinal products to cover its own needs provided observation of the requirement of paragraph 1 shall have:

1. therapeutic establishments according to Article 5 of the Law on Healthcare establishments that provide hospital care;

2. healthcare establishments for hospital care;

3. dispensaries and

4. hospices with stationary according Article 10, point 5 from the Law for Therapeutic Establishments.

(4) Pharmacies of therapeutic establishments for outpatient care at the Ministry of Defence and Ministry of Interior can be managed from assistant pharmacist after proposal by the corresponding administration and after issued approval from the Minister of Health.

(5) In settlements, where there is not opened pharmacy according to paragraph 1, the corresponding municipality has right to obtain approval for retail trade with medicinal products by sole municipal trade company after contracting an agreement or agreement for management of pharmacy with master of pharmacy.

Article 223. (1) Master - pharmacist and assistant pharmacist can be manager of only one pharmacy and shall obligatorily work in it.

(2) Master of pharmacy or assistant pharmacist who is the manager of a pharmacy cannot be hired to work upon agreement with sole trader or trade company having as its objectives manufacture, import, wholesale or retail trade in medicinal products or to work in another place.

(3) A sole trader or trade company who have received authorisation to retail trade with medicinal products cannot be an owner or participate in trade companies that have as their objectives manufacture, import, or wholesale trade in medicinal products including companies of related persons within the meaning of the Commercial Law.

Article 224. The manager of a pharmacy must be:

1. has a master in pharmacy, respectively assistant pharmacist in the cases stipulated by the law;

2. not be deprived of the right to practice the profession;

3. not to be convicted for crimes associated with practicing of his profession, for crimes against property and economy, or for intentional crimes against personality;

4. has at least one year practice like the person obtaining a master in pharmacy.

Article 225. (1). In settlement on the territory, which does not have another pharmacy, right for retail trade with medicinal products, after opening a pharmacy has the assistant pharmacist, registered like a sole trader to the Trade Law, until receiving authorisation for retail trade by a master of pharmacy.

(2) The assistant pharmacist who has authorisation for retail trade with medicinal products according to paragraph 1 is the manager of the pharmacy and he/she obligatory works in it.

Article 226. (1) Pharmacies for selling medicinal products to citizens can be opened on the territory of healthcare establishments for outpatient care.

(2) Pharmacies for selling medicinal products to citizens cannot be opened on the territory of healthcare establishments to Art. 21, paragraph 2 of the Health Law, therapeutic establishments for hospital care, and healthcare establishments according to Article 10 of the Law on Healthcare Establishments.

Article 227. The requirements relating to the location and to the premises of the pharmacy shall be laid down in the regulation according to Article 219, paragraph 2.

Article 228. (1) Authorisation for retail trade with medicinal product shall be issued by the minister of health on the grounds of a formal application accompanied with the following documents:

1. actual certificate of court registration inscription, document for actual court registration respectively or a copy of the constituent act for the establishment of the persons according to Article 222, paragraph 3;

2. investment project pf the premises approved under the terms of the Law on the Organization of the Territory and a document evidencing the legal grounds for the use of the premises;

3. documents certifying that the requirements of Article 224 have been met;

4. certificate of clean court record of the master of pharmacy, respectively of the assistant pharmacist indicated as manager of the pharmacy;

5. medical certificate of the master of pharmacy, respectively of the assistant pharmacist indicated as manager of the pharmacy;

6. authorisation to use the premises or another substituting document issued under the terms of he Law on the Organization of the Territory;

7. hygiene opinion of the corresponding Regional Inspectorate for the Protection and Control of Public Health;

8. certificate for register inscription in regional association of Bulgarian Pharmacists Union - for the manager of the pharmacy;

9. statement of Bulgarian Pharmacists Union for opening of pharmacy;

10. document for paid state fee to the amount as laid down in the tariff according to Article 21, paragraph 2.

(2) The pharmacies of the therapeutic establishments according to Article 222, paragraph 3, 4, 5 shall be opened and closed according to the request of the person representing the healthcare establishment or Municipality Company

(3) For opening a pharmacy, in which medicinal products containing narcotic substances, the requirements of the Law on the Control of Narcotic Substances and Precursors shall also be applied.

(4) In the cases according to paragraph 3, the application for the issue of a license for retail trade and storage of medicinal products containing narcotic substances included in Annexes № 2 and 3 to Article 3, paragraph 2 of the Law on the Control of Narcotic Substances and Precursors can be submitted simultaneously with the application for retail trade to paragraph 1. Besides the documents according to paragraph 1, the following documents shall also be submitted:

1. certificate to the effect that no accusation of intended general crime has been raised against the master of pharmacy managing the pharmacy;

2. applicant's certificate of clean court record being the master of pharmacy, sole trader, or manager/executive director of the legal person, as well as of the person responsible for the conduct of the activities according to Article 34 of the Law on the Control of Narcotic Substances and Precursors;

3. court certificates to the effect that the applicant has not been declared insolvent and is not in the course of a liquidation procedure;

4. certificate of registration according to BULSTAT;

5. document certifying that the applicant has no public obligations to the state;

6. copy of the security contract with the bodies of the Ministry of Interior or a physical or legal person possessing license to conduct private security activity and a copy of that license;

7. rules for the conduct of activities with narcotic substances approved by the manager of the pharmacy;

8. order for the appointment of the persons who, in the absence of the manager, will be responsible for the safe where the medicinal products containing narcotic substances will be stored;

9. protocol issued by the inspector of narcotic substances at the regional healthcare centre in the district on the territory of which the premises of the pharmacy are situated certifying the absence of factual conditions with respect to the submitted documentation.

(5) For the cases according to paragraph 4, the fee according to this law, as well as the corresponding fee under the terms of Law on the Control of Narcotic Substances and Precursors.

Article 229. (1) The Higher Council of Pharmacy shall make a motivated proposal to the minister of health to issue an authorisation or refusal for retail trade with medicinal product in the pharmacy..

(2) The minister of health shall issue authorisation for retail with medicinal products or make a motivated refusal to issue an authorisation within one month of the receipt of the documentation according to Article 228. The authorisation or refusal shall be delivered to the person who has submitted the application.

(3) Where discrepancies with or omissions in the submitted documentation shall be established, the Higher Council of Pharmacy shall notify the candidate in writing and give instructions as to their elimination. In these cases the term according to paragraph 2 shall cease to run as from the date of the notification till the elimination of the defects.

(4) The refusal of the minister of health to issue an authorisation shall be subject to appeal under the terms of the Administrative procedure code.

Article 230. (1) The Ministry of Health shall keep a register of the issued authorisations for retail trade with medicinal products, which shall contain:

1. authorisation number and date;

2. name, place of business and address of management of the person who has received the authorisation;

3. name, personal data, and address of the manager of the pharmacy;

4. address of the pharmacy;

5. activities, which will be conducted in the pharmacy;

6. date of cancelling the authorisation and its deletion from the register and reason therefore;

7. remarks relating to the inscribed circumstances.

(2) Data from the register shall be published on the internet site of the Ministry of Health.

Article 231. (1) In case of change of the circumstances inscribed in the register according to Article 230, paragraph 1, points 2-5, the person who has received authorisation to carry out retail trade with medicinal products shall submit an application under the terms of Article 228, paragraph 1, and shall append the documents associated with the change.

(2) at issuing the authorisation allowing the change according to paragraph 1, the provisions in Article 229 shall applied.

Article 232. (1) Physicians and physicians in dental medicine can keep medicinal products according to a list determined by the minister of health.

(2) Where there is no pharmacy in a settlement, the persons according to paragraph 1 can only keep and sell medicinal products provided that they have received authorisation therefore according to an order laid down in a regulation of the minister of health.

Article 233. The manager of the pharmacy takes the responsibility for the activities according to Article 219, paragraph 1.

Article 234. (1) Prohibited shall be the sale of medicinal products through automatic machines except for the medicinal products indicated in a list determined to the regulation according to Article 219, paragraph 2.

(2) The automatic machines according to paragraph 1 can be possession only on the persons according to Article 222 and Article 238, paragraph 2.

(3) The bargain trade with drug products shall be prohibited

(4) The sale of medicinal products dispensed on medical prescription via internet shall be prohibited.

Article 235. (1) The authorisation to carry out retail trade with medicinal products shall be cancelled with the termination of the activity of the persons according to Article 222.

(2) The Minister of Health shall cancel the authorisation for retail trade with medicinal products:

1. according to an application by the person who has received authorisation for carrying out retail trade with medicinal products:

2. wherever it has been established that the manager of the pharmacy does not comply with the requirements laid down in Article 224 and 225.

(3) The persons according to Article 222 and 225 shall notify the minister of health in writing within 14 days of the termination of the activity according to paragraph 1.

Article 236. (1) The pharmacy cannot be closed for more than 30 days within a calendar year due to the absence of the manager.

(2) Where the manager of the pharmacy is not in a position to fulfil his obligations due to a leave for temporary incapacity of work, pregnancy, birth, or adoption and breeding of a child, the pharmacy can operate under the management of another master of pharmacy, respectively another assistant pharmacist, in the cases to Art. 225 complying with the requirements of Article 224 for not more than two years. In all these cases a permission of the minister of health shall be issued.

(3) The permission according to 2 shall be issued within 30 days.

Article 237. Upon termination of the activity of the person who received authorisation to retail trade with medicinal products, the medicinal products can be sold by persons who have received authorisation for wholesale trade in medicinal products.

Article 238. (1) Products of importance for human health and medicinal products, which are dispensed without medical prescription as paid down in lists of the minister of health, can be sold in a drugstore.

(2) Entitled for carry out retail trade with medicinal products, as opening drugstores shall have all natural or legal person registered according to the Commercial Law, the legislation of a Member State, or the legislation of a State Party to the Agreement on the European Economic Area.

(3) The manager of a drugstore must be a medical specialist.

Article 239. (1) Drugstores shall be opened after registration with the BDA.

(2) The persons according to Article 238, paragraph 2, shall submit to the BDA a registration application accompanied by the following documents:

1. actual certificate of actual court registration;

2. education document and certificate of clean court record or the person appointed as manager of the drugstore;

3. medical certificate of the person according to point 2;

4. authorisation to use the premises or another substituting document issued under the terms of he Law on the Structure of the Territory;

5. hygiene opinion of the corresponding Regional Inspectorate for the Protection and Control of Public Health;

6. document for paid state fee to the amount as laid down in the tariff according to Article 21, paragraph 2.

Article 240. (1) The executive director of the BDA shall issue a certificate of registration of the drugstore or make a motivated refusal within 30 days or the receipt of the documentation according to Article 239, paragraph 2.

(2) The refusal of the executive director of the BDA to issue certificate of registration shall be subject to appeal under the terms of the Administrative procedure code.

Article 241. (1) The BDA shall keep a record of the issued certificates for a drugstore authorisation, which shall contain:

1. number and date of the issued certificate;

2. place of business and address of management of the persons who have received certificates for registration of drugstore;

3. name, personal data, and address of the manager of the drugstore;

4. address of the drugstore;

5. date of cancelling the registration and reason therefore;

6. remarks relating to the inscribed circumstances.

(2) Data of the register shall be published on the internet site of the BDA.

Article 242. In case of change of the address of the drugstore of the manager, the person who has received the authorisation to open the pharmacy shall submit an application under the terms of Article 239, paragraph 2, and documents associated with the change.

Article 243. The conditions and order for the organization of work in a drugstore shall be paid down in a regulation of the minister of health.

Chapter Eleventh

ADVERTISING OF MEDICINAL PRODUCTS

Article 244. (1) Advertising of medicinal products shall be any form of information, provision, promotion, or offers aimed at stimulating the prescribing, sale, or use of a medicinal product and shall include:

1. advertising intended for the population;

2. advertising, intended for medical specialists;

3. visit of a medical trade representative with medical specialists;

4. provision of samples to medicinal products;

5. sponsorship of promotional meetings and scientific congresses visited by medical specialists including taking their travel and stay expenses in the respective country where the event is taking place.

(2) The following shall not be considered advertising of medicinal products:

1. text on the secondary packaging and in the patient information leaflet, which has been approved in the procedure for marketing authorisation;

2. correspondence on the occasion of a specific issue or problems associated with a given medicinal product;

3. informative announcements and instructions as to changes in the packaging, warnings for adverse drug reactions as a part of the overall safety measures for the medicinal product, trade catalogues and pricelists provided that these do not contain data of advertising character with respect to the medicinal product;

4. statements relating to human health or diseases provided that when these do not directly or indirectly bear on treatment, prophylaxis, or diagnostics with c medicinal products;

5. campaigns carried out by the Ministry of Health for vaccination of the population where the associated materials do not contain data for a specific medicinal product.

Article 245. (1) The marketing authorisation holder shall be obliged to establish a scientific unit for the proliferation of information fir the medicinal products for which he has received marketing authorisation under the terms of this law.

(2) The marketing authorisation holder shall be obliged to:

1. guarantee that the advertising of a medicinal product is presented to the population and medical specialists in an appearance corresponding to the requirements of this chapter and in compliance with the advertising authorisation issued by the BDA;

2. have at his disposal data and materials of all advertising campaigns undertaken within the framework of his activity including information about the groups, which the advertising is intended for, about the method of its realization, as well as the starting date of the advertising campaign;

3. guarantee the training of the medical trade representatives;

4. accurately and timely fulfil the instructions of the persons responsible for the control of advertising.

(3) The medical trade representatives must report to the scientific units according to paragraph 1 any information about the use of the advertised medicinal products, particularly with respect of the information of adverse drug reactions communicated to them by the medical specialists.

Article 246. (1) The content of the advertising must comply with the data of the approved during the marketing authorisation procedure summary of product characteristics and only present the indications approved therein.

(2) Advertising of a medicinal product must only bear on its correct use by objectively presenting the therapeutic indications of the medicinal product without exaggerating its therapeutic, prophylactic, and diagnostic capacities.

(3) The advertising must not contain misleading information.

Article 247. Advertising to the population shall only be allowed for medicinal products dispensed without medical prescription.

Article 248. Besides the cases according to Article 247, advertising campaigns carried out by marketing authorisation holders in connection with vaccination shall be permitted provided observation of the requirements of Article 251.

Article 249. The requirements to the advertising of medicinal products shall be paid down in a regulation of the minister of health**.**

Article 250. Application for authorisation of advertising of medicinal product shall be submitted by the marketing authorisation holder of the medicinal product or a duly empowered person.

Article 251. (1) For advertising authorisation the person according to Article 250 shall submit to the BDA a formal application as approved by the executive director of the agency accompanied by:

1. design of the advertising;

2. notarized power of attorney issued by the marketing authorisation holder where the application shall be submitted by another person;

3. bibliographical references of the used quotations, tables, or other materials, if any;

4. document for paid fee to the amount as paid down in the tariff according to Article 21, paragraph 2.

(2) The presented advertising drafts - designs to Art. 1 issue 1 must be clear and if there is text, it must be understandable providing possibility to assess all of its elements - text and illustrations.

(3) Expert Council of Advertising shall be established to the BDA. It shall involve physicians and specialists with practical experience in the field of advertising. The executive director of the BDA shall appoint by an order the composition of the council, where a representatives of the Professional Ethic Commission of the Bulgarian Medical Association, Bulgarian Dental Association and Bulgarian Pharmacists Union, the amount of the remuneration of its members, and shall approve rules for the condition and order for its work. In the Council representatives of patients organizations may be included.

(4) The council according to paragraph 3 shall prepare examination to the advertising design and shall establish an opinion for the executive director of the BDA.

(5) In case of establishment of discrepancies between the advertising and the requirements of this law, the BDA shall, within 7 days of the submission of the application according to paragraph 1, give written instructions for their elimination by the applicant within one month of the notification date. This decision term shall cease to run as from the notification date till the elimination of the discrepancies.

(6) If the applicant shall not fulfil the instructions within one month of the notification date according to paragraph 5, the authorisation procedure shall be terminated.

Article 252. (1) The executive director of the BDA shall authorise or issue a motivated refusal of the advertising by an order within one month of the submission of the documentation according to Article 251, paragraph 1, on the grounds of the opinion according to Article 251, paragraph 4, and shall notify the marketing authorisation holder.

(2) The refusal of the executive director of the BDA shall be subject to appeal under the terms of the Administrative procedure code.

Article 253. (1) The issued advertising authorisation to Art. 252, paragraph 1 shall refer to a concrete medicinal product within the validity of its marketing authorisation.

(2) Where there have been variations in the marketing authorisation of a medicinal product resulting in changes of an authorised advertising of this product, the marketing authorisation holder shall submit to the BDA an application for change.

Article 254. In case of change in the authorised advertising, the person according to Article 250 shall submit an application under the terms of Article 251.

Article 255. (1) The proliferation of samples of medicinal products containing narcotic substances within the meaning of the Law on the Control of Narcotic Substances and Precursors shall be prohibited.

(2) The direct provision of samples of medicinal products to the population by medical trade representatives according to Article 244, paragraph 1, point 3 shall be prohibited.

Article 256. Samples of medicinal products shall be provided to medical specialists under the conditions and order laid down in the regulation according to Article 249.

Article 257. (1) The medical trade representatives according to Article 245, paragraph 2, point 3, must have passed special education organized by the marketing authorisation holder who has employed them and must possess scientific knowledge about the presented medicinal product.

(2) During any visit, the medical trade representatives must dispose of the summary of the product characteristics and price data of the medicinal product and about the conditions of its payment and shall provide these upon request.

(3) While presenting medicinal products before medical specialists, the medical trade representatives cannot offer gifts and other material and immaterial benefits.

Chapter Twelve

PRICES OF MEDICINAL PRODUCTS

Article 258. (1) The state shall regulate the ceiling of the medicinal products included in the Positive List pursuant Art. 262, paragraph 4 and paid by the public funds in correspondence to the lower referent prices in the Member States, which are dispensed on medical prescription.

(2) The state regulates the ceiling of the prices of medicinal products, which are dispensed with medicinal prescription, except those according paragraph 1.

(3) The state shall register the maximum retail sales prices of the medicinal products dispensed without medical prescription.

Article 259. (1) The council of ministers by proposal of the minister of health creates Medical Product Pricing Committee and determines its composition.

(2) The Medicinal Product Pricing Committee shall obligatorily involve representatives of the Ministry of Health, the Ministry of Finance, the Ministry of Economy and Energetic, the Ministry of Labour and Social Policy, the NHIF, and of the BDA.

(3) The members of the Medicinal Product Pricing Committee shall have a mandate of 4 years.

(4) Person, which is member of Medicinal Product Pricing Committee shall not be a member of the committees according to Article 261 and Article 265.

(5) Every two years one half of the membership of the committee, according to paragraph 1 is changed.

(6) The conditions and order of work of the Medical Product Pricing Committee Council of Ministers.

(7) The committee according to paragraph 1 has a session at least once monthly.

(8) Informational-analytical section is created at the Medicinal Product Pricing Committee. The section collects analyses and presents on the committee the information for prices of medicinal products in Member States under the terms set out in a regulation according to paragraph 6.

(9) The Medicinal Product Pricing Committee maintains Internet site, on which it publishes information about its activity.

Article 260. (1) The Council of Ministers, according to a proposal of the minister of health, shall determine by a regulation the terms, conditions, and rules for the pricing regulation of the medicinal products according to Article 258, paragraph 1, for the regulation of the ceiling prices of dispensed on medical prescriptions medicinal products according to Article 258, paragraph 2, in their retail sale and the conditions and order for the registration of the prices of those dispensed without medical prescription.

(2) The Medical Product Pricing Committee is expressed an opinion in term of:

1. 45 days – for drug products according to Article 258, paragraph 1 and 2;

2. 30 days – for drug products according to Article 258, paragraph 3.

(3) The term, according to the paragraph 2 starts from the date of the application submission pursuant to the order of regulation in paragraph 1.

(4) Medicinal product application submission for set up, registration or change of the set up price, the ministry of health collects fee in amount, determined in the tariff according to Article 21, paragraph 2.

Article 261. (1) A Committee for Positive Drug List shall be established to the Council of Ministers.

(2) The Positive Drug List Committee shall review and make decisions on applications for inclusion, change, and/or exclusion of medicinal products from the Positive Drug List of the Republic of Bulgaria.

(3) The members of the Positive Drug List Committee shall have a mandate of 4 years.

(4) Every two years one half of the composition of the committee pursuant to Art.1 shall be renewed.

(5) The composition of the Positive Drug List Committee shall be determined by the Council of Ministers according to a proposal of the minister of health.

(6) Equal number of representatives of the Ministry of Health, Ministry of Work and Social Policy, the NHIF, and the BDA, Bulgarian Medical Association, Bulgarian Dental Association shall obligatorily be included in the Positive Drug List Committee.

(7) Medical specialists, lawyers, and economists with scientific achievements and/or practical experience in the field of medicinal products and in the respective spheres of their application can be appointed as members of the Positive Drug List Committee.

(8) A person who is a member of the Positive Drug List Committee, shall not be a member of the committees according to the Articles 259 and 265.

(9) The protocols from the Committee sessions according to the paragraph 1 are published at its internet site

Article 262. (1) the Positive Drug List shall include medicinal products dispensed on medical prescription, which are necessary to cover the healthcare needs of the population and are paid by monies from the budget of the NHIF, from the national budget outside the scope of the obligatory health insurance, and from the budget of the healthcare establishments according to Article 5 of the Law on Healthcare Establishments and from the budget of the therapeutic establishments with state and or/municipal participation, according to Article 9 и 10 of the Law on the Healthcare Establishments with state participation.

(2) Positive Drug List shall be a list of medicinal products drawn by pharmacological groups with the respective international non-proprietary names, the respective defined daily doses, reference price (value) for the defined daily dose, and level of payment.

(3) Therapeutic course and respective reference value shall be determined for medicinal products, which have no defined daily dose.

(4) The Positive Drug List shall include:

1. medicinal products for treatment of diseases paid under the terms of Law for Health Insurance;

2. medicinal products paid by the budget of the healthcare establishments according to Article 5 of the Law on Healthcare Establishments and by the budget of the therapeutic establishments according to Article 9 и 10 of the Law on the Healthcare Establishments with state and or municipality participation;

3. medicinal products proposed for treatment of diseases out of range of Law for Health Insurance, paid under the terms of Article 82, paragraph 1, point 8 from the Law of Health;

4. medicinal products intended for treatment of rare diseases, AIDS, and infectious diseases.

(5) Level of payment of medicinal products according to paragraph 4, point 1 is determined according to the budget of NHIF for the corresponding year.

(6) For submission of application for inclusion or change of included in the list according to paragraph 1 medicinal product, the ministry of health collects fee in amount, determined in the tariff according to Article 21, paragraph 2.

Article 263. (1) The medicinal products in the Positive Drug List shall be selected according to evidence of efficacy, therapeutic effectiveness, safety, and analysis of pharmaco-economic indices.

(2) The term for inclusion of medicinal products in the Positive Drug List shall be 90 days from the date of submission of an application under the terms of the regulation according to Article 264.

Article 264. The Council of Ministers, according to a proposal of the minister of health, shall determine in a regulation the conditions, rules, and criteria for inclusion in, change, and/or exclusion medicinal products from the Positive Drug List, as well as the conditions and order for the Positive Drug List Committee.

Article 265. (1) The Council of Ministers shall establish a Transparency Committee.

(2) The composition of the Transparency Committee shall be determined by the Council of Ministers according to a proposal by the minister of health. In it representatives of

the Ministry of Health, the BDA, the NHIF, the Bulgarian Medical Association, Bulgarian Dental Association, Bulgarian Pharmacists Union, the professional organization of the pharmacists, and organizations of the patients and the pharmaceutical industry are obligatory included.

(3) The Council of ministers shall determine the conditions and order of the work of the Transparency Committee by a regulation.

(4) The Council of Ministers determines with a regulation the condition and the order for work of the Transparency Committee.

Article 266. (1) The Transparency Committee shall be a body before which decisions of the committees according to Article 259, paragraph 1, and Article 261, paragraph 1, can be appealed.

(2) The decisions of the Transparency Committee shall be taken by a majority of two thirds of its members.

(3) The decisions of paragraph 2 could be appealed under the terms of the Administrative procedure code and the appeal has no suspensive effect.

Chapter Thirteen

STATE CONTROL ON THE MEDICINAL PRODUCTS

Article 267. (1) The Ministry of Health shall exercise the state control on the medicinal products. The immediate management shall be executed by the chief state health inspector, the executive director of the BDA, and the directors of the regional inspectorates for the protection and control of public health (RIPCPH) who shall be state inspectors for the control of the medicinal products.

(2) Bodies for state control of the medicinal products shall be the BDA and RIPCPH.

(3) The immediate control shall be exercised by officials – inspectors and experts appointed by orders of the director of the BDA or the director of corresponding RIPCPH depending on their subjection.

(4) For the execution of their control functions, the bodies according to paragraph 1 can request the assistance of the bodies of the Ministry of Interior.

Article 268. (1) The BDA shall exercise control on:

1. the compliance of the premises, equipment, and conditions for manufacture, control, storage, and trade in medicinal products and for the observation of the Good Manufacturing Practice for medicinal products and the Good Distribution Practice;

2. the activity of the manufacturers, importers, marketing authorisation holders wholesalers of medicinal products, pharmacies, and drugstores;

3. the quality, safety, and efficacy of the medicinal products;

4. the clinical trials with medicinal products and the control of the observation of the requirements of the Good Clinical Practice;

5. drug information associated with marketing and advertising authorisation;

6. the pharmacovigilance system of the marketing authorisation holders.

(2) the regional inspectorates for the protection and control of public health shall exercise control over the premises, equipment, and conditions for storage of and trade in

medicinal products, as well as over the activity of the wholesalers, pharmacies, and drugstores situated on the territory of the respective region.

(3) Investment projects for construction of new and/or refurbishment of existing sites associated with the manufacture of medicinal products in compliance with the rules for Good Manufacturing Practice of medicinal products shall be coordinated with the BDA.

Article 269. (1) The control according to Article 267 shall be exercised through inspections and laboratory tests.

(2) The inspections and laboratory tests according to paragraph 1 shall be conducted:

1. in connection with issuing marketing, manufacture, and import authorisations and certificates under the terms of this law;

2. in connection with exercising surveillance on the medicinal products market;

3. in case of application on the part of the European Commission, the European Medicines Agency, or on the part of a competent body of another Member State;

4. in case of application on the part of a manufacturer, importer, or marketing authorisation holder outside the cases according to point 1.

(3) The BDA shall conduct inspections as a part of the certification procedure, which in connection with European Pharmacopoeia monographs.

(4) The BDA shall conduct inspections of manufacturers of medicinal products established in a third country in connection with a submitted application for receipt of marketing or import authorisation.

(5) Where compliance of the conditions with the requirements of the Good Manufacturing Practice shall be established as a result of the inspection, the BDA shall issue a Good Manufacturing Practice certificate within 90 days of the inspection.

(6) The BDA shall notify European Medicines Agency the issued Good Manufacturing Practice certificates.

(7) Where discrepancies with the requirements of the Good Manufacturing Practice shall be established the as a result of the inspection the BDA shall notify the European Medicines Agency.

Article 270. (1) Within the framework of their competence, the officials according to Article 267, paragraph 3, shall be entitled to:

1. Access to all documents, connected directly and indirectly with violation of this law or of legislation of the Member States, implementing requirements of Directive 2001/83/EC of the European Parliament and the Council for approval of the Community code concerning medicinal products for human use, as last amended by Directive 2004/27/EC of the European Parliament and the Council, independently from the form of the document;

2. to order of each person to present information for violations according to point 1, which are familiar to him;

3. at any time inspect the sites subject to control and require, check, or make copies of all documents relating to the overall activity of the controlled site;

4. take samples of medicinal products, active substances, and excipients for laboratory tests;

5. inspect the premises, records, and documents of marketing authorisation holders or person to whom a marketing authorisation holder has assigned the conduct of the activities according to chapter eight;

6. draw up statements of administrative infringements.

(2) The officials according to Article 267, paragraph 3, shall draw up reports of the conducted inspection, which shall be provided to the inspected manufacturer/marketing authorisation holder of the medicinal product.

(3) The Executive Director of BDA of the corresponding director of RIPCPH, depending of the administrative person, who determined the violence, has right to:

1. order in written form to the violator to cease the violation according to paragraph 1, point 1;

2. requires from the violator to declare that it will cease the violation according to paragraph 1, point 1 and when it is necessary to makes the declaration matter publicly available.

3. to order cease or prohibition of each violation according to paragraph 1, point 1 and when it is necessary to order for cease or prohibition of violation matter publicly available..

Article 271. (1) The regional inspectorates for the preservation and control of the public health shall be entitled to:

1. stop construction and issue directions where violations of hygienic norms and requirements have been established in the course of construction; notify the Directorate for National Construction Control or the municipal technical office in case of illegal construction of sites and equipment for manufacture, storage, and sale of medicinal products shall be established;

2. prohibit the commissioning and stop the operation of sites and equipment in case of violation of the hygienic norms for the manufacture, storage, and sale of medicinal products – until the elimination of the violations;

3. block medicinal products in case of available documented information of discrepancies with the quality requirements; medicinal products imported or manufactured in infringement of this law; as well as medicinal products, which are offered in packaging non-complying with the requirements of this law; order the recall of such medicinal products from pharmacies and drugstores, wholesale warehouse, manufacturers, and healthcare establishments in case of necessity and notify for that the Ministry of Health;

4. give conclusions of the compliance of the controlled sites with the legal determined requirements;

5. issue orders, directions, and instructions in the filed of their competency, which shall be obligatory for all persons on the territory of the respective district.

(2) The compulsory administrative measures according to paragraph 1 or pursuant to art.270, paragraph 3 shall be imposed by an order of the director of RIPCPH,

(3) The orders according to paragraph 2 shall be subject to appeal under the terms of the Administrative Proceeding Code whereas the appeal shall not stop their execution.

Article 272. (1) The BDA shall:

1. prohibit the commissioning and stop the operation of sites and equipment in case of violation of the rules for Good Manufacturing Practice for medicinal products until the elimination of the violations;

2. prohibit the manufacture, import, export and trade with medicinal products, which directly or indirectly threaten the health of the population and shall order destruction, reprocessing or otherwise use of such medicinal products;

3. temporarily stop the operation of sites for wholesale and retail trade in medicinal products where the conditions under which the respective authorisation has been issued have not been fulfilled;

4. block medicinal products in case of available documented information of discrepancies with the requirements for: quality, efficacy, and safety, medicinal products imported or manufactured in infringement of this law, as well as medicinal products, which are offered in packaging with leaflets non-complying with the requirements of this law; order the recall of such medicinal products from pharmacies and drugstores, wholesale warehouse, manufacturers, and healthcare establishments in case of necessity and notify for that the Ministry of Health;

5. stop clinical trials in case of established violation until the elimination thereof or order heir termination;

6. issue orders, directions, and instructions, in the field of its competency, which shall be obligatory to persons.

(2) The compulsory measures according to paragraph 1 shall or pursuant to Art. 270, paragraph 3 shall be imposed by an order of the director of the BDA.

(3) The orders according to paragraph 2 shall be subject to appeal under the terms the Administrative procedure code whereas the appeal shall not stop their execution.

Article 273. (1) The conditions and order for taking samples, conduct of teats, and payment thereof shall be laid down in a regulation of the minister of health.

(2) Repeated tests shall be conducted in case of litigation of the results of conducted laboratory tests. These shall be conducted upon a written request by the interested party made within 7 days of the date of receipt of the results of the initial test.

(3) The repeated tests according to paragraph 2 shall be conducted by experts appointed by the executive director of the BDA who have not participated in the initial test and in the presence of a representative on the interested party.

Article 274. (1) The conditions and order for blocking and recall of medicinal products, which have shown discrepancies with the requirements to quality, efficacy, and safety shall be paid down in a regulation of the minister of health.

(2) The conditions and order for destruction, reprocessing, and otherwise use of medicinal products shall be paid down in a regulation of the minister of health.

Article 275. (1) During exercising control, the BDA shall undertake all necessary measures to ensure correct validation of the processes of manufacture and purification of the medicinal products obtained from human blood or human plasma, consistency of batch quality, and guaranteeing the absence of specific viral contamination in so far as technology allows.

(2) Manufacturers shall notify the BDA of the method used for decreasing or elimination of pathogenic viruses, which can be transmitted through medicinal products obtained from human blood or human plasma.

(3) The BDA shall test or forward to another official laboratory for control of medicinal products in Republic of Bulgaria or another Member State samples of bulk product and/or medicinal product for a test or in the course of assessment of an application for marketing authorisation according to Article 46, paragraph 1, point 2, or after issuing a marketing authorisation.

Article 276. The executive director of the BDA shall temporarily stop, bereave, or amend by an order the marketing authorisation of a medicinal product or its registration where it shall be established that:

1. there is an inadmissible adverse drug reaction during correct use or

2. there is lack of therapeutic efficacy (lack of therapeutic shall be where it has been established that the declared therapeutic results cannot be achieved at its marketing authorisation), or

3. the benefit/risk ratio is unfavourable during correct use, or

4. the quantitative and qualitative composition of a medicinal product does not comply with that declared at the marketing authorisation, or

5. the data in the dossier according to Articles 27 - 32 are untrue, or

6. the data in the dossier according to Articles 27 - 32 have not been supplemented of amended in compliance with the requirements of chapter three, section six, or

7. the control tests are not conducted in compliance with the methods laid down in Article 27, paragraph 1, т. 8, or

8. the data on the packaging and/or leaflet is not in compliance with those approved at the issuing of the marketing authorisation.

Article 277. (1) The executive director of the BDA irrespective of the measures according to Article 276, shall prohibit by an order the supply with the medicinal product and shall order its blocking and recall from the market where:

1. there is an inadmissible adverse drug reaction during correct use or

2. there is lack of therapeutic efficacy, or

3. the benefit/risk ratio is unfavourable during correct use, or

4. the quantitative and qualitative composition of a medicinal product does not comply with that declared at the marketing authorisation, or

5. the control of the medicinal product and/or its ingredients and on the intermediate stages of the manufacturing process has not been done or the requirements under which the manufacture authorisation ahs been granted are not met.

(2) The executive director of the BDA can also impose a ban according to paragraph 1 on concrete batches of a medicinal product.

Article 278. (1) The executive director of the BDA shall, by an order, temporarily stop or bereave the marketing authorisation of a group of or all medicinal products, for which the requirements as regards the place manufacture for which the manufacturing authorisation has been granted are not met.

(2) The executive director of the BDA besides the measures according to Article 276, can, by an order, temporarily stop the import of a group of or all medicinal products from third countries or bereave the issued import authorisation for a group of or all medicinal products where these do not comply with the requirements of chapter five.

(3) The executive director of the BDA besides the measures according to Article 276, can, by an order, temporarily stop or bereave the manufacturing authorisation for a group of or all medicinal products, which are not in compliance with the requirements of chapter five.

Article 279. (1) The orders according to Articles 276, 277, or 278 shall be delivered to the marketing authorisation holder, the manufacturer, or importer, respectively.

(2) The orders according to paragraph 1 shall subject to appeal under the terms of the Administrative procedure code and the appeal does not stop their execution.

Article 280. (1) In case that infringement of the provisions of chapter eleventh, respectively of the regulation according to Article 249 are established, executive director of the BDA shall order termination of the proliferation of advertising.

(2) By the order according to paragraph 1 the executive director of the BDA can oblige the advertiser to publish or proliferate in a manner coordinated with the BDA a disclaimer of the statements in the advertising through the same media and in the same format and volume.

(3) The order according to paragraph 2 shall be subject to appeal under the terms of the Administrative procedure code.

Chapter Fourteen

ADMINISTRATIVE PENAL PROVISIONS

Article 281. (1) Whoever manufactures, imports, sells, stores, or provides for use in Republic of Bulgaria medicinal products, which have no marketing authorisation, except for the cases according to Articles 8, 9, and 10, shall be penalized with a fine from BGN 10,00 to BGN 50,000, if not subject to more severe penalty.

(2) The same penalty shall also be imposed on the persons who manufacture, import, sell, or permit the use in Republic of Bulgaria of medicinal products, which do not comply with the requirements of the acting pharmacopoeia and the conditions of their marketing authorisation.

(3) Where the infringements according to paragraphs 1 and 2 are associated with unauthorised medicinal products containing narcotic substances or in case repeated perpetration the authorisation issued under the terms of this law shall be bereaved provided that the deed shall not constitute a crime.

(4) Medical specialists who manufacture, sell, or provide for use unauthorised medicinal products shall be deprived of the right to exercise the profession for a term of 6 months to two years.

(5) The penalty according to paragraph 4 shall be imposed by and order of the minister of health according to a proposal by the executive director of the BDA.

Article 282. (1) Whoever sells medicinal products in packaging or with patient information leaflets, which do not comply with the requirements of this law, shall be penalized with a fine from BGN 750 to BGN 1,500 and in case of a repeated perpetration of the same infringement - with a fine from BGN 1,500 o BGN 3,000.

(2) Whoever sells medicinal products without patient information leaflets shall be penalized with a fine from BGN 750 to BGN 1,500 and in case of a repeated perpetration of the same infringement - with a fine from BGN 1,500 to BGN 3,000.

Article 283. (1) Whoever imports, trades with, or provides for same medicinal products with expired validity term shall be penalized with a fine from BGN 10 000 to BGN 20 000.

(2) Whoever breaks the primary/secondary packaging or sells/provides medicinal products with broken primary/secondary packaging shall be penalized with a fine from BGN 750 to BGN 1500 and in case of a repeated infringement with a fine from BGN 1,500 to BGN 3,000.

Article 284. (1) Whoever manufactures, imports, or conducts wholesale with medicinal products, or sells without respective authorisation or in infringement of an issued authorisation shall be penalized with a fine from BGN 50,000.

(2)) Whoever manufactures, imports, or conducts wholesale with medicinal products, or sells without respective authorisation or in infringement, or sell, storage or provides medicinal products, which of uncertain origin, shall be penalized with a fine from BGN 25,000 to BGN 50,000.

(3) In the cases according to paragraph 1 the bodies of the state control shall stop the operation of the site by an order.

(4) The order according to paragraph 3 shall be subject to appeal under the terms of the Administrative procedure code; however, the appeal shall not stop its execution.

Article 285. (1) Whoever trades in medicinal products without certificate of batch release shall be penalized with a fine from BGN 5,000 to BGN 10,000 and in case of repeated perpetration of the same infringement – with a fine from BGN 10,000 to BGN 20,000.

(2) A wholesaler who supplies drugstores with medicinal products outside the lists approved by the minister of health shall be penalized with a property sanction from BGN 3,000 to BGN 2500 to 5000 and in case of repeated infringement with a fine from BGN 5,000 to BGN 10,000.

(3) A qualified person who has permitted sale of batches of medicinal products without certificate of batch release of any separate batch shall be penalized with a fine from BGN 2,500 to BGN 5,000.

Article 286. (1) In case of clinical trials conducted in infringement of this law, provided no crime has been committed, the guilty persons shall be penalized with a fine from BGN 5,000 to BGN 10000 and in case of repeated permission or commitment of the same infringement – with a fine from BGN 10000 to BGN 20000.

(2) Medial specialists who have permitted or committed infringements according to paragraph 1 can be imposed the penalty of "deprived of the right to exercise the profession" for a term from 6 months to two years.

(3) The measure according to paragraph 2 shall be imposed by the minister of health according to a proposal by the executive director of the BDA.

Article 287. (1) Whoever conducts retail trade in medicinal products without having respective authorisation/certificate shall penalized with a fine from BGN 5,000 to BGN 10,000.

(2) The penalty according to paragraph 1 shall also be imposed on persons who conduct retail trade in pharmacy or drugstore after the authorisation/certificate has ceased to be in effect.

(3) Whoever sells in a drug store medicinal products outside the lists according to Article 238, paragraph 1, and by repeated perpetration of the infringement the issued registration of the drug store will be deprived.

(4) In the cases according to paragraphs 1 and 2, the bodies of the state control on the medicinal products shall stop the operation of the site by an order.

(5) The order according to paragraph 4 shall be subject to appeal under the terms of the Administrative procedure code; however, the appeal shall not stop its execution.

(6) In case of established infringements according to paragraphs 1 and 2, the minister of health can deprive the respective medical specialist of the right to exercise the profession for a term of up to two years.

Article 288. (1) A retailer in medicinal products who has permitted an incapable person to exercise activities, pointed out in Art. 219, shall be penalized with a property sanction from BGN 5,000 to BGN 10,000 and in case of repeated perpetration of the infringement the issued retail trade authorisation shall be bereaved.

(2) In the cases according to paragraph 1 the bodies of the state control shall stop the operation of the site by an order.

Article 289. Whoever sells medicinal products on prices different from those formed under the terms of this law shall be penalized with a fine from BGN 5,000 to BGN 10,000 and in case of repeated perpetration of the same infringement – with a fine from BGN 6,000 to BGN 12,000.

Article 290. (1) Whoever advertises medicinal products, which are not authorised under the terms this law and/or ascribes or directs properties associated with prophylaxis or diagnostics, or treatment of diseases in man shall be penalized with a fine from BGN 10000 to BGN 20000.

(2) Whoever advertises medicinal products in infringement of this law shall be penalized with a fine from BGN 10000 to BGN 20000.

(3) The penalties according to paragraph 2 shall also be imposed on persons who have permitted the emission, publication, and proliferation of the advertisement.

Article 291. (1) Property sanctions shall be imposed in case the infringements according to Articles 281-287, Article 289, Article 290, Article 292 and Article 294 have been committed by legal persons or sole traders in amount of the property sanction cannot be less than the triple amount of the respective fines and cannot be more than the triple amount of the stipulated maximum amounts of the respective fines.

(2) For infringements according to Article 289 the property sanction shall be the nine-fold amount of the overdrawn amount provided that it exceeds the maximum amount of the sanction according to paragraph 1.

(3) The imposing of a property sanction shall not exclude fining of the guilty officials.

(4) The imposing of property sanctions shall not exclude the imposing of the stipulated measures regarding the right of the medical specialists and qualified persons.

Article 292. (1) Whoever shall not execute an order, directions, or instruction of the bodies of the state control, except in the cases pursuant to Article 270, paragraph 1, issue 2 and paragraph 3 shall be penalized with a fine from BGN 1,500 to BGN 3,000.

(2) For failure to execute an order, pursuant Article 270, paragraph 1, issue 2 and 3, the blamed persons shall be penalized with a fine of from BGN 500 to BGN1000.

Article 293. (1) In cases according Article 281, paragraph. 1-3, Article 283, paragraph 1, as and of non-observance of the condition under which the authorisations to retail trade with medicinal products the minister of health shall issue an order for the bereavement thereof.

(2) In case of non-observance of the conditions under which the authorisations/certificates for manufacture, import, parallel import, wholesale trade in medicinal products, or for registration of drugstore and as in the cases according to Articles 281, paragraph 1-3, and Article 283, paragraph 1 and 287, paragraph 3 the executive director of the BDA shall issue an order for the bereavement thereof.

(3) In case of non-observance of the obligation to notify according to Article 204, paragraph 3, for the termination of the activity on the part of a wholesaler of medicinal products,

the executive director of the BDA shall issue an order for the bereavement the issued authorisation.

(4) In case of non-observance of the obligation to notify according to Article 235, paragraph 3, for the termination of the activity on the part of a holder of an authorisation to retail trade with medicinal products, the minister of health shall issue an order for bereavement of the issued authorisation.

(5) The orders according to paragraphs 1 - 4 shall be subject to appeal under the terms of the Administrative procedure code, however, the appeal shall not stop their execution.

Article 294. Whoever infringes the provisions of this law or the regulations for its implementation, except for the cases according to Articles 281-293, shall be penalized with a fine from BGN 1,000 to BGN 3,000 and in case of repeated perpetration of the same infringement – with a fine from BGN 3,000 to BGN 5,000.

Article 295. (1) The infringements according to this law shall be established by virtue of deeds drawn up by state inspectors of the BDA or of the RIPCPH

(2) The infringements according to Article 289 shall only be established by officials appointed by the minister of health.

(3) The penal ordinances shall be issued by the minister of health, the chief state health inspector, and the directors of the BDA and RIPCPH depending on the subjection of the official, who has established the infringement.

Article 296. The drawing of the deeds and the issue, appeal and the execution of penal ordinances shall be made in compliance with the provisions of the Law on Administrative Infringements and Penalties.

Article 297. In the cases pursuant Article 281, 282, 283, 284, 285 and 287 the penalty body enact a bereavement of the medicinal products for state benefit, the subject of the infringement by rules and order, determined in a regulation by the minister of health.

ADDITIONAL PROVISIONS

§ 1. Within the meaning of this law:

1. "Active substance" shall mean any substance (ingredient) intended to be used as a pharmacologically active ingredient of a pharmaceutical form.

2. "Bioequivalence" shall be in place where medicinal products are pharmaceutically equivalent or pharmaceutical alternatives and if their bioavailabilities after administration of the same molar dose are similar to such extent that their effects with respect to efficacy and safety are essentially similar.

3. "Bioavailability" shall mean the rate and degree at which an active substance or its therapeutically active part is absorbed from the pharmaceutical form and it becomes available at its site of action. Where the medicinal substance is intended to exert a systemic therapeutic effect, bioavailability shall mean the rate and degree at which the medicinal substance or its therapeutically active part is released from the pharmaceutical form and passes into the total circulation.

4. "Researcher's brochure" shall mean the aggregate of clinical and non clinical data of tests of medicinal product(s), which are relevant to the clinical test of the product(s) in man.

5. “Valid documentation” shall mean any documentation which is compliant with the requirements laid down in a give procedure pursuant to this Law both with respect to content and completeness.

6. “Substance with well established use in medical practice” shall mean a substance to which the following criteria can be applied:

a) the period for proving the well established use in medical practice is not less than 10 years from the date of the first systematized and documented use of the substance as a medicinal product in the European Union or in the European Economic Area;

b) quantitative aspects of the use of the substance, taking into consideration the degree of use in medical practice, the degree of use on geographical principle, and the degree of follow-up through the pharmacovigilance system including pre- and postmarketing studies and published scientific literature for epidemiological studies and comparative epidemiological studies in particular;

c) high degree of scientific interest in the use of the substance (number of scientific publications) and coherence in scientific assessments.

7. “Outer packaging” shall mean the packaging, which does not come in immediate contact with the medicinal product.

8. “Contracting authority” shall mean a natural or legal person, institution, or organization responsible for the start-up, management, and/or financing of a clinical test.

9. “Generic medicinal product” shall mean a medicinal product, which has the same qualitative and quantitative composition as regards the active substances and the same pharmaceutical form as the reference medicinal product and its bioequivalence compared to the reference medicinal product has been proven in adequate bioavailability studies. Various immediate release oral pharmaceutical forms shall be regarded as the same pharmaceutical form. Various salts, esters, ethers, isomers, mixtures of isomers, complexes, or derivatives of an active substance shall be regarded as the same active substance except if these are significantly different in respect of safety and/or efficacy.

10. “Principal researcher” shall mean an appointed by the contracting authority medical doctor or doctor in dental medicine who is managing the overall conduct of a clinical test in compliance with an approved protocol and the rules for Good Clinical Practice and is responsible for the work of the researchers.

11. “Defined daily dose” shall be the mean daily maintenance dose of a given medicinal product, which administered to adults according to the main indication of a medicinal product.

12. “Good clinical practice” shall mean the aggregate of internationally recognized ethical and scientific quality requirement, which shall be observed during the planning, conduct, accounting, and reporting of clinical trials.

13. “Good laboratory practice” shall mean a system of rules in respect if the conditions for planning, processes of organizing, conduct, follow up, and documenting of laboratory tests.

14. “Good manufacturing practice” shall mean a system of rules encompassing all aspects of manufacture: personnel, premises, equipment, materials, documentation, and quality control and has the purpose of ensuring safety, efficacy, and compliance with a specification.

15. “Member State” shall mean a state member of the European Union.

16. “Labelling” shall mean information on the immediate or outer packaging of a medicinal product.

17. ”Immunological medicinal product” shall mean a medicinal product, which contains vaccines, toxins, sera, or allergens. Agents used to create active immunity or establish a condition of immunity or invoke passive immunity shall be involved in the scope of vaccines, toxins, and sera. Allergens shall mean medicinal products, which are intended to identify or stimulate specific purposeful change in the immunological response to an allergens agent.

18. “Bioequivalence study” shall mean a clinical test aimed at proving that two medicinal products are bioequivalent provided that they are pharmaceutically equivalent or pharmaceutical alternatives and provided that their bioavailability after administration of the same molar dose are similar to a degree, which is a condition for equivalence in respect of efficacy and safety.

19. “Bioavailability study” shall mean a clinical test aimed at showing what is the rate and degree which an active substance or a therapeutically significant part of a studied medicinal product reach from the pharmaceutical form to the systemic circulation of the blood.

20. “Study medicinal product” shall mean a pharmaceutical form of an active substance or placebo, which are investigated or used as comparators in a clinical test including products with granted marketing authorisation but are used in an unauthorised indication or with a view of obtaining additional information for an authorised form, or are made up (in a pharmaceutical form or packaged) in a manner, which is different from the authorised form.

21. “Researcher” shall mean an appointed by the contracting authority and the principal researcher medical doctor or doctor in dental medicine who practically conducts a clinical test under the management of a principal researcher in compliance with an approved protocol and the guidelines for Good Clinical Practice in an investigational site for the conduct of a clinical test. If a clinical test is not conducted by a team, the researcher shall be the manager responsible for the team and shall be called principal researcher.

22. „Informed consent” shall mean a decision to participate in a clinical test, which must be in writing, dated and signed and taken freely by any person capable of giving his consent or – where a person is incapable of giving his consent by his legal representative after being duly informed about the essence, importance, consequences and risks of a clinical test and documented in an adequate manner.

23. “Kit” shall mean any substance, which – usually before use – shall be dissolved, suspended, diluted, or combined with radionuclides as a result of which procedure the finished radioactive medicinal product is obtained.

24. “Clinical test of a medicinal product” shall mean any study in man intended for discovering or confirming clinical, pharmacological, and/or other pharmacodynamic effects of one or more study medicinal products, and /or for determination of the adverse reactions to one or more study medicinal products, and/or for studying the absorption, distribution, metabolism, and excretion of one or more study medicinal products with the purpose of establishing their safety and/or efficacy.

25. “Clinical advantage” shall mean a significant therapeutic or diagnostic advantage of a medicinal product compared to a medicinal product, which has already received marketing authorisation.

26. „Coordinating researcher” shall mean a researcher appointed for the purpose of coordinating the researchers or various sites participating in a multicentre test.

27. “Patient information leaflet” shall mean a leaflet accompanying a medicinal product and containing information for the customer.

28. ”Medicinal product obtained from human plasma or human blood” shall mean a medicinal product produced from human blood constituents and by a method involving industrial

process. The following shall be ascribed to this group: immunoglobulins, coagulating factors and antiproteases, solutions of plasma proteins, and other plasma fractions and combinations thereof.

29. “Medicinal product intended for treatment, prophylaxis, and diagnostics of rare diseases” shall mean a product, which:

а) is intended for diagnostics, prophylaxis, or treatment of life-threatening diseases or chronic diseases taking progressive course, which affect not more than 5 of 10,000 people on the territory of a state or

б) is intended for diagnostics, prophylaxis, or treatment of life-threatening diseases and severely health damaging chronic disease (diseases with high percentage of disease-related incapacity of work or disability) and are there is evidence appended that the sale of the product does ensure satisfactory return, which can justify the required investment for scientific research and development without having stimuli for the creator of the product, and

в) where the is no satisfactory method of diagnostics, prophylaxis, or treatment of a given condition or where there is such method the proposed medicinal product has significantly more advantages and benefits for the people affected by this condition.

30. "Pharmaceutical form" shall mean an adequate for intake structure containing active substance(s), which can include or cannot include excipients and which is obtained through application of certain technological operations ensuring the desired healing effect and stability at storage within the expiry term.

31. “Person established on the territory of a Member State or a state of the European Economic Area” shall mean a legal subject registered according to the civil or trade legislation of a Member State or a state of the European Economic Area or established pursuant to a normative act and having place of business in a Member State or a state of the European Economic Area.

32. “Magisterial formula” shall mean a prescription for a medicinal product prepared in a pharmacy according to a prescription of a medical specialist or according to an established recipe and intended for a definite patient.

33. "International non-proprietary name" shall mean a recommended name of an active substance approved and published by the World Health Organization.

34. “Medical specialists” shall mean medical doctors, doctors in dental medicine, masters of pharmacy, nurses, midwives, medical laboratory assistants, medical auxiliaries and pharmacy assistants.

35. “Medical trade representative” shall mean a person who has passed special training and possessing scientific knowledge for the presentation of accurate and comprehensive information about the medicinal product he is advertising.

36. “Multicentre clinical test” shall mean a clinical test, which is conducted according to a single protocol but in more than one site and by more than one researcher. Researcher sites can be situated in the territory of one Member State, more than one Member State, and/or in Member States and third states.

37. „Name of a medicinal product” shall mean the name given to a medicinal product, which can be:

a) a freely selected name (trade name);

b) a common name together with the trade mark or manufacturer’s name;

c) scientific name together with the trade mark or manufacturer’s name.

38. "Scientific literature" shall mean publication(s) of results from scientific research in specialized international scientific editions.

39. “New active substance” shall mean:

a) chemical, biological, or radiopharmaceutical substance, which has not been authorised to market in the European Union as a medicinal product;

b) isomer, mixture of isomers, complex or derivative or salt of a chemical substance, which has been authorised to market in the European Union as a medicinal product but is different with respect to safety and efficacy from a formerly authorised substance;

c) biological substance, which has been authorised to market in the European Union as a medicinal product but has different molecular structure, different origin with respect to the starting material, or has been obtained through a different manufacturing process;

d) radiopharmaceutical substance the radionuclides or molecular bonds (ligands) of which have not been authorised in the European Union as a medicinal product or the mechanism of bonding in a couple of the molecules and radionuclides has not been authorised in the European Union.

40. “Adverse event” shall mean any untoward unfavourable change the health condition observed during the administration of a medicinal product in a patient or a clinical test subject and which has not necessarily a causal relationship with this treatment.

41. “Adverse drug reaction” shall mean any untoward and unpredicted response to a medicinal product, which occurs during the administration of a product in doses normally used for treatment, prophylaxis, or diagnostics of a disease in human subjects or for correction or modification of a physiological function. In case of a clinical test – any untoward and unpredicted response to a study medicinal product irrespective of the administered dose. The types of adverse reactions shall be:

a) “unexpected” – an adverse drug reaction, which has not been mentioned in the summary of product characteristics of the character, severity, and outcome of which do not comply with those mentioned in the summary of product characteristics. In case of a clinical test – an adverse drug reaction the character, severity, and outcome of which do not comply with the information for the study medicinal product mentioned in the researcher’s brochure;

b) “suspected” – and adverse drug reaction fore which the reporter or the marketing authorisation holder supposes that there is a possible causal relationship with a taken medicinal product;

c) “serious” – any unfavourable effect on the health condition, which has become the reason for a lethal outcome, immediate threat to life, hospitalization, or prolongation if hospitalization, significant or durable injury, disability, and innate anomalies;

d) combination of reactions according to subsections “a”, “b”, and “c”.

42. “Common name" shall mean the international non-proprietary name (INN) of a medicinal substance or excipient recommended by the World Health Organization; if not any, the name in the European Pharmacopoeia shall be used; if there is no such name there, another pharmacopoeia name shall be used; if there is no pharmacopoeia name, the common name shall be used.

43. "Batch" shall mean a definite quantity of a medicinal product manufactured according to an established reproducible technological scheme ensuring the required batch homogeneity with respect to the required quality characteristics.

44. “Maintenance of a marketing authorisation” shall include all required activities with regard to the maintenance of an updated registration status of a medicinal product including pharmacovigilance.

45. “Benefit” shall mean a positive result/therapeutic efficacy of a medicinal product for a definite patient, patient group, or the society. Quantitative assessment of the anticipated benefit shall include approximate calculation of the probability of this positive result.

46. "Excipient" shall mean a substance complying with a given specification, with definite quality characteristics, which is included in the composition of a pharmaceutical form and ensures the structure, stability, and regulates its activity.

47. “Postmarketing study” shall mean any study conducted during the use of a medicinal product within the approved summary of product characteristics during the period after the authorisation to market.

48. “Postmarketing safety study” shall mean a pharmaco-epidemiological study or a clinical test conducted in compliance with the conditions of a marketing authorisation aimed at the identification or quantitative assessment or the risks associated with the use of a product in the clinical practice.

49. “Potential serious risk for the population” shall exist where there is a high probability a medicinal product to cause irremovable, irremediable, and irreversible consequences. The assessment process shall identify the threat of causing damages to the health of the population and its actual exposition during wide use of the product. The serious risk for the health in the context of the use of a given medicinal can be assessed under the following conditions:

a) efficacy – the submitted therapeutic efficacy data with regard to the proposed indication(s), the proposed target group, and the proposed dosage mentioned in the proposed patient information leaflet do not scientifically defend to the full extent the efficacy claims;

b) safety – the assessment of the data for preclinical toxicity/pharmacological safety and clinical safety cannot convincingly defend the conclusion that all potential safety aspects with regard to the target patient group(s) have been accurately and comprehensively reflected in the proposed patient information leaflet or the absolute risk degree is unacceptable;

c) quality – the proposed method of manufacture and control methods cannot guarantee the lack of an essential defect in the quality of the product, which can affect the product safety and/or efficacy;

d) benefit/risk ratio: the assessment of the benefit/risk ratio and the potential benefit for the proposed indication(s) and the patient group(s).

50. “Representative of the person according to Article 26, paragraph 1, or of a marketing authorisation holder” shall mean a person residing on the territory of the Republic of Bulgaria appointed by the person according to Article 26, paragraph 1, or by the marketing authorisation holder to represent them before the regulatory bodies on the territory of the Republic of Bulgaria.

51. "Acceptable safety level" shall be in place where the submitted data shall be accepted as statistically reliable safety according to clinical trials conducted in compliance with the Good Clinical Practice.

52. "Manufacture of a medicinal product" shall mean all operations relating to the supply of materials, their processing during the manufacturing process including packaging and labelling, quality control, batch release, storage, shipment, and operations control relating there to.

53. “Clinical test protocol” shall mean a document describing the purpose(s), design, methodology, statistical processing, and organization of a clinical test. The protocol shall also include all subsequent amendments thereto.

54. “Placing on the market” shall mean the distribution of a medicinal product in the trade network on the territory of the Republic of Bulgaria outside the direct control of the marketing authorisation holder.

55. "Immediate packaging" shall mean the packaging, which enters in immediate contact with a product.

56. “Radiopharmaceutical” shall mean a medicinal product, which when in a ready for use form contains one or more radionuclides (radioactive isotopes) included with medical purpose.

57. “Radionuclide generator” shall mean any system, which includes a fixed maternal radionuclide from which a filial radionuclide is obtained, which is separated by elusion or other methods and is used in a radiopharmaceutical.

58. “Radionuclide precursor” shall mean any other radionuclide manufactured for radioactive marking of another substance immediately before its introduction in a patient’s body.

59. “Herbal medicinal product” shall mean a medicinal product containing as active ingredient one or more herbal substances or one or more herbal preparations, or one or more herbal substances in a combination with one or more herbal preparations.

60. “Herbal substances” shall basically mean plants or parts of plants, seaweed, mushrooms, and lichens, which are whole, broken, or cut, usually dried or sometimes fresh. Certain exudates, which have not been subjected to specific processing, shall also be assigned to the herbal substances. Herbal substances shall have be accurately defined botanical scientific name of the plant wherefrom they originate according to the binominal system (species, sort, variety, and author).

61. “Herbal preparation” shall mean the product obtained after extraction, distillation, pressing, fractionation, purification, concentration, or fermentation of herbal substance. The herbal preparation can also represent ground or powdered herbal substances, tinctures, extracts, essential oils, and processed herbal liquids/juices.

62. "Rare diseases" shall mean the diseases, which are characterized with incidence of not more than 5 in 10,000 of the population.

63. “Reference medicinal product” shall mean a medicinal product authorised under the terms of Article 23 in compliance with the requirements of Article 27.

64. “Reference value of a defined daily dose” on an international non-proprietary name with the corresponding pharmaceutical for according to the anatomo-therapeutic classification of medicinal products shall mean the lowest value of a defined daily dose determined on the basis of the values of a defined daily dose for various medicinal products for the international non-proprietary with the corresponding pharmaceutical form according to the anatomo-therapeutic classification of medicinal products.

65. “Reference value of a therapeutic course” shall be the lowest value of a therapeutic course determined on the basis of the values of a therapeutic course of the medicinal products according to international non-proprietary name with the corresponding pharmaceutical form.

66. “Risk during the use of a medicinal product” shall mean:

a) risk for the health of the patient or risk for the health of the population, which is associated with the quality, safety, or efficacy of a medicinal product;

b) risk of undesirable effects on the environment.

67. “Serious adverse event” shall mean any unfavourable change in the health condition, which has become the cause of lethal outcome, immediate threat to life,

hospitalization or extension of hospitalization, significant or durable injury, disability, and innate anomalies.

68. "Batch release certificate" shall mean a document issued for each batch by the qualified person of the manufacturer or importer and shall include the requirements according to the specification, as well as all results from the tests for the release of the batch.

69. “Additional protection certificate” shall mean a document, which shall provide additional patent protection for a medicinal product of maximum 5 years after the lapse date of the main patent.

70. “Urgent limitation safety measures” shall mean temporary changes in the product information with respect of one or more parts of the summary of product characteristics, indications, method of administration, contraindications, and warnings, which result from new information associated with the safe use of a medicinal product.

71. “Spontaneous report” shall mean a voluntarily report for a suspected adverse reaction during the use of a medicinal product forwarded to the marketing authorisation holder, to the bodies for supervision on the medicinal products, or to other organizations, which is not originating from a study or another organized system for data capturing.

72. "Expiry period of a medicinal product" shall mean the interval of time during which, if a medicinal product is stored under the prescribed conditions, it shall comply with the specification developed on the grounds of stability tests of several batches of the finished form.

73. “Medicinal product equivalent to a herbal medicinal product” shall mean a product containing the same active substances irrespective of the composition of the excipients and which is intended for the same purpose, has equivalent quantity of the medicinal substance, the same dosage and the same or similar method of administration as the product for which an application has been submitted.

74. “Adverse drug reaction reports” shall mean documented information for one or more suspected adverse reactions associated with the use of one or more medicinal products by one patient. Required to recognize the validity of an adverse drug reaction report shall be minimum data for the identification of the reporter (initials or age, or date of birth, or gender) and data about the adverse reaction/event and the suspected medicinal product.

75. “Essential amendment in a clinical test protocol” shall mean any amendment in the protocol and/or in the information of the accompanying documentation, which can affect:

a) the safety or physical and mental validity of the participants;

b) the scientific value of the study;

c) the conduct or the organization of the study;

d) the quality or the safety of any study medicinal product.

76. “Third country” shall mean a state outside the Member States of the European Union, the European Economic Area, and the Confederation of Switzerland.

77. "Wholesale distribution" shall mean all activities for the acquisition, storage, supply, import, or export of medicinal products except for the cases of provision of medicinal products directly to the population.

78. ”Subject” shall mean a person taking part in a clinical test irrespective whether taking the study medicinal product or a medicinal product used for comparison.

79. “Vulnerable patient groups" shall mean persons whose wish to participate in s clinical test can be affected by the anticipation of benefits or affected by eventual penalty on the part of higher officials in the hierarchical structure associated with the person’s participation or refusal to participate in the clinical test. Examples of such group in the hierarchical structures shall be students in medicine, pharmacy, dental medicine or nursing, laboratory personnel,

employees in the pharmaceutical industry, members of the armed forces or persons deprived of freedom. Other vulnerable groups shall be patients with incurable diseases, persons in hospices, unemployed and beggars, patients in critical conditions, waifs and strays, under-aged and minors and persons who are unable to give consent.

80. "Pharmacopoeia" shall mean a collection of approved specifications and respective requirements in connection with the manufacture, investigation, storage, and marking of active substances, excipients, pharmaceutical forms, packaging materials, and components of the medicinal products.

81. "Pharmacopoeia recipe" shall mean a prescription for a medicinal product prepared in a pharmacy according to a recipe from an acting pharmacopoeia and intended for provision to the patients in the same pharmacy.

82. "Homeopathic medicinal product" shall mean a medicinal product prepared from substances called homeopathic source according to the manufacturing procedures of the European Pharmacopoeia and – in the absence of such – according to the national pharmacopoeia of a Member State.

83. "Price calculated on the basis of a referent value" shall be the price formed for any medicinal product included in the Positive Drug List calculated on the basis of the determined reference value for a defined daily dose or therapeutic course.

84. "Site" shall mean a structure in a healthcare establishment where a clinical test is conducted.

85. "Abuse of medicinal products" shall mean permanent or incidental intentional excessive use of medicinal products accompanied by noxious physical or mental effects.

§ 2. The name of the Executive Drug Agency shall be written in Latin as "Bulgarian Drug Agency".

§ 3. The Council of Ministers shall determine the conditions and order for the supply, storage and renewal of the medicinal products kept in the State Agency "State Reserve and War-time Reserves".

§ 4. This law shall implement the provisions of Directive 2001/83/EC of the European Parliament and the Council on the Community code relating to medicinal products for human use subsequently amended by Directive 2004/27/EC of the European Parliament and the Council

§ 5. The data protection periods for reference medicinal products shall be applied according to the provisions of Article 89 of Regulation (EC) № 726/2004 of the European Parliament and the Council and Article 2 of Directive 2004/27/EC of the European Parliament and the Council

TRANSITIONAL AND FINAL PROVISIONS

§ 6. The Law for the Medicines and Pharmacies in the Human Medicine (State Gazette, No 36 from 1995; No 61 from 1996 - Decision No 10 of the Constitutional Court from 1996; amended, State Gazette No 38 from 1998, No 30 from 1999, No 10 from 2000, No 37 from 2000 - Decision No 3 of the Constitutional Court from 2000; amended, State Gazette No 59 from 2000 , No 78 from 2000 - Decision № 7 of the Constitutional Court from 2000; amended, State Gazette No 41 from 2001, No 107 and 120 from 2002; amended, State Gazette No 2 from 2003; amended, State Gazette No 56, 71 and 112 from 2003, No 70 and 111 from 2004, No 37, 76, 85, 87, 99 and 105 from 2005, No 30, 31, 34, 75 и 105 from 2006) is repealed, with

exception of the Regulation of Article 10, paragraph 2, which is applied for term to one year since the day of the coming in the force of this Law.

§ 7. (1) The marketing authorisations fro medicinal products published before the entering into force of this Law under national procedure, which are authorised also in a Member States under centralised procedure shall cease to be valid as from 1 January 2007.

(2) The marketing authorisations for medicinal products issued up to the entering into force of this Law under national procedure shall be brought into line with the requirements at the date of their renewal.

(3) The marketing authorisations for medicinal products falling within the scope of Regulation (EC) 726/2004 of the European Parliament and the Council and which have issued marketing authorization under the terms of the repealed Law for Medicines and Pharmacies in Human Medicine as materially similar products, but which have no marketing authorisation in European Union under the centralised procedure shall cease to be valid.

(4) The medicinal products which have been issued marketing authorisation in the European Union under the centralised procedure, which national marketing authorisation is ceased under the terms of paragraph 1, can be sold on the territory of Republic of Bulgaria in packages and with leaflets according to the ceased national marketing authorisation for a time limit not longer than one year since the date of its cessation.

§ 8. (1) The setting up of ceiling prices and the registered prices under the terms of the repealed Law for Medicines and Pharmacies in the Human Medicine of the medicinal product, which have marketing authorisation in the European Union according to the centralised procedure, which national marketing authorisation is suspended under the terms of § 7, paragraph 1, remain in force for a time limit of one year from the date of its cessation.

(2) The setting up of ceiling prices and registered prices under the terms of the repealed Law for Medicines and Pharmacies in the Human Medicine of the medicinal products, other then those according to paragraph 1 remain in force for a time limit expiring on 31 December 2007.

§ 9. (1) The applications for marketing authorisation, renewal, modification of the published authorisation, which are submitted up to the entering into force of this Law are reviewed and closed according to the terms and the conditions provided for herein.

(2) The submitted applications and documentations for marketing authorisation for medicinal products falling within the scope of the procedure provided for in Article 74 and also according to Article 75 shall be brought into line with the requirements of this Law within three months from its entering into force.

(3) When in the case provided for in paragraph 2, the application and the documentation under paragraph 2 have not been brought into line with the requirements of this Law, the procedure of their review shall be terminated.

§ 10. (1) The clinical trials which were approved before this law comes in force shall be finished according to under the conditions prevailing hitherto.

(2) The applications for conduction of the clinical trial on the territory of Republic of Bulgaria are submitted, reviewed and closed according to the terms and conditions of this Law after the regulation according Article 82, paragraph 3 comes in force.

(3) The applications for amendments in approved clinical trials, which were submitted before this law comes in force, are reviewed and closed according to the terms and conditions provided for herein.

§ 11. The applications for publishing of the authorisations for manufacture and wholesale with medicinal products, which are submitted before this law comes in force are reviewed and are reviewed and closed according to the terms and conditions provided for herein.

§ 12. (1) The manufacturers of medicines, which received authorisation for manufacture under the terms of the repealed Law for Medicines and Pharmacies in the Human Medicine shall put their manufacture activity in compliance with the requirements of this Law according to the requirements of this Law regarding the qualified person according to Article 148, point 2 within three months of the entering into force of this Law.

(2) The established state manufacturers which shall carry out their activity according to their authorisations, issued under the terms of the repealed Law for Medicines and Pharmacies in the Human Medicine**.**

§ 13. (1) The persons, who have been granted authorisation for wholesale with medicines under the terms of the repealed Law for Medicines and Pharmacies in Human Medicine shall set their activity according to the requirements of this Law in term of 12 months after it is in force.

(2) Until the publishing of authorization for wholesale with medicinal products under the terms of this Law, but not later than the expiration of the term according to paragraph 1, the persons according the paragraph 1 shall carry out their activity based on the published authorization for wholesale with medicines under the terms of the repealed Law for Medicines and Pharmacies in the Human Medicine.

(3) With the publishing of the authorisation for wholesale with medicinal products, according to this Law, and also with expiration of the term according the paragraph 1, the published authorisation for wholesale with medicines under the terms of the repealed Law on Medicines and Pharmacies in Human Medicine is terminated.

§ 14. (1) The persons, who received authorization for wholesale with medicines under the terms of the repealed Law for Medicines and Pharmacies in Human Medicine may import medicinal products on the territory of Republic of Bulgaria from third countries based on this authorization till receiving of the authorization for import under the terms of this Law not more late than 12 months after it comes in force.

(2) In the term of one month since this law comes in force the persons according to paragraph 1 shall give in BDA the notification for the person who will fulfil the functions of the qualified person according to the Article 161, paragraph 2, point 1.

§ 15. The term for action of the authorisations for wholesale with medical devices, which are published under the terms of the repealed Law for Medicines and Pharmacies in Human Medicine is prolonged officially to 31 December 2007.

§ 16. (1) The M.Sc. Pharmacists who have approval for opening of pharmacy like sole trader, medicinal establishments, and also the municipalities, which correspond of the conditions according to Article 222, paragraph 5, which had received approval for opening of pharmacy under the terms of the repealed Law for Medicines and Pharmacies in the Human Medicine carry out their activity according to their published authorisations.

(2) Outside the cases according to paragraph 1 the established state pharmacies shall set their activity in compliance with its requirements in term of one year after this law comes in force.

(3) The persons, who fulfil retail commercial with medicinal products and who received authorization for opening of pharmacy under the terms of the repealed Law for Medicines and Pharmacies in the Human Medicine, submit in term according the paragraph 2 in the Ministry of Health application with sample, which is approved from the Minister of Health for re-registration in compliance with the requirements of this Law, at which they apply:

1. Certified copy from court decision for registration;

2. Actual certificate for inscribing in the commercial register;

3. Copy from the published authorization for opening of pharmacy under the terms of the repealed Law for the Medicines and Pharmacies in Human Medicine.

4. Document for only once paid fee in amount of 100 BGN.

(4) In the term according to paragraph 2 the M.Sc. Pharmacists which received license for retail commercial with medicinal products, which contain narcotic substances and their precursors give in together with the documents according to paragraph 3 application for change in the published license. The number of the authorisation for retail trade and storage of the medicinal product containing narcotic substances.

§ 17. (1) The established state drugstores till the moment when that Law comes in force carry out their activity based on their published authorisations under the terms of the repealed Law for the Medicines and Pharmacies in the Human Medicine.

(2) The applications for publication of the certifications, which are granted before the entering into force of this Law, are reviewed and closed under the terms and conditions provided for herein.

§ 18. Until coming into force the Positive Drug List, pursuant to paragraph 1 the medicinal products negotiation, based on Article 45, paragraph 4 and 5 of the |Law on Health Insurance shall be made at least once a year, in accordance with the current Positive Drug List at moment of starting the negotiating procedure.

§ 19. (1) Within three months after the entering into force of this Law:

1. The Council of ministers shall amend and supplement the ordinance for the structure of BDA in compliance with this law.

2. The minister of health shall issue regulation, pursuant Article 82, paragraph 3.

(2) In six month period of time, after the entering into force of this Law, the Council of Minister shall adopt and the minister of health shall issue the remaining legislative documents for the implementation of this Law.

§ 20. After the first two years of the mandate of the members of the committees according to Articles 104, 107, 259, and 261 half of the members whose mandate is terminated shall be elected by drawing lots.

.§ 21. In a year period of time of the entering into force of this Law, the BDA shall take the necessary actions for accreditation of the laboratory for control of the medicinal products and active substances BY the European Directorate for Quality of Medicines and Healthcare

§ 22. (In force from 14.04.2008) in the Law on Health Insurance (promulgated, SG, 70 of 1998; amended and supplemented, 93 and 153 of 1998, 62, 65, 67, 69, 110, and 113 of 1999, 1, 31, 64 of 2000, 41 of 2001, 1, 54, 74, 107, 112, 119, and 120 of 2002, 8, 50, 107, and 114 of 2003, 28, 38, 49, 70, 85, and 111 of 2004, 39, 45, 76, 99, 102, 103 and 105 of 2005, and

17, 18, 30, 33, and 34, 59, 95 and 105 from 2006 , 11 from 2007, 26 from 2007- Decision № 3 off the Constitution court of 2007):

1. In Article 45:

a) paragraphs 4, 5, 6, and 7 shall be repealed;

b) in paragraph 8 the shall be amended as follows:

(8) The terms and conditions for payment of the medicinal product, included in the Positive Drug List pursuant to Art. 262 of the Law of Medicinal Product in the Human Medicine, of medical devices and of the diet foot for special medical purposes are laid down with a regulation of the minister of health.

2. In Art 55, paragraph 2, shall be amended as follow:

7. The lists of the medical devices, diet foots for special medical purposes and the prices, fully or partially paid; condition of prescribing and receiving, medical devices and diet foots for special medical purposes.

§ 23 In the Law on Healthcare Establishments (promulgated, SG, 62 of 1999; amended and supplemented, 88, 113 и 114 of 1999, amended 36, 65 и 108 of 2000; Decision № 11 of the Constitutional Court of 2001 – 51 of 2001; amended and supplemented, 28 и 62 of 2002 , 83, 102 и 114 of 2003, 70 of 2004 , 46, 76, 85, 88 and 105 of 2005. and 30, 34, 59 and 105 of 2006 following amendments are maid.

1. In Art. 17 a new paragraph shall be introduced:

"(4) Clinical trials of medicinal products can be conducted in the diagnostic – consultancy centre under the terms of the Law on Medicinal Products in Human Medicine."

2. In Art. 26 new paragraph 4 shall be inserted:

(4) In the dispensary clinical trials of medicinal products can be conducted under the terms of the Law on Medicinal Products in Human Medicine.

§ 24. In § 14 Of Transitional and Final Provisions in the amended Law of the Law of the society organization of physicians and dentists (SG, N. 76 from 2005) following amendments and supplementation shall be made:

1. The text in Art 1 shall be amended as follow:

(1) The individual and group of practices for dental assistance, dentist and medico-dental centres, which are registered as traders under he Commercial Law or as a cooperative under the Law on Cooperatives, shall apply their names in compliance according § 2 of that Law and shall inscribe that change in the Commercial Register, Register BULSTAT and in the Regional health centre until 31 of December 2007.

2. New Articles 2, 3 and 4 are inserted:

The individual dental assistance practices, which are nor registered as traders upon the Commercial Law, shall apply their names in compliance with c § 2 of that Law and inscribe the change in the BULSTAT register and in the Regional health centre in the period provided in paragraph 1.

(3) The registration of the change of the name of the practices and the centres according to paragraph 1 in the Commercial Register and BULSTAT shall be carried out as follows:

1. until 1 of July 2007 - upon the rules in the Commercial Law, Law on the Cooperatives, Law of BULSTAT Register.

2. until 1 of July 2007 – under the procedures of the Commercial Register

(4) State fees for modification in the registration under paragraphs 1 and 2 shall not be required.

§ 25. In the Patent Law and Registration of the Useful Models (promulgated SG, 27 from 1993; amended, 83 from 1996, 11 from 1998, 81 from 1999, 45 and 66 from 2002 ,17, 30 and 64 from 2006) in Article 20, issue 7 is repealed

§ 26. In the Law of the society organisation of master of pharmacists SG, 75 from 2006, amended 105 from 2006, Article 5, point 9 shall be amended as follow:

"9. Provides statements for opening of pharmacies, pursuant Art. 228, paragraph 1, issue 9 from the Law on Medicinal Product in Human Medicine.

§ 27 In § 1, point 5 of the Additional provisions of the Law of human integration and the injures (promulgated SG, N81 from 2004, amended .,N. 28, 88, 94, 103 и 105 from 2005, N 18, 30, 33, 37, 63, 95, 97 and 108 from 2006) the second sentence shall be amended as follow "Medical devices are not auxiliary devices, installations and equipment ".

§ 28. In the Law on Excise Duty and Bonded Warehouses (promulgated, SG, No 91 of 2005; amended and supplemented, No 105 of 2005. and No 30 and 34, 63, 81, 105 and 108 from 2006 of 2006) the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

§ 29. In the Law on Genetically Modified Organisms (promulgated, SG, 27 of 2005; amended and supplemented, 88 and 99 of 2005 and 30 of 2006) the paragraph 2 in Art. 2, issue 3 the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

§ 30. In Law on the Protection of Customers (promulgated, SG, No 99 of 2005; amended and supplemented, No 30 and 51, 53, 59, 105 and 108 of 2006 г.) in Art. 186, paragraph 2, issue 4 the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

§ 31. The following amendments shall be introduced in the Law on Health (promulgated, SG, 70 of 2004; amended and supplemented, 46, 76, 85, 88, 94 and 103 of 2005 and 18, 30, and 34, 59,71,75, 81,95 and 102 of 2006):

1. In Article 4 the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

2. In Article 21, paragraph 3, the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

§ 32. The following amendments shall be introduced in the Law on the Control of Narcotic Substances and Precursors (promulgated, SG, 30 of 1999; amended and supplemented, 63 of 2000, 74, 75, and 120 of 2002, 56 of 2003, 76, 79, and 103 of 2005, and 30,75 and 82 of 2006):

1. In Article 32, paragraph 3 the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

2. In Article 33, paragraph 1, item 1 the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

3. In Article 34 after the word "issued" the words "on master of pharmacy" are deleted.

4. In Article 39, paragraph 2 the words „Article 55, item 2 of Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Article 197, paragraph 2 of Law on Medicinal Products in Human Medicine".

5. In Article 44 a, paragraph 3 is deleted.

6. In Article. 44b the words master of pharmacy are deleted.

7. In § 1, item 14 of the Additional provision the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

§ 33. In the Law on Blood, Blood Donation, and Blood Transfusion (promulgated, SG, 102 of 2003; amended and supplemented, 70 of 2004 and 30 and 65 of 2006) in Article 8, paragraph 4, the words „Law on Drugs and Pharmacies in Human Medicine" shall be replaced by „Law on Medicinal Products in Human Medicine".

§ 34. In Article 140 of Law on Preservation of the Environment (promulgated, SG, 91 of 2002; correction, 98 of 2002; amended and supplemented, 86 of 2003, 70 of 2004, 74, 77, 88, 95, and 105 of 2005, and 30,65, 82, 99, 102 and 105 of 2006.) in the Article 140 after the words „pharmaceutical products and medical devices" the expression „within the meaning of the Law on Medicinal Products in Human Medicine" shall be added and the words „within the meaning of § 1, item 40 of the additional provisions of the Law on Drugs and Pharmacies in Human Medicine and medical devices " shall be deleted.

§ 35. In Law on Foods (promulgated, SG, 90 of 1999; amended and supplemented, 102 of 2003, 70 of 2004, 87, 99, and 105 of 2005 and 30, 31, 34, and 51,55 and 96 of 2006) in Art.2, paragraph 3, issue 4 shall be amended:

"4. medicinal product within the meaning of the „Law on Medicinal Products in Human Medicine".

§ 36 Until coming into force of the provisions pursuant to § 19 the issued normative acts for applying the repealed "Law on Medicinal Products and Pharmacy in Human Medicine" shall be applied, until they shall not contradict to that Law.

§ 37. This law shall take effect as from the date of is promulgation in State Gazette, except § 22, which shall take effect after one year from the date of the promulgation of this Law,.

This law has been adopted by the 40 National Assembly on 30 of March 2007 and has been sealed with the official seal of the National Assembly.

Relevant legislative Documents from the European Legislation:

Directive 2001/83/EC OF THE EUROPEAN PARLIAMENT AND THE COUNCIL of 6 November 2001 on the Community code relating to medicinal product for human use

DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use

DIRECTIVE OF COUNCIL 93/16/EEC of 5 April 1993 to facilitate the free movement of doctors and the mutual recognition of their diplomas, certificates and other evidence of formal qualifications.

COUNCIL DIRECTIVE FROM 14 OF JUNE 1989 extending the scope of application of the Directive 65/65/EEC and (89/381/EEC) and 75/319/EEC for the approximation of the laws,

regulations and administrative provisions regarding the medicinal products and establishing specific provisions for the medicinal products derived from human blood and plasma

COUNCIL DIRECTIVE 87/18/EEC OF 18 DECEMBER 1986 on the harmonization of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for trials on chemical substances.

COUNCIL DIRECTIVE 85/433/EEC of 16 September 1985 concerning the mutual recognition of diplomas, certificates and other evidence of formal qualifications in pharmacy, including measures to facilitate the effective exercise of the right of establishment relating to certain activities in the field of pharmacy

SECOND COUNCIL DIRECTIVE 75/319/EEC of 20 May 1975 on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to proprietary medicinal products

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

REGULATION (EC) NO 726/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

COMMISSION REGULATION (EC) NO 1084/2003 of 3 June 2003 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use and veterinary medicinal products granted by a competent authority of a Member State.

REGULATION (EC) NO 141/2000 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 1999 on orphan medicinal products.