Medicinal Products in Human Medicine Act

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Chapter One
GENERAL TERMS
Section I
General Provisions

Article 1. This Act shall specify the terms and procedure for:

1. Authorisation of the use or of the registration of medicinal products that have been manufactured industrially or using a method involving an industrial process, and which are destined for human medicine;
2. Authorisation of the manufacturing and importation of medicinal products and active substances;
3. Authorisation and conduct of clinical trials;
4. Wholesale and retail trade in medicinal products;
5. Parallel importation of medicinal products;
6. Advertisement of medicinal products;
7. Monitoring the safety of medicinal products placed on the market;
8. Classification of the manner in which medicinal products are prescribed and dispensed for use;
9. Control of the manufacturing and importation, of the wholesale and retail trade, of the conduct of clinical trials, of advertisement and of the safety monitoring system for medicinal products placed on the market;
10. The pricing of medicinal products;
11. Drafting of a Positive Drug List.

Article 2. This Act shall have the purpose of making conditions available for placing medicinal products on the market in compliance with the requirements for quality, safety and efficacy.

Article 3. (1) (Amended, *SG* No. 71/2008) A medicinal product in human medicine shall be:

1. any substance or combination of substances presented as possessing properties for the treatment or prevention of human disease, or
2. any substance or combination of substances that can be used or administered to humans for the purpose of:

a) restoring, correcting or changing human physiological functions through their pharmacological, metabolic or immunological action, or

b) for medical diagnostic purposes.

(2) A substance shall be any matter of which the origin may be:

1. Human (human blood, human blood products, etc.);
2. Animal (microorganisms, animal organs, extracts, secretions, toxins, blood products, etc.);
3. Vegetal (microorganisms, plants, plant parts, plant extracts, secretions, etc.);
4. Chemical (elements, natural chemical material, synthetic or semi-synthetic substances, etc.).

Article 4. Where a product simultaneously qualifies, based on its characteristics, as a medicinal product and as a product regulated in another Act, the requirements hereof shall apply.

Article 5. Medicinal products shall be classified in accordance with an Anatomic Therapeutic Chemical Classification system in compliance with the requirements of the World Health Organisation (WHO).

Article 6. This Act shall not apply to:

1. Hermetically closed radionuclides;
2. Blood, plasma or blood cells of human origin, except plasma obtained through a method involving an industrial process.

Article 7. (1) Manufacturing, importation, wholesale and retail trade, advertising and treatment, prevention and diagnosis shall only be allowed with medicinal products that have been granted authorisation for use for use in compliance with:

1. This Act or
2. Regulation (EC) No. 726/2004 of the European Parliament and of the Council.

(2) The importation of, trade in, and the treatment, prevention and diagnosis using medicinal products whose shelf life has expired shall be prohibited.

(3) Holding authorisation or a certificate for the use, manufacturing or clinical trials of medicinal products, which have been issued in compliance with this Act, shall not serve as grounds for the exemption from liability under the legislation in force.

Article 8. No authorisation for use in compliance with this Act shall be required for:

1. medicinal products prepared under a magisterial formula in a pharmacy;
2. medicinal products prepared under an official formula in a pharmacy;
3. intermediate products intended for industrial processing to be carried out by a person having obtained a manufacturing authorisation under this Act;
4. active substances and excipients;
5. medicinal products being developed and/or tested;
6. medicinal products intended for exportation.
7. (New, *SG* No. 71/2008, effective 12.08.2008) medicinal products for a highly technological therapy, prepared for a concrete patient following individual physician's prescription in accordance with specific quality standards, and administered in a medical institution at the exceptional professional responsibility of the physician.

Article 9. (1) The treatment of a specific patient may entail the administration of a medicinal product that has not been authorised under Chapter Three, following a special order of the in-patient care establishment under the terms and conditions set out in an Ordinance of the Minister of Health.

(2) The head of the medical establishment shall incur liability for the administration of treatment under Paragraph 1.

Article 10. (1) The Minister of Health, following a motivated proposal of the chief state health inspector, in coordination with the Executive Director of the Bulgarian Drugs Agency (BDA), may allow by an order for a specified period a treatment using a medicinal product which has not been authorised under Chapter Three, in the event that an epidemic has been declared in the country, caused by pathogenic microorganisms or toxins, or an alleged or confirmed spread of chemical agents or nuclear radiation exist and there is no suitable medicinal product allowed for use.

(2) In the cases under Paragraph 1, holders of an authorisation for use, manufacturers and medical specialists shall incur no civil or penal administrative liability for the effects from the use of a non-authorised indication of a medicinal product or of a medicinal product which has not been authorised under Chapter Three.

(3) The provision of Paragraph 2 shall not exclude liability for faulty goods under the Consumer Protection Act.

Article 11. (1) The Minister of Health may, for reasons concerned with protecting the health of the population, give orders to the BDA Executive Director to authorise the use of a medicinal product which has not been authorised on the territory of the Republic of Bulgaria and for which no licensing application has been submitted, but which is authorised in another Member State.

(2) In the cases under Paragraph 1, the BDA Executive Director or an official authorised by him shall:

1. inform the holder of the authorisation for use of the medicinal product about the launching of a procedure for authorising the use of the product;
2. register the person under item 1 as the holder of the issued authorisation;
3. obtain from the regulatory body of the Member State in which the authorisation for use has been delivered a copy of the evaluation report and a copy of the authorisation for use.

(3) The Bulgarian Drugs Agency must ensure compliance of the label, patient brochure, classification, advertisement and safety monitoring of the medicinal product placed on the market under Paragraph 1 with the requirements of this Act.

(4) The BDA Executive Director shall inform the European Commission of the authorisations issued under Paragraph 1, of the name and address of the authorisation holder, as well as of the date of termination of their validity.

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

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

(3) The Minister of Health shall specify by order the dates of entry into force of the up-to-date issue of the official pharmacopoeia and of the supplements thereto.

(4) The order under Paragraph 3 shall be promulgated in the *State Gazette* and posted on the BDA website.

Article 13. (1) The European Pharmacopoeia monographs shall be mandatory for all substances, preparations and pharmaceutical forms contained therein. In case no European Pharmacopoeia monographs exist, the requirements of up-to-date editions of pharmacopoeias of the Member States, the USA and Japan shall apply, provided they are in line with the general rules of the European Pharmacopoeia.
(2) Where the specification contained in a monograph of the European Pharmacopoeia or in another national pharmacopoeia is insufficient to ensure the quality of the substance or pharmaceutical form, BDA may require that the specification be supplemented by the applicant/holder of the authorisation for use.

Chapter Two
MANAGEMENT AND FINANCE BODIES
Section I
Management Bodies

Article 14. (1) The medicinal policy shall be part of the state health policy of the Republic of Bulgaria and it shall be implemented by the Minister of Health.
(2) The Minister of Health shall:
1. be the national coordinator for any issues pertaining to medicinal products;
2. participate in international bodies and organisations carrying out operations in the area of medicinal products;
3. issue licenses for retail trade in medicinal products in pharmacies, and close down pharmacies;
4. carry out other activities provided for under the law.
(3) When carrying out the activities under Paragraph 2, item 3, the Ministry of Health shall collect fees in amounts set out in the Tariff under Article21, Paragraph 2.
Article 15. (1) A Pharmacopoeia Committee shall be set up with the Minister of Health as an advisory body on any issues concerning the effective pharmacopoeia.
(2) The Minister of Health, based on a proposal by the BDA Executive Director, shall specify by order the composition of the Pharmacopoeia Committee and of the expert groups attached to it, and he shall endorse their Rules of Operation.
(3) The operations of the Pharmacopoeia Committee shall be funded from the budget of the Ministry of Health.
Article 16. (1) A High Pharmacy Council shall be established with the Minister of Health to be composed of five members designated by the Minister of Health, five members designated by the Bulgarian Pharmacy Union, two members designated by the National Health Insurance Fund (NHIF) and one member designated by each Pharmacy Department of the Higher Medical Schools. The Minister of Health shall be the Chairperson of the Council without voting rights.
(2) The High Pharmacy Council shall be an advisory body to discus and give opinion on:
1. the general directions and the main priorities in the area of pharmacy;
2. ethical issues in pharmacy;
3. draft legislation connected with pharmacy;
4. the research priorities in the area of pharmacy;
5. programmes for public education campaigns in the field of medicinal products.
(3) The High Pharmacy Council shall examine applications for retail trade in medicinal products and shall submit motivated proposals to the Minister of Health for the issuance of an authorisation or a refusal, as well as for the withdrawal of licenses already issued.
(4) The organisation and the activities of the High Pharmacy Council shall be specified in Rules issued by the Minister of Health based on a proposal by the High Pharmacy Council.
Article 17. (1) The Bulgarian Drugs Agency shall be a specialised body of the Minister of Health that supervises the quality, safety and efficacy of drugs.
(2) The Bulgarian Drugs Agency shall be a public budget legal entity with a seat in Sofia, a secondary spender of budget appropriations attached to the Minister of Health.
(3) The Bulgarian Drugs Agency shall be headed and represented by an Executive Director appointed under the Public Administration Act.
(4) The structure, functions and organisation of the work of the BDA shall be specified in Rules adopted by the Council of Ministers.
(5) The Bulgarian Drugs Agency shall:

1. issue licenses for the manufacturing of medicinal products;
2. issue licenses for use and certificates for registration of medicinal products;
3. (Supplemented, *SG* No. 71/2008, effective 12.08.2008) issue licenses and certificates for wholesale trade in medicinal products;
4. issue licenses for parallel importation of medicinal products;
5. issue certificates for registration of drugstores;
6. issue licenses for conducting clinical trials of medicinal products;
7. carry out quality, efficacy and safety evaluations of medicinal products in relation to their authorisation for use;
8. issue authorisations for the advertisement of medicinal products;
9. exercise control on the manufacturing, importation, storage, wholesale and retail trade, clinical trials, safety and advertisement of medicinal products;
10. conduct laboratory analyses in case of suspected deviations in the quality, efficacy and safety of medicinal products, and take the measures provided for under the law;
11. set up a system of drug safety and take appropriate measures;
12. issue certificates in accordance with the WHO certification scheme;
13. issue certificates of Good Manufacturing Practice;
14. coordinate construction development projects for new sites and/or for the reconstruction of existing sites related to the manufacturing of medicinal products in accordance with the rules of Good Manufacturing Practice;
15. carry out the functions of a coordinator and of a consultative body on issues of quality, efficacy and safety of medicinal products;
16. carry out consultancy, scientific, information and publishing activities in the drugs sector;
17. coordinate and take part in activities connected with the European Pharmacopoeia and with the development of the Bulgarian pharmacopoeia;
18. take part in activities in the area of medicinal products, which concern the work of the European Medicines Agency, the European Directorate for the Quality of Medicines and Healthcare, of international bodies and organisations, as well as the enforcement of international treaties to which the Republic of Bulgaria is a party;
19. carry out other activities provided for under the law.

(6) The BDA shall coordinate its operations in the area of medicinal products control with the Regional Inspectorates for the Protection and Control of Public Health (RIPCPH).

Section II
Registries

Article 18. The Ministry of Health shall keep and maintain a public register of licenses issued for retail trade in medicinal products in pharmacies.

Article 19. (1) The Bulgarian Drugs Agency shall keep and maintain registries of:
1. the manufacturers of medicinal products on the territory of the Republic of Bulgaria and of the individuals qualified under Article 148, item 2;
2. the importers of medicinal products on the territory of the Republic of Bulgaria and of the individuals qualified under Article 161, Paragraph 2, item 1;
3. the medicinal products authorised for use and registered on the territory of the Republic of Bulgaria;
4. wholesale traders in medicinal products on the territory of the Republic of Bulgaria;
5. the certificates of registration of drugstores issued;
6. the authorised clinical trials;
7. the authorisations for parallel importation issued.

(2) Data on the registries under Paragraph 1, items 1-5 and 7 shall be posted within 14 days of issuance of the respective authorisation on the BDA website.

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

Section III
Funding

Article 20. (1) The activities of the Bulgarian Drugs Agency shall be funded by the public budget and with revenues therefrom.

(2) A public budget subsidy shall be provided from the budget of the Ministry of Health.

Article 21. (1) The Bulgarian Drugs Agency shall administer the revenues from its own activities generated from:

1. chemical and pharmaceutical expert assessments;
2. laboratory analyses and trials;
3. evaluations of documents and the issuance of licenses, certificates, attestations and other documentation specified herein;
4. evaluations upon the renewal, modification and deletion of licenses for use and certificates of registration of medicinal products;
5. maintaining licenses for use or certificates of registration of medicinal products;
6. fines and pecuniary sanctions imposed by penal decrees issued for violations of this Act;
7. consultancy, publishing and research activities in the drug sector;
8. coordination of construction development projects for new sites and/or for the reconstruction of existing sites related to the manufacturing of medicinal products;
9. inspections for evaluation of compliance of the manufacturing conditions with the requirements of Good Manufacturing Practice;
10. other sources.

(2) When conducting activities under Paragraph 1, items 1-5, and 7-9, the BDA shall collect fees in the amounts specified in a Tariff adopted by the Council of Ministers.

(3) (New, *SG* No. 71/2008, effective 12.08.2008) The Tariff under Paragraph 2 shall provide for lower fees of different amounts for the procedures for licensing the use, production and import of medicinal products for small and medium-sized enterprises in the pharmaceutical sector under the Small and Medium-Sized Enterprises Act.

Article 22. (1) The financial resources under Article 21 shall be spent for:

1. control operations of the Bulgarian Drugs Agency;
2. payment for activities under Article 21, Paragraph 1, items 1 and 2, in cases these have been assigned by BDA to other persons under contract;
3. acquisition, maintenance and repairs of the fixed assets of the Bulgarian Drugs Agency;
4. creation, maintenance and keeping of registries under Article 19, Paragraph 1;
5. maintenance of systems for the electronic exchange of data with the regulatory bodies of other Member States, the European Commission and the European Medicines Agency;
6. information and publishing activities pertaining to the quality, efficacy and safety of medicinal products;
7. providing support for the activities of specialised commissions under Article 47, Paragraphs 1 and 2, and of the Council under Article 251, Paragraph 3;
8. carrying out training programmes for BDA staff;
9. participation in international and national interlaboratory trials;
10. supplementary material incentives for BDA staff amounting to 40 per cent of the resources under Article 21, Paragraph 1 under the terms and conditions set out in the Internal Rules by the BDA Executive Director.

(2) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) The financial resources under Article 14, Paragraph 3, Article 260, Paragraph 4 and Article 262, Paragraph 6 shall be spent for:

1. activities of the High Pharmacy Council;
2. activities of the Pharmacopoeia Committee;
3. activities of the Commission for the Prices of Medicinal Products; the Commission for the Positive Drug List; the Commission for Transparency, the Central Commission for Ethics and the Commission for Ethics in Multi-Centre Trials;
4. implementation of programmes for the training of Ministry of Health staff in the area of drug policy;
5. (Supplemented, *SG* No. 71/2008, effective 12.08.2008) Additional material incentives for staff members of the Ministry of Health amounting to up to 40 per cent of the resources under Article 14, Paragraph 3, Article 260, Paragraph 4 and Article 262, Paragraph 6 under the terms and conditions set out in the Internal Rules of the Minister of Health.

Chapter Three
MARKET PLACEMENT OF MEDICINAL PRODUCTS
Section I

General Terms

Article 23. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) An industrially manufactured medicinal product or a medicinal product obtained through a method involving an industrial process may only be placed on the market after obtaining authorisation for use or a certificate of registration, issued under this Act or in compliance with Regulation (EC) No. 726/2004 of the European Parliament and of the Council, and in full compliance with the requirements of Regulation (EC) No. 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use, and for amendments to Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No. 726/2004, referred to below as "Regulation (EC) No. 1901/2006", and of Regulation (EC) No. 1394/2007 of the European Parliament and of the Council of 13 November 2007 on medicinal products for modern therapy and for amendments to Directive 2001/83/EO and to Regulation (EC) No. 726/2004 (*OJ*, L 324/121 of 10 December 2007

(2) Authorisation for use under Paragraph 1 shall also be required for a radionuclide generator, a radionuclide precursor and for a kit.

(3) The types of procedures under Paragraph 1 shall be:

1. centralised;
2. procedure of mutual recognition/decentralised;
3. national.

(4) (New, *SG* No. 71/2008, effective 12.08.2008) Only medicinal products whose holder of the authorisation for use/certificate of registration is established on the territory of a Member State may be released on the territory of the Republic of Bulgaria.

Article 24. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) No authorisation for use shall be required for radio pharmaceuticals prepared immediately prior to their use in radionuclide generators, radionuclide precursors or kits authorised for use in compliance with the instructions of their manufacturer.

(2) Products under Paragraph 1 shall be prepared by qualified persons in laboratories or institutes authorised to conduct such operations in compliance with the Safe Use of Nuclear Energy Act.

(3) The preparation, use and administration of products under Paragraph 1 shall be carried out in accordance with the medical standard in nuclear medicine.

Article 25. (1) The criteria for the qualification of medicinal products intended for the treatment, prevention or diagnosis of rare diseases shall be provided for in Regulation (EC) No. 141/2000 of the European Parliament and of the Council.

(2) The terms and conditions for issuance of licenses for the use of medicinal products under Paragraph 1 shall be provided for in Regulation (EC) No. 726/2004 of the European Parliament and of the Council.

Article 26. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) An authorisation for the use of a medicinal product, a certificate of the registration of a homeopathic medicinal product under Article 35 or a certificate of the registration of a traditional herbal medicinal product under Article 37 on the territory of the Republic of Bulgaria shall be issued by the Bulgarian Drugs Agency Executive Director to a natural or legal person established on the territory of a Member State.

(2) Where the person under Paragraph 1 is not established on the territory of the Republic of Bulgaria, he shall designate au authorised representative.

(3) The holder of an authorisation for use shall incur liability for medicinal products placed on the market. Designating a person under Paragraph 2 shall not exempt the holder of an authorisation for use from liability in accordance with the effective legislation in the Republic of Bulgaria.

Section II

Requirements to the documentation for the issuance of licenses for use

Article 27. (1) (Amended and supplemented, *SG* No. 71/2008, effective 12.08.2008) A person under Article 26, Paragraph 1 shall file a model-based application for the issuance of an authorisation for use with the Bulgarian Drugs Agency to be accompanied by a dossier in the format of an Electronic General Technical Document, which shall contain:

1. the name and business/permanent address of the applicant and of the representative under Article 26, Paragraph 2; where the applicant is a person other than the manufacturer or manufacturers – the address of the production sites;
2. the name of the medicinal product;

3. data about the quantitative and qualitative composition of the medicinal product, stating the international non-patented name recommended by WHO, if available, or the respective chemical name;
4. therapeutic indications, counterindications and adverse reactions;
5. (Amended, *SG* No. 71/2008, effective 12.08.2008) the dosage, pharmaceutical forms, mode and route of administration, and proposed shelf life;
6. precautionary and safety measures for the storage of the product, for its administration to patients and for the destruction of product waste accompanied by instructions about the potential environmental hazards of the medicinal product;
7. a description of the manufacturing process;
8. a description of the control methods used by the manufacturer;
9. an evaluation of the potential environmental hazard of the medicinal product in each specific case and measures foreseen for its limitation;
10. the results from:
a) pharmaceutical (physical and chemical, biological or microbiological) trials;
b) preclinical (toxicological and pharmacological) trials;
c) clinical trials;
11. a declaration to the effect that during clinical trials performed outside the territory of Member States, the ethical principles of Good Clinical Practice have been complied with;
12. a description of the system for drug safety that will be introduced and, where appropriate, also a description of the risk management system;
13. data about the person under Article 186, Paragraph 1: name, address and professional qualifications;
14. a product summary in accordance with Article 34;
15. a model of the immediate and outer packaging of the product and a proposal for a brochure in compliance with the requirements under Chapter Six;
16. a copy of the manufacturing authorisation issued by the regulatory body of the state in which the manufacturing takes place, accompanied by a certificate of Good Manufacturing Practice or a certificate to the effect that the manufacturing of the medicinal product and of the active substances in its composition is carried out in compliance with standards that are at least equivalent to those for Good Manufacturing Practice;
17. a copy of a document, whereby the medicinal product has been designated for the treatment, prevention or diagnosis of rare diseases, accompanied by a copy of the opinion of the European Medicines Agency;
18. a copy of all licenses for use, issued in another Member State or in a third country, for the medicinal product for which an authorisation for use is requested;
19. a list of the Member States in which an application has been filed for the issuance of an authorisation for the use of a medicinal product;
20. (Amended, *SG* No. 71/2008, effective 12.08.2008) a copy of the summary of product characteristics proposed by the person under Article 26, Paragraph 1, or a copy of the Summary of Product Characteristics approved by a regulatory body of a Member State(s) which has already issued an authorisation for use;
21. a copy of the refusal to grant an authorisation for use in a Member State or in a third country accompanied by reasons; information about any provisional suspension or about the termination of the effect of an authorisation for use;
22. a copy of the proposed patient information leaflet accompanied by a summary of the results from the evaluation of brochure content understanding by a target group of patients selected by the applicant or a copy of the brochure approved by a regulatory body of a Member State which has already delivered an authorisation for use;
23. a document evidencing the payment of a fee in the amount set out in the Tariff under Article 21, Paragraph 2;
24. (New, *SG* No. 71/2008, effective 26.07.2008) the documents under Article 7 of Regulation (EC) 1901/2006.
(2) The documents under Paragraph 1, item 18, with regard to Member States, respectively under item 19, shall only be filed in procedures under Section VII.

(3) The following documents shall be submitted in respect to radionuclide generators, in addition to data under Paragraph 1:
1. a description of the system together with a detailed description of its components which could influence the composition or quality of daughter radionuclides;
2. qualitative and quantitative characteristics of the eluate or sublimate.
(4) Documents and data from pharmaceutical, preclinical and clinical trials shall be accompanied by summary reports prepared by experts with the required level of technical and professional qualifications. A CV for the experts who have drafted the report shall be attached to them.
(5) The dossier of the medicinal product shall be provided in the Bulgarian and/or the English language.
Article 28. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) The person under Article 26, Paragraph 1, insofar as such person does not infringe upon any industrial or commercial property rights, shall not submit data under Article 27, Paragraph 1, item 10, b) and c) to the Bulgarian Drugs Agency, where it may prove that a medicinal product listed in the application is the generic product of a reference medicinal product which is or has been authorised for use in a Member State no less than 8 years previously.
(2) The holder of an authorisation for use of the generic product under Paragraph 1 may not place it on the market before 10 years have elapsed from the date of the initial authorisation for use of the reference medicinal product.
(3) The person under Article 26, Paragraph 1, subject to the terms of Paragraphs 1 and 2, may also file an application with the Bulgarian Drugs Agency for an authorisation for the use of the generic product of a reference medicinal product, where the latter has not had any authorisation for use issued on the territory of the Republic of Bulgaria.
(4) In cases under Paragraph 3, the person under Article 26, Paragraph 1 shall indicate in the application under Article 27, Paragraph 1 the Member State in which the reference product is or has been authorised for use.
(5) In cases under Paragraph 3, the Bulgarian Drugs Agency shall obtain from the regulatory body of the Member State specified in the application under Article 27, Paragraph 1 a confirmation of the information under Paragraph 4, the quantitative and qualitative composition of the reference product and, if necessary, additional documentation.
(6) The Bulgarian Drugs Agency shall provide, upon request from a regulatory body of a Member State in which an application for the generic product of a reference medicinal product has been filed, the latter being or having been authorised for use on the territory of the Republic of Bulgaria, the necessary information under Paragraph 5 within one month of the date of request.
(7) The ten-year period under Paragraph 2 may be extended by no more than one year upon request by the holder of the authorisation for use of the reference medicinal product where within the first 8 years following the issuance of the authorisation for use of the reference medicinal product its holder obtains, in respect to the same product, an authorisation for a new therapeutic indication whose significant clinical advantages compared to existent treatment courses have been scientifically substantiated.
Article 29. (1) The person under Article 26, Paragraph 1 shall submit to the Bulgarian Drugs Agency the results from the required preclinical and/or clinical trials in cases where a medicinal product listed in the application:
1. may not be defined as generic, or
2. the trials for bioavailability do not prove bioequivalence, or
3. (Supplemented, *SG* No. 71/2008, effective 12.08.2008) A change has occurred in the active substance or substances, in the quantity of the active substance or substances in the dose unit, in the therapeutic indications, in the pharmaceutical form and in the route of administration compared to the reference medicinal product.
4. (Repealed, *SG* No. 71/2008, effective 12.08.2008).
(2) Where a biological medicinal product listed in the application, similar to the reference biological medicinal product, does not meet the requirements for qualification as a generic medicinal product, due to a difference in the manufacturing process or to different input material compared to the reference product, or due to any other reasons, the applicant shall submit to the Bulgarian Drugs Agency the results from the required preclinical and/or clinical trials associated with those requirements.
(3) In the cases under Paragraphs 1 and 2, the documentation specified by the Ordinance under Article 42 shall also be submitted.

Article 30. (1) The person under Article 26, Paragraph 1, insofar as that person does not violate industrial and commercial property rights, shall not submit to the Bulgarian Drugs Agency the data under Article 27, Paragraph 1, item 10, b) and c) where he can prove, subject to the conditions specified in the Ordinance under Article 42, that the active substance in the composition of the medicinal product proposed to be authorised for use has an established use in medical practice, a recognised efficacy and an acceptable level of safety. In such cases the results from trials and the trials may be replaced by the respective scientific publications.
(2) The person under Paragraph 1 shall submit the results of the required preclinical and clinical trials in the case of a medicinal product containing active substances with a well established use, which have not been used in the proposed combination for therapeutic purposes. In this case no documentation with regard to each and every separate active substance shall be submitted.
(3) Where the active substance under Paragraph 1 has a new therapeutic indication proven on the basis of significant preclinical and clinical data associated with the new indication, no subsequent applicant may refer to data about the new indication of the active substance for a one-off period of one year.
Article 31. In case where a medicinal product contains active substances used in the composition of medicinal products authorised for use but which are not used in the proposed combination for therapeutic purposes, the person under Article 26, Paragraph 1 shall submit the results of the preclinical and of the clinical trials associated with this combination. In this case the applicant shall not submit any documentation with regard to the safety and efficacy of each and every active substance.
Article 32. The holder of an authorisation for the use of a medicinal product may authorise the use of the pharmaceutical, preclinical and clinical documentation, contained in the dossier of the medicinal product, in the evaluation of subsequent applications for medicinal products with the same qualitative and quantitative composition, with regard to the active substances, and in the same pharmaceutical form.
Article 33. Carrying out the required research and trials with the aim of preparing the documentation for an authorisation for use and in order to comply with any subsequent practical requirements in relation to authorising the medicinal products under Articles 28 and 29 for use shall not be a violation of the patent or of the certificate for additional protection of a medicinal product.
Article 34. (1) The summary of the product shall specify the following information:
1. the name of the medicinal product, the quantity of the active substance per dosing unit and the pharmaceutical form;
2. the qualitative and quantitative composition, in terms of active substances, and of those of the excipients, the information about which is of significance for the regular administration of the product; the common name or the chemical description shall be used;
3. the pharmaceutical form;
4. clinical data:
a) therapeutic indications;
b) dosage and route of administration for adults and for children;
c) counterindications;
d) special warnings and precautions for use; for immunological medicinal products – precautions for persons who will handle and administer them to patients, as well as any precautionary measures to be taken by the patient;
e) interaction with other medicinal products or other forms of interaction;
f) use during pregnancy or breast-feeding;
g) effects on the ability to drive and to use machines;
h) adverse reactions;
i) overdose (symptoms, antidotes, emergency procedures);
5. pharmacological data:
a) pharmacodynamic properties;
b) pharmacokinetic properties;
c) preclinical safety data;
6. Pharmaceutical data:
a) a list of excipients;
b) main incompatibilities;

c) shelf life; shelf life after dissolving the medicinal product (where necessary) or after opening the immediate packaging for the first time;
d) special instructions for storage;
e) type and composition of packaging;
f) special instructions for disposing of the remaining medicinal product or of the waste material from it;
7. the holder of the authorisation for use;
8. the registration number;
9. the date of the first authorisation for use or of the renewal of the authorisation for use;
10. the date on which a modification of the summary content for the product is made;
11. for radiopharmaceuticals – exhaustive information about the internal radiation dosimetry;
12. for radiopharmaceuticals – detailed instructions for their extemporaneous preparation and for the quality control thereof and, where appropriate, the maximum storage time during which any intermediate product, such as an eluate or the ready-to-use pharmaceutical, will conform to its specifications.
(2) The summary of medicinal products under Articles 28-33 may not include those parts of the summary of the reference medicinal product, which refer to the indications and pharmaceutical forms, having been the object of patent protection when the generic product was on the market.
(3) The requirements to the form and content of the product summary shall be specified in the Ordinance under Article 42.

Section III
Specific requirements applicable to homeopathic medicinal products

Article 35. (1) A certificate of registration for a homeopathic medicinal product shall be issued in compliance with a simplified procedure where the product meets the following conditions:
1. It is administered orally or externally;
2. No specific therapeutic indication appears on the labelling of the medicinal product or in any information relating thereto;
3. There is sufficient dilution to guarantee the safety of the medicinal product; in particular, the medicinal product may not contain either more than one part of the mother tincture per 10,000 or more than 1/100th of the smallest dose used in allopathy, as regards active substances whose presence in an allopathic medicinal product results in mandatory medical prescription.
(2) In order to obtain a certificate of registration for a homeopathic medicinal product, the person under Article 26, Paragraph 1 shall file a model-based application with the Bulgarian Drugs Agency, which could specify a series of medicinal products obtained from the same homeopathic stock or from the same stocks.
(3) The following documentation shall be attached to the application under Paragraph 2 in order to prove the pharmaceutical quality and the batch-to-batch homogeneity of the medicinal product concerned:
1. (Amended, *SG* No. 71/2008, effective 12.08.2008) the scientific name or other name of the homeopathic stock or stocks given in a pharmacopoeia, together with a statement of the various routes of administration, the pharmaceutical forms and degree of dilution;
2. the 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. a dossier of the manufacturing and control methods for each pharmaceutical form and a description of the methods of dilution and potentiation;
4. a manufacturing authorisation accompanied by a certificate of Good Manufacturing Practice or a certificate testifying that the product has been manufactured under conditions equivalent to the requirements of Good Manufacturing Practice;
5. copies of any registrations or licenses obtained for the same medicinal product in other Member States;
6. a mock-up of the immediate and/or outer packaging of the product;
7. data concerning the stability of the product.
(4) The requirements to the data under Paragraph 3 shall be specified in the Ordinance under Article 42.
Article 36. (1) The provisions of Articles 27-32 shall apply to homeopathic medicinal products other than those listed in Article 35, Paragraph 1.

(2) The person under Article 26, Paragraph 1 shall submit no results from preclinical and clinical trials for homeopathic medicinal products under Paragraph 1, where such person may prove, using bibliographic data from scientific literature, the established safe homeopathic use of the medicinal product concerned or of the homeopathic stocks within its composition.
(3) In the cases under Paragraph 2, bibliographic data must establish:
1. the homeopathic nature of the raw materials and their traditional administration, in presence of the indication applied for;
2. the non-harmful nature of the homeopathic medicinal product, in terms of the level of dilution of each of its ingredients.

Section IV
Specific requirements applicable to traditional herbal medicinal products

Article 37. (1) A certificate of registration for a traditional herbal medicinal product shall be issued in compliance with a simplified procedure where the product meets the following conditions:
1. it has therapeutic indications inherent to the use of traditional herbal medicinal products and, bearing in mind its composition and intended use, is destined for use without prescription by a doctor and without medical supervision;
2. it is only administered as a set quantity of the medicinal substance per dosing unit, at a set dose;
3. it is administered orally, through inhalation or is intended for external use;
4. the period of traditional use under Article 38, Paragraph 1, item 5 has expired;
5. data about the traditional use of the medicinal product prove that it is not harmful under the set conditions for use and the pharmacological effect or efficacy of the medicinal product has been established through its long-term use and the experience accumulated.
(2) The Bulgarian Drugs Agency may apply the procedure under Paragraph 1 to a herbal medicinal product containing vitamins or minerals whose safety has been documentally proven and whose action in respect to herbal medicinal substances in the product, as regards the latter's specific indications, is auxiliary.
Article 38. (1) In order to obtain a certificate of registration for a traditional herbal medicinal product, the person under Article 26, Paragraph 1 shall submit an application to the Bulgarian Drugs Agency accompanied by the following documents:
1. the data specified in Article 27, Paragraph 1, items 1-9 and item 10, a);
2. (Amended, *SG* No. 71/2008, effective 12.08.2008) A product summary, with the exception of data under Article 34, Paragraph 1, item 5;
3. in the case of an herbal medicinal product under Article 37, Paragraph 2, or of a combined medicinal product – the information under Article 37, Paragraph 1, item 5, as regards the combination; where the active substances of the combined product are not sufficiently known, if taken separately, data about the traditional use of each shall be submitted;
4. a copy of the authorisation for use or of the certificate of registration for the herbal medicinal product issued by a Member State or a third country, and/or a copy of a refusal accompanied by the reasoning of the decision concerned;
5. (Amended, *SG* No. 71/2008, effective 12.08.2008) bibliographic data or expert opinions proving that the herbal medicinal product, for which an application for registration has been filed, or that a corresponding product has been in use, until the date on which the application for registration was filed, for more than 30 years in world medical practice, of which at least 15 years on the territory of a Member State;
6. bibliographic data about the safety of the product accompanied by a report of experts;
7. a copy of the manufacturing authorisation accompanied by a certificate of Good Manufacturing Practice or by a certificate proving that the product is manufactured under conditions that are equivalent to the requirements of Good Manufacturing Practice.
(2) The Bulgarian Drugs Agency may require from the applicant additional information in order to evaluate the safety of medicinal products under Paragraph 1.
(3) The Bulgarian Drugs Agency may request the opinion of the Committee on Herbal Medicinal Products with the European Medicines Agency as regards the truthfulness of data under Paragraph 1, item 5, providing it with the necessary parts of the medicinal product dossier.
(4) Data submitted under Paragraph 1, item 5 shall also be valid in cases where, in the 30-year period of use in medical practice:

1. the medicinal product corresponding to the one for which an application for registration is submitted has been on the market without authorisation or registration for use, or
2. where the number of ingredients in the medicinal product, for which an application for registration is filed, is reduced or their quantity per dosing unit is reduced.

Article 39. (1) Where the herbal medicinal product has been on the Community market for less than 15 years, but it meets the conditions of Article 37, Paragraph 1, the Bulgarian Drugs Agency shall submit the documentation under Article 38, Paragraph 1 to the Committee on Herbal Medicinal Products with the European Medicines Agency, in order to obtain its opinion.

(2) The Bulgarian Drugs Agency shall make a final decision after publication of the monograph of the Committee under Paragraph 1 with regard to the compliance of the product with registration criteria for traditional use.

(3) In the cases under Paragraph 1, the period under Article 44 shall be suspended.

Article 40. The Bulgarian Drugs Agency may require the applicant, in case of a herbal medicinal product, to file the documentation under Articles 27-32 or under Article 35.

Article 41. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) The Bulgarian Drugs Agency shall post on its website a list, to be prepared by the Committee on Herbal Medicinal Products with the European Medicines Agency, of the herbal substances, preparations or combinations thereof used in traditional herbal medicinal products. For each herbal substance the list shall specify its therapeutic indications, the active ingredient content per dosing unit, the route of administration and other information required for the safe use of the herbal substance as a traditional medicinal product.

(2) Where the product, as proposed in the traditional use application for registration, contains a herbal substance, preparation or a combination thereof, as per the list under Paragraph 1, the applicant shall not submit data specified in Article 38, Paragraph 1, items 4-6.

(3) Where the herbal substance, preparation or the combination thereof is excluded from the list under Paragraph 1, the holder of a certificate for registration of the herbal medicinal product must submit to the Bulgarian Drugs Agency the full documentation set under Article 38 within a period of three months after any such change.

(4) In case the holder of a certificate of registration for a herbal medicinal product fails to perform the duty under Paragraph 3, the Bulgarian Drugs Agency shall terminate the certificate of registration for the product.

Section V
Procedure for issuance of an authorisation for the use of medicinal products and for registration of homeopathic and traditional herbal products

Article 42. The requirements to data and documents in the dossiers under Articles 27-32, Article 35, Paragraph 3, Article 36, Paragraph 2 and under Article 38 shall be specified in an Ordinance of the Minister of Health.

Article 43. (1) Within a period of 30 days from the date of submission of the documentation under Articles 27-32, Article 35, Paragraph 3 or under Article 38, the BDA shall examine the various sections of the dossier for completeness and their compliance with the requirements for issuance of the authorisation for use or of the certificate of registration under this Act.

(2) Where no incompleteness or discrepancies are found in the documentation submitted, the Bulgarian Drugs Agency shall notify the applicant in writing, within the period under Paragraph 1, that the documentation is valid. The notification shall specify the date from which the period under Article 44 is to start running.

(3) Where incompleteness and/or discrepancies are found in the documentation under Paragraph 1, the Bulgarian Drugs Agency shall notify the applicant in writing to submit additional information and/or a verbal or written explanation of the incompleteness and discrepancies found, within a period of 14 days of the date of the notification.

(4) Where the requirements under Paragraph 3 are not met within the specified period, the BDA shall notify the applicant in writing that the application is not valid. In that case, the BDA shall return within 14 days the documentation submitted and shall reimburse 75 per cent of the fee paid by the applicant.

(5) Where the requirements under Paragraph 3 are met within the specified period, the Bulgarian Drugs Agency shall notify the applicant in writing that the documentation is valid, the notification specifying the date from which the period under Article 44 is to start running.

Article 44. The procedure for issuance of an authorisation for use or of a registration of a medicinal product shall start on the date specified in the notification under Article 43, Paragraph 2 or under Article 43, Paragraph 5, correspondingly, and shall terminate within a period of 210 days.

Article 45. (1) Where an application has been filed with the Bulgarian Drugs Agency for an authorisation for use or for the registration of a medicinal product, for which information is available from data under Article 27, Paragraph 1, item 18 that an authorisation for use of the same medicinal product has been issued in a Member State, the Bulgarian Drugs Agency shall notify the applicant in writing of the application of the procedure under Article 74.

(2) Where an application with the Bulgarian Drugs Agency has been filed for an authorisation for use or for the registration of a medicinal product, for which information is available from data under Article 27, Paragraph 1, item 19, that the dossier of the same medicinal product in the Member State is under evaluation, the Bulgarian Drugs Agency shall not examine the documentation under Articles 27-32 or under Article 35, Paragraph 3, or under Article 38, and shall notify the applicant in writing of the application of the procedure under Article 75.

(3) For the purposes of applying the provisions of Paragraphs 1 and 2, a medicinal product authorised in another Member State shall be considered as being the same or as a product for which the file is under evaluation in another Member State, where two medicinal products:

1. are of identical quantitative and qualitative composition, in terms of the active substance(s) and are offered as the same pharmaceutical form, variation being allowed with regard to the excipients, provided it has no impact over safety and efficacy, and where

2. they belong to the same company or an application for the medicinal products is filed by persons belonging to the same company or group of companies, or an application is filed for the medicinal products by persons who have entered a licensing or another agreement or who take joint actions relating to the marketing of the respective medicinal product in the different Member States.

Article 46. (1) When evaluating the documentation, the Bulgarian Drugs Agency shall:

1. be able to test the end product, the intermediate product or the raw materials for the medicinal product concerned, as well as to send them for testing to a laboratory within the system of official medicine control laboratories in a Member State, in order to establish whether the control methods of analysis used by the manufacturer and described in the dossier meet the relevant requirements;

2. following an on-site or document-based inspection, confirm whether manufacturers of medicinal products from third countries carry out manufacturing in accordance with data described in Article 27, Paragraph 1, item 7 and/or exercise control in accordance with the methods described in Article 27, Paragraph 1, item 8;

3. inspect the manufactured object specified in the application where the manufacturer(s) of medicinal products from third countries have, by way of exception, outsourced certain stages of the manufacturing or control of the medicinal product concerned to another manufacturer.

(2) Where the Bulgarian Drugs Agency conducts an on-site inspection of a manufacturing site, the period under Article 44 shall be suspended until the report containing the outcomes of the inspection comes out.

(3) In the cases under Paragraph 1, items 2 and 3, manufacturers shall pay a fee in the amount specified in the Tariff under Article 21, Paragraph 2.

Article 47. (1) The following specialised commissions shall be set up as consultative bodies with the Executive Director of the Bulgarian Drugs Agency:

1. Commission for Medicinal Products;
2. Commission for Immunological Medicinal Products;
3. Commission for Homeopathic Medicinal Products;
4. Commission for Herbal Medicinal Products;
5. Commission for Radiopharmaceuticals.
6. (New, *SG* No. 71/2008, effective 12.08.2008) Commission for Medicinal Products for Paediatric Use;
7. (New, *SG* No. 71/2008, effective 12.08.2008) Commission for Medicinal Products for Highly Technological Therapies.

(2) Where necessary, the BDA Executive Director may also set up other specialised commissions outside those specified in Paragraph 1.

(3) The specialised commissions shall be composed of specialists with scientific achievements and practical experience in the respective fields of application of the medicinal products.

(4) External experts with scientific knowledge and practical experience in the area of the specific class of drugs could also be used in addition to the permanent composition of the commissions.
(5) The BDA Executive Director shall specify, by order, the composition of commissions for a period of three years, the amount of their remuneration and shall endorse Rules on the terms and conditions of their work.
(6) No later than 30 January of each year, the BDA Executive Director shall endorse lists of experts outside the composition of the commissions under Paragraph 1, subject to approval by the Minister of Health.
(7) The BDA Executive Director may relieve prematurely a member of a specialised commission from office, upon his request, in case of failure to discharge his duties for a period of more than three months or in case of negligent performance of his functions.
(8) The composition of the commissions and the list of experts under Paragraph 6 shall be posted on the Bulgarian Drugs Agency website.
Article 48. (1) The members of specialised commissions under Article 47, Paragraph 1 and the experts under Article 47, Paragraph 4 shall sign a declaration, thereby taking the obligation not to:
1. disclose data and circumstances of which they have become aware while or on the occasion of carrying out their operations;
2. take part in operations associated with the manufacturing or wholesale and retail trade in medicinal products.
(2) In case individuals under Paragraph 1 have taken part in any of the stages in the preparation of documentation required for the authorisation of the use of the medicinal product concerned, they may not take part in the sessions of the respective specialised commission under Article 47.
(3) Individuals under Paragraph 1 shall not vote when decisions are made on matters in which they or members of their families have commercial, financial or other interests.
Article 49. (1) Within a period of up to 200 days from receiving valid documentation, the Bulgarian Drugs Agency, together with the respective commission under Article 47, shall evaluate the quality, safety and efficacy of the medicinal product concerned and shall prepare an evaluation report which it shall submit to the BDA Executive Director. The evaluation report shall be updated upon receipt of new information concerning the quality, safety and efficacy of the product.
(2) Where the medicinal product contains genetically modified organisms, the Bulgarian Drugs Agency shall provide the Ministry of Environment and Waters with the necessary documentation from the medicinal product's dossier and shall obtain an opinion, within a period of 60 days, on the potential risk to the environment. The 60-day period shall be within the period under Paragraph 1.
(3) In the case of radiopharmaceuticals, the Bulgarian Drugs Agency shall provide the necessary documentation from the medicinal product's dossier and shall obtain an opinion within a period of 60 days from the Nuclear Regulation Agency with regard to the quality and safety of the product. The 60-day period shall be within the period under Paragraph 1.
(4) Where the Ministry of Environment and Waters and the Nuclear Regulation Agency fail to rule within the periods set under Paragraphs 2 and 3, it shall be considered that their opinion is positive.
Article 50. (1) Where the Bulgarian Drugs Agency finds lack of compliance in the dossier with the requirements for issuance of an authorisation for use or of a certificate of registration under this Act, it shall notify the applicant in writing to submit additional information relating to the documentation under Articles 27-32 or under Article 35, Paragraph 3, or under Article 38, and/or to submit a verbal or written explanation with regard to the incompleteness and discrepancies found, within a period of 180 days from the date of notification.
(2) In the cases under Paragraph 1, the period under Article 44 shall be suspended from the date of notification until submission of the requested information.
(3) The Bulgarian Drugs Agency Executive Director shall terminate the procedure for issuance of an authorisation for use or of a certificate of registration of a medicinal product, where:
1. the applicant fails to submit the information under Paragraph 1 within the specified period;
2. the persons under Article 26, Paragraph 1 request its termination in writing.
Article 51. Within a period of 10 days from preparing the evaluation report under Article 49, Paragraph 1, the BDA Executive Director shall issue an authorisation for use/certificate of registration of the medicinal product or issue a motivated refusal.

Article 52. (1) Within 5 days from issuance, the authorisation for use/certificate of registration shall be entered in the register under Article 19, Paragraph 1, item 3, which shall contain:
1. a registration number;
2. a number and date of the authorisation for use/certificate of registration of the medicinal product;
3. the name of the medicinal product;
4. the international non-patent name of each active substance;
5. the name and address of the holder of an authorisation for use/certificate of registration;
6. the date of the change introduced in the authorisation for use/certificate of registration;
7. the date of termination of the authorisation for use/certificate of registration;
8. other data.
(2) The authorisation for use/certificate of registration of the medicinal product shall be served on the person under Article 26, Paragraph 1, and shall enter into force on the date of entry into the register under Article 19, Paragraph 1, item 3.
Article 53. (1) The Bulgarian Drugs Agency shall post on its website data under Article 52 concerning the issued authorisation for use/certificate of registration and the approved summary of the product within a period of 14 days following issuance thereof.
(2) Based on the evaluation report under Article 49, Paragraph 1, the Bulgarian Drugs Agency shall prepare a public evaluation report, including the reasoning for the decision made, without the data constituting commercial secrecy. The report shall be posted on the Bulgarian Drugs Agency website.
Article 54. (1) The holder of the authorisation for use/certificate of registration of a medicinal product shall notify the Bulgarian Drugs Agency in writing of the date on which the medicinal product shall be placed on the market.
(2) The holder of the authorisation for use/certificate of registration of a medicinal product shall notify the Bulgarian Drugs Agency in writing of each case in which sales of the medicinal product have been stopped, whether temporarily or permanently.
(3) In case of a planned stop of sales of the medicinal product, the holder of the authorisation for use/certificate of registration of the medicinal product shall notify the BDA in writing at least two months in advance.
(4) In case the sales of the medicinal product have been stopped as a result of unforeseeable circumstances, the holder of the authorisation for use/certificate of registration of the medicinal product shall notify the BDA in writing within a period of 24 hours from establishing the circumstances.
Article 55. (1) The authorisation for use/certificate of registration of the medicinal product shall be issued by the BDA Executive Director for a period of 5 years.
(2) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) Following the expiry of the term under Paragraph 1, the authorisation for use/certificate of registration of the medicinal product may be renewed by the Bulgarian Drugs Agency, based on an evaluation of the benefit/risk ratio under Article 59a.
(3) (Amended, *SG* No. 71/2008, effective 12.08.2008) The authorisation for use/certificate of registration may also be terminated before the term under Paragraph 1 expires, if its holder demands that in writing from the BDA Executive Director, citing the reasons for the request.
(4) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) The authorisation for use/certificate of registration shall become unlimited in time following its renewal, except in the cases under Paragraph 5.
(5) (Amended, *SG* No. 71/2008, effective 12.08.2008) If valid reasons concerning the safety of the product exist, the Bulgarian Drugs Agency may require from the holder of the authorisation for use/certificate of registration to submit an application for its renewal under Article 59a for 5 more years.
(6) (Amended, *SG* No. 71/2008, effective 12.08.2008) Upon expiry of the term of the authorisation for use/certificate of registration, or upon their termination, the medicinal product may be sold until the quantities available in the country are depleted, but for not more than one year after the date of expiry or termination, with the exception of the cases when the reasons for the termination are connected with the safety of the medicinal product.
(7) The BDA Executive Director shall by order withdraw the authorisation for use/certificate of registration of a medicinal product, where:
1. its holder has not placed the medicinal product on the market within up to three years from the date of issuance of the authorisation for use, or

2. the sales of the medicinal product have been suspended for a period of up to three consecutive years after its release on the market.
(8) The order under Paragraph 7 shall be subject to appeal under the Administrative Procedure Code.
(9) By way of exception and in the interest of public health, the provision of Paragraph 7 may not be applied if the holder of the authorisation for use of the medicinal product provides valid reasons. In such cases the BDA Executive Director shall provide reasoning for his decision.
(10) The holder of an authorisation for use shall pay an annual fee in the amount set in the Tariff under Article 21, Paragraph 2 for maintaining the authorisation for use issued.
Article 56. (1) By way of exception, when objective reasons have been provided and the relevant evidence submitted, the BDA Executive Director, following consultations with the applicant, may issue a conditional authorisation for use.
(2) The type and scope of the conditions under Paragraph 1 and the terms for their enforcement shall be specified in annexes to the authorisation for use/certificate of registration issued.
(3) The authorisation for use in the cases under Paragraph 1 shall be issued for a period of one year and it shall be extended for each subsequent year on the basis of an evaluation of the compliance with the conditions in Paragraph 2 by the Bulgarian Drugs Agency.
(4) The conditions under Paragraph 2 and the deadlines for their enforcement shall be posted on the Bulgarian Drugs Agency website.
(5) The BDA Executive Director shall withdraw an authorisation for use where the conditions under which the authorisation was issued are not complied with within the periods set under Paragraph 2.
Article 57. (1) The BDA Executive Director shall refuse an authorisation for use or a certificate of registration of a medicinal product where, after evaluation of the dossier under Articles 27-32, he finds that:
1. the benefit/risk ratio is unfavourable, or
2. the efficacy of the medicinal product is not convincingly defended by the applicant, or
3. the quantitative and qualitative composition of the medicinal product does not correspond to the one described in the dossier.
(2) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) The BDA Executive Director shall refuse to issue an authorisation for use or a certificate of registration of a medicinal product where some of the data in the dossier do not comply with the requirements of Articles 27-32 or with the Ordinance under Article 42.
(3) The BDA Executive Director shall refuse the registration of a traditional herbal medicinal product when it is found, after evaluation of the documentation, that the product does not meet the conditions under Article 37, Paragraph 1, data in the dossier do not comply with Article 38, or:
1. the quantitative and qualitative composition does not comply with the description in the dossier;
2. the medicinal product may be harmful with correct use;
3. data about its traditional use are insufficient, especially if pharmacological properties or efficacy are not proven through long-term use based on the accumulated experience;
4. the pharmaceutical quality of the medicinal product has not been sufficiently justified.
Article 58. The holder of the authorisation for use shall incur liability for the completeness and truthfulness of the data in the dossier.
Article 59. (1) The refusal by the BDA Executive Director to issue an authorisation for use/certificate of registration of a medicinal product may be appealed under the Administrative Procedure Code.
(2) A refusal by the BDA Executive Director and the reasons for it shall be posted on the Agency website.
Article 59a. (New, *SG* No. 71/2008**,** effective 12.08.2008) (1) In the cases under Article 55, Paragraphs 2 and 5, not later than six months prior to the expiry of the authorisation for use/certificate of registration, its holder shall file an application for its renewal before the BDA, accompanied by a summarised dossier concerning the quality, safety and efficacy of the medicinal product, which shall include all approved changes after the issuance of the authorisation for use/certificate of registration.
(2) The requirements to the data and the documents in the dossier under Paragraph 1 shall be determined in the Ordinance under Article 42.
(3) Within 120 days after the filing of the application and of the documentation under Paragraph 1, the BDA shall assess the safety, quality and efficacy of the medicinal product and shall draft an evaluation report, which shall be presented to the BDA Executive Director.

(4) In the event that incompleteness or non-compliance is found in the documentation submitted under Paragraph 1, the BDA shall inform in writing the holder of the authorisation for use/certificate of registration and shall give instructions for their elimination. The owner of the authorisation for use/certificate of registration shall eliminate the incompleteness and/or the non-compliance in the documentation within 30 days of receiving the notification.
(5) Within 10 days after receiving the evaluation report under Paragraph 3, the BDA Executive Director shall issue the permission for the renewal of the authorisation for use/certificate of registration of the medicinal product, or shall give a motivated refusal.
Article 59b. (New, *SG* No. 71/2008, effective 12.08.2008) (1) The BDA Executive Director shall refuse to renew the authorisation for use/certificate of registration of a medicinal product in the event that the assessment of the dossier under Article 59a, Paragraph 1, reveals that:
1. the medicinal product is harmful with correct usage, or
2. therapeutic efficacy is lacking, or
3. the benefit/risk ratio is unfavourable with correct usage, or
4. the qualitative and the quantitative composition of the medicinal product does not correspond to the composition described in the dossier, or
5. the data in the dossier under Article 59a, Paragraph 1, are untrue, or
6. no control has been performed on the medicinal product and/or on the components and intermediary stages of the production process, or some other requirement for the issuing of the permission for production has not been met, or
7. some data in the dossier do not meet the requirements under Article 59a, Paragraphs 1 and 2.
(2) The refusal by the BDA Executive Director to renew an authorisation for use/certificate of registration of a medicinal product may be appealed under the Administrative Procedure Code.
(3) The refusal by the BDA Executive Director and the motives thereof shall be posted on the BDA's website.

Section VI
Changes in an authorisation for use that has already been issued

Article 60. (1) The holder of an authorisation for the use of a medicinal product shall be obliged to immediately notify the Bulgarian Drugs Agency of each change in the conditions under which the authorisation was issued.
(2) The changes could be minor – of type IA and IB, or significant – of type II.
(3) Criteria on the basis of which changes are defined as being of type IA or IB shall be specified in the Ordinance under Article 42.
(4) All changes, other than those of type IA or IB, shall be significant changes of type II.
Article 61. (1) In case of type IA or IB changes, or of type II changes, the person under Article 26, Paragraph 1 shall file an application with the Bulgarian Drugs Agency, accompanied by:
1. documentation concerning the changes, as specified in the Ordinance under Article 42;
2. a document evidencing the payment of a fee in the amount specified in the Tariff under Article 21, Paragraph 2.
(2) The application under Paragraph 1 shall also include a proposed date for the entry of the changes into force.
(3) For each type IA, IB or II change, the holder of an authorisation for use of a medicinal product shall file a separate application.
(4) Where the holder of an authorisation for the use of a medicinal product makes more than one change in the authorisation for use issued, he shall file a separate application for each change, whereby each of the applications shall set out information about the type of changes for which other applications have been submitted.
(5) Where the change applied for results in subsequent interconnected changes of the same type, the holder of the authorisation for use of the medicinal product shall file a single application, stating therein the connection between the main change and those related thereto.
(6) Where a type IB change results in subsequent interconnected type IA or IB changes, the holder of the authorisation for use of a medicinal product shall file a single IB type of application, therein stating the connection between the main change and those related thereto.

(7) Where a change results in modification of the data in the product summary, the packaging and/or the brochure, these changes shall be taken as part of the change applied for and no separate application for them shall be filed.

Article 62. (1) The BDA Executive Director shall approve the type IA changes within 14 days following the submission of an application, provided the requirements under Article 60, Paragraph 3 and Article 61 have been met.

(2) Where the requirements under Articles 60 and 61 have not been met, the Bulgarian Drugs Agency shall notify the applicant within the period under Paragraph 1 that the application is not valid and the changes have not been accepted.

Article 63. (1) The BDA Executive Director shall approve type IB changes within a 30-day period following the submission of the application and shall issue an authorisation for the change concerned, indicating therein the date on which the said changes shall enter into force.

(2) Where the Bulgarian Drugs Agency finds lack of compliance of the submitted documentation with the requirements under Article 61, Paragraph 1, item 1, it shall notify the holder of the authorisation for use.

(3) The holder of the authorisation for use shall amend or supplement the documentation within a period of 30 days from the date of receiving the notification. In this latter case the period under Paragraph 1 shall be suspended.

(4) Where in the period under Paragraph 3 the holder of an authorisation for the use of the medicinal product concerned fails to submit the requested documentation, the BDA Executive Director shall terminate the procedure and shall notify the holder of the authorisation thereof.

Article 64. (1) Within a period of 60 days from the date of submission of a valid application for a type II change, the Bulgarian Drugs Agency shall prepare an evaluation report concerning the said change.

(2) The period under Paragraph 1 may be:

1. reduced in urgent cases connected with the safe use of the medicinal product, or
2. extended to 120 days in the event of a change that amends or supplements a therapeutic indication.

(3) Where the Bulgarian Drugs Agency finds non-compliance of the documentation submitted with the requirements under Article 61, Paragraph 1, item 1, it shall notify the holder of the authorisation for use and shall set a deadline for the submission of additional information.

(4) In the cases under Paragraph 3, the deadline under Paragraph 1 shall be suspended until the additional information concerned has been submitted.

(5) The Bulgarian Drugs Agency Director, based on the evaluation report under Paragraph 1, shall approve the changes and shall issue an authorisation for changing the authorisation for use, or shall give a motivated refusal. The authorisation shall specify the date on which changes shall enter into force.

(6) A refusal under Paragraph 5 shall be subject to appeal under the Administrative Procedure Code.

Article 65. (1) Where the holder of an authorisation for use finds a health hazard associated with the use of the medicinal product, he shall take urgent restrictive measures and shall immediately notify the BDA in writing.

(2) The Bulgarian Drugs Agency shall rule on these measures within 24 hours of notification.

(3) Where the Bulgarian Drugs Agency fails to rule within the period under Paragraph 2, the measures shall be considered approved.

(4) Where the Bulgarian Drugs Agency finds that there is a risk to human health associated with the use of the medicinal product, it shall order the holder of the authorisation for use to take immediate restrictive measures.

(5) In the cases under Paragraphs 1 and 4, the holder of the authorisation for use of the medicinal product concerned shall agree with the BDA the manner and terms for implementing the measures taken.

(6) The holder of an authorisation for use of the medicinal product concerned shall file an application for change with the BDA Executive Director under Article 64 no later than 15 days after the date on which the measures were taken.

Article 66. (1) The holder of an authorisation for the use of the medicinal product concerned shall file an application for extending the scope of the authorisation for use issued if there is:

1. a change in the quality of the active substance indicated in the dossier, which does not significantly change the safety and efficacy characteristics of the medicinal product and the changed substance shall not be defined as new where:

a) the medicinal substance(s) are replaced by a different salt/esther complex/derivatives (having the same therapeutic section);
b) a blend with an isolated polymer is replaced by a different isomer or a different blend of isomers.
c) a biologically active substance or a biotechnological product is replaced by a substance or product with a slightly changed molecular structure; the vector used to obtain the antigen/raw material is modified, including a new primary cell bank from a different source;
d) a new ligand or connection mechanism is available in the case of radio pharmaceuticals;
e) a change is found in the extracting solvent or in the herbal substance/herbal preparation ratio;
2. a change in the bioavailability;
3. a change in the pharmacokinetics, such as a change in the rate of discharge;
4. a change or addition of a new amount/activity of the active substance;
5. a change or addition of a new pharmaceutical form;
6. (Amended, *SG* No. 71/2008, effective 12.08.2008) a change or addition of a new route of administration – in the case of parenteral administration a distinction needs to be made between the intra-arterial, intravenous, intramuscular, subcutaneous and other routes of administration.
(2) The application under Paragraph 1 shall be filed together with the documentation under Article 27, Paragraph 1, item 10, concerning the changes under Paragraph 1.
(3) The requirements to the documentation under Paragraph 2 shall be specified in the Ordinance under Article 42.
(4) The name of the medicinal product shall not be changed in the authorisation issued expanding the scope of the initial authorisation for use.
(5) The issuance of an authorisation expanding the scope of an authorisation for the use of a medicinal product already issued shall take place in compliance with the terms and conditions of Articles 49-51.
Article 67. (1) The holder of an authorisation for the use of the medicinal product shall file an application for the issuance of a new authorisation for use where:
1. one or more active substances, including antigen components for vaccines, have been added or removed;
2. the quality of the active substance has been changed as specified in the dossier, significantly changing the safety and efficacy characteristics of the medicinal product, the changed substance thereby being defined as new;
3. an indication for the treatment, prevention or diagnostics has been added in another therapeutic area, or has been changed.
(2) (New, *SG* No. 71/2008, effective 12.08.2008) The holder of the authorisation for the use of the medicinal product shall file an application for the issuance of a new authorisation for use when the application for the renewal of the authorisation for use had not been filed before the deadline specified in Article 59a, Paragraph 1.
(3) (Renumbered from Paragraph 2, *SG* No. 71/2008, effective 12.08.2008) The application shall be accompanied by the documentation specified in the Ordinance under Article 42.
(4) (Renumbered from Paragraph 3, supplemented, *SG* No. 71/2008, effective 12.08.2008) In the cases under Paragraphs 1 anf 2 the procedure under Articles 49-51 shall apply.
Article 68. (1) The holder of an authorisation for the use of a medicinal product shall be obligated to immediately inform the Bulgarian Drugs Agency of:
1. any new information that may influence the benefit/risk ratio and necessitate a change in the data under Articles 27-32 and in the product summary;
2. any prohibition or restriction imposed by regulatory bodies of other states in which the medicinal product is on sale and of the reasons on account of which such measures have been imposed.
(2) The holder of an authorisation for use shall be obligated, upon request from the Bulgarian Drugs Agency, to submit data:
1. in support of a favourable risk/benefit ratio with regard to the medicinal product;
2. relating to the volume of sales of the medicinal product and data from the medical prescriptions issued for the product, if available to it.
Article 69. (1) The holder of an authorisation for the use of a vaccine or an immunological medicinal product intended for immunisation shall be obligated, prior to placing each batch of the product concerned on the market, to submit to the Bulgarian Drugs Agency the following:
1. a sample of the end product and/or a sample of the product in bulk/not poured into bottles;

2. manufacturing and quality control protocols;
3. a document evidencing the payment of a fee at the amount set out in the Tariff under Article 21, Paragraph 2.
(2) The holder of an authorisation for use of new immunological medicinal products or of immunological medicinal products manufactured using new or changed technologies or using technologies that are new to a particular manufacturer, shall discharge the obligations under Paragraph 1 for the specific period stated in the authorisation for use.
(3) Within a period of 60 days following the date of submission of the full set of documents, the Bulgarian Drugs Agency shall evaluate the manufacturing and quality control protocols for live vaccines, immunological and new immunological medicinal products and for testing the samples provided in an accredited laboratory, in order to establish whether the medicinal products under Paragraphs 1 and 2 have been manufactured in accordance with the approved specifications.
(4) In case of a positive testing outcome, the Bulgarian Drugs Agency shall issue a certificate for release of the batch.
(5) The terms, conditions and the requirements to the documentation for issuance of a certificate for release of the batches of products under Paragraphs 1 and 2 shall be specified in an Ordinance of the Minister of Health.
(6) Where the testing and evaluation under Paragraph 3 for the respective batch of the medicinal products have been carried out by an official medicinal product control laboratory in another Member State, the holder of the authorisation for use shall submit the certificate of release issued by the regulatory body of the Member State for the batch of medicinal products to the BDA.
(7) In the cases under Paragraph 6, the Bulgarian Drugs Agency shall carry out the operations under Paragraphs 3 and 4.
Article 70. (1) The holder of an authorisation for the use of a medicinal product obtained from human blood or plasma, prior to placing each product batch on the market, shall be obligated to submit to the Bulgarian Drugs Agency the following:
1. a sample of the end product and/or a sample of the product in bulk/not poured into bottles;
2. manufacturing and quality control protocols;
3. a document evidencing the payment of a fee at the amount set out in the Tariff under Article 21, Paragraph 2.
(2) Within a period of 60 days following the submission of the full set of documents, the Bulgarian Drugs Agency shall evaluate the manufacturing and quality control protocols for the medicinal product concerned obtained from human blood or plasma and for testing the samples provided in an accredited laboratory, in order to establish whether the medicinal product under Paragraph 1 has been manufactured in compliance with the approved specifications.
(3) In case of a positive testing outcome, the Bulgarian Drugs Agency shall issue a certificate of release for the batch.
(4) The terms, conditions and the requirements to the documentation for issuance of a certificate for release of the batches of products under Paragraph 1 shall be specified in the Ordinance under Article 69, Paragraph 5.
(5) Where the testing and evaluation under Paragraph 2 for the respective batch of medicinal products have been carried out by an official medicinal product control laboratory in another Member State, the holder of the authorisation for use shall submit the certificate of release issued by the regulatory body of the Member State for the batch of the medicinal product to the BDA.
(6) In the cases under Paragraph 5, the Bulgarian Drugs Agency shall not carry out the operations under Paragraphs 2 and 3.
Article 71. (1) The holder of an authorisation for use shall be obligated to maintain a system for the prohibition and market withdrawal of medicinal products falling short of the requirements for quality, safety and efficacy.
(2) The holder of an authorisation for use shall be obligated to prohibit and withdraw from the market medicinal products that have demonstrated lack of compliance with the quality, efficacy and safety requirements in compliance with the Ordinance under Article 274, Paragraph 1.
Article 72. (1) The holder of an authorisation for use of the medicinal product shall be obligated to update the information under Article 27, Paragraph 1, items 7 and 8 in accordance with changes in the generally accepted methods as a result of scientific and technological progress.

(2) The changes under Paragraph 1 shall be approved by the BDA Executive Director in compliance with this section.

Article 73. (1) The holder of an authorisation for use may transfer the rights on the authorisation for use of the medicinal product to another legal person or to groups having no legal personality, established on the territory of the Member States.

(2) The holder of an authorisation for use shall submit to the BDA an application to which the documentation specified in the Ordinance under Article 42 shall be attached, proposing a date for the transfer.

(3) Where incompleteness of the documentation under Paragraph 2 is found, the Bulgarian Drugs Agency shall notify the holder of the authorisation for use in writing to submit the necessary additional information within a period of 30 days. The period under Paragraph 5 shall stop running from the date of notification until the requested information is provided.

(4) Where the holder of the authorisation for use fails to supplement the documentation within the period under Paragraph 3, the procedure for transfer of the authorisation for use of the medicinal product shall be terminated.

(5) Within a period of 30 days from the date of submission of the application under Paragraph 2, the BDA Executive Director shall issue an authorisation for change, thereby approving the transfer. The authorisation for change shall also specify the date of transfer of the authorisation for use.

(6) The new holder of the authorisation for use shall fully assume the rights and obligations of the previous authorisation for use holder.

(7) Where the authorisation for use has been transferred in compliance with Paragraphs 1-6, its term of validity shall not be changed.

Section VII
Mutual recognition and decentralised procedures

Article 74. (1) Where the person under Article 26, Paragraph 1 holds an authorisation for use issued in another Member State for the same medicinal product within the meaning of Article 45, Paragraph 3, for which an application for authorisation for use has been submitted with the Bulgarian Drugs Agency, this person shall file a request with the regulatory body of a Member State it has designated in the application, hereinafter referred to as "reference Member State", to proceed with an evaluation report or to update the existent one.

(2) Together with the application, the person under Paragraph 1 shall also file with the BDA a dossier identical to the one filed in the reference Member State and in the other Member States designated in the application, hereinafter referred to as "concerned states."

(3) The Bulgarian Drugs Agency and the applicant shall obtain through official channels the evaluation report, together with the approved product summary, packaging mock-up and patient brochure from the regulatory body of the reference state under Paragraph 1.

(4) The Bulgarian Drugs Agency shall examine the documents under Paragraph 3 and shall inform in writing the reference state of the decision made within 90 days of the date of their receipt.

(5) Within a period of 30 days from receiving the notification that the reference state has terminated the procedure, the BDA Executive Director shall issue an authorisation for the use of the medicinal product on the territory of the Republic of Bulgaria with the approved product summary, packaging mock-up and patient brochure.

Article 75. (1) Where the person under Article 26, Paragraph 1 simultaneously submits with the Bulgarian Drugs Agency and in other Member States an application for authorisation to use a medicinal product for which no authorisation for use has been issued on the territory of a Member State, that person shall indicate in the application the regulatory body of the Member State, hereinafter referred to as "reference Member State", which shall prepare a draft evaluation report, a draft product summary and a project for a mock-up packaging and a draft patient brochure.

(2) Together with the application, the person under Paragraph 1 shall submit a dossier with the Bulgarian Drugs Agency, identical to the one filed in all other Member States designated in the application, hereinafter referred to as "concerned states."

(3) The Bulgarian Drugs Agency and the applicant shall obtain through official channels the draft evaluation report, the draft product summary, the project for a packaging mock-up and the draft patient brochure from the regulatory body of the reference Member State.

(4) The Bulgarian Drugs Agency shall examine the documents under Paragraph 3 and shall inform the reference Member State in writing of the decision made within 90 days from the date of their receipt.
(5) Within a period of 30 days from receiving a notification that the reference Member State has terminated the procedure, the BDA Executive Director shall issue an authorisation for the use of the medicinal product on the territory of the Republic of Bulgaria with the approved product summary, packaging mock-up and patient brochure.
Article 76. (1) Where the Republic of Bulgaria is a reference Member State under Article 74, the Bulgarian Drugs Agency shall:
1. within a period of 90 days from the date of submission of valid documentation, send the regulatory bodies of the concerned states and the applicant an evaluation report accompanied by the approved product summary, packaging mock-up and patient brochure.
2. close the procedure and notify the applicant and the concerned states, where all concerned states have approved thereof.
(2) Within a period of 30 days from closing the procedure under Paragraph 1, item 2, the BDA Executive Director shall issue an authorisation for the use of the medicinal product on the territory of the Republic of Bulgaria with the approved product summary, packaging mock-up and patient brochure.
(3) Where the Republic of Bulgaria is a reference state under Article 75, the BDA shall:
1. within a period of 120 days from the date of submission of valid documentation, send the regulatory bodies of the concerned states and the applicant the draft evaluation report, a draft product summary, a project for a packaging mock-up and a draft patient brochure.
2. close the procedure and notify the applicant and the concerned states, where all concerned states have approved thereof.
(4) Within a period of 30 days from closing the procedure under Paragraph 3, item 2, the BDA Executive Director shall issue an authorisation for the use of the medicinal product on the territory of the Republic of Bulgaria with the approved product summary, packaging mock-up and patient brochure.
Article 77. (1) Where the Bulgarian Drugs Agency fails to approve the documentation submitted under Article 74, Paragraph 3 or under Article 75, Paragraph 3, due to potential serious risk to the health of the population, it shall prepare a detailed motivated report to the reference Member State, the other concerned states and to the applicant.
(2) The disputed issues under Paragraph 1 shall be examined by the Coordination Group of the Member States. The applicant may give a statement on the issues examined in writing or verbally.
(3) The Bulgarian Drugs Agency shall take part in the Coordination Group under Paragraph 2 until the reference state closes the procedure.
(4) Within 30 days from receiving a notification that the reference state is closing the procedure, the BDA Executive Director shall issue an authorisation for use of the medicinal product with the approved product summary, packaging mock-up and patient brochure.
Article 78. (1) Where the Member States fail to reach agreement within the procedure under Article 77, Paragraph 2, taking place before the Coordination Group, the disputed issues shall be examined by the Committee for Medicinal Products for Human Use with the European Medicines Agency in an arbitration procedure. A copy of the documentation shall be sent to the applicant.
(2) The applicant shall submit the dossier of the medicinal product and the product summary to the European Medicines Agency.
(3) In the cases under Paragraph 1, if the Bulgarian Drugs Agency has approved the evaluation report, the draft product summary, the project for a packaging mock-up and the draft patient brochure, provided by the reference state, the BDA Executive Director, at the request of the applicant, may issue an authorisation for the use of the medicinal product prior to the completion of the arbitration procedure under Paragraph 1.
(4) Following completion of the arbitration procedure, the BDA Executive Director shall bring the authorisation for use issued under Paragraph 3 in line with the decision of the European Commission.
Article 79. (1) Where regulatory bodies of one or more Member States have adopted differing decisions with regard to the authorisation for use of the same medicinal product or for its temporary suspension or withdrawal, the Bulgarian Drugs Agency shall bring the issue to the Committee for Medicinal Products for Human Use with the European Medicines Agency for the implementation of an arbitration procedure. The applicant or the holder of the authorisation for use may, if they so deem appropriate, bring the

issue to the Committee for Medicinal Products for Human Use with the European Medicines Agency for the implementation of an arbitration procedure.
(2) Where the use of the product creates a risk to public health, the Bulgarian Drugs Agency or the applicant or the holder of an authorisation for use may bring the issue of delivering an authorisation for use of a specific medicinal product, its temporary suspension, the termination of the validity of such licenses or of its modification in relation to the information under Chapter eight to the Committee under Paragraph 1 for an arbitration procedure to be carried out.
(3) In the cases under Paragraphs 1 and 2, the BDA or the applicant for/holder of the authorisation for use of the medicinal product concerned shall provide the European Medicines Agency with the full available information on a particular issue.
(4) Depending on the decision of the European Commission, following termination of the arbitration procedure, within 30 days of receiving the notification, the BDA shall:
1. issue or terminate an authorisation for use, or
2. require that changes be made in an issued authorisation in order to make it compliant with the decision of the European Commission.
(5) The Bulgarian Drugs Agency shall notify the European Commission and the European Medicines Agency of the act issued under Paragraph 4.
Article 80. The terms and conditions for changing the authorisations issued under this section are provided for in Regulation (EC) No. 1084/2003 of the European Commission.

Chapter Four
CLINICAL TRIALS
Section I
General provisions

Article 81. Clinical testing of medicinal products on humans may take place, in order to:
1. discover or confirm the clinical, pharmacological or pharmacodynamic effects of one or more medicinal products tested;
2. identify the adverse reactions to one or more medicinal products tested;
3. study the absorption, distribution, metabolism and excretion of one or more medicinal products tested and/or establish their safety and/or efficacy.
Article 82. (1) Clinical testing on humans shall be carried out subject to the fundamental principles of protection of human rights and dignity in each medico-biological study in accordance with the Helsinki Declaration.
(2) (Amended, *SG* No. 71/2008, effective 12.08.2008) All clinical trials of medicinal products on humans, including trials of bioavailability and bioequivalence, shall be planned, carried out and reported in compliance with the rules of Good Clinical Practice, the requirements of this Act and Regulation (EC) No. 1901/2006.
(3) The rules of Good Clinical Practice shall be specified in an Ordinance of the Minister of Health.
Article 83. (1) The rights, safety and health of the subjects in a clinical trial shall be placed above the interests of science and the public.
(2) Any available preclinical and/or clinical data about the medicinal product tested must be adequate to justify the clinical trial being carried out.
Article 84. (1) A clinical trial must be scientifically justified and described in a clear and detailed way in the testing protocol.
(2) When developing the documentation and when carrying out the clinical trial for a medicinal product, the sponsor and the researcher shall take into account all available guidelines published by the European Commission and the European Medicines Agency and the scientific committees attached to it.
Article 85. (1) Clinical testing of medicinal products on humans shall be carried out in conformity to the required procedures for assuring the quality of every aspect of clinical testing.
(2) The entire information about clinical testing shall be recorded, processed and stored in a way that shall ensure its accurate reporting, interpretation and validation, the personal data of subjects being protected.
Article 86. (1) All persons conducting a clinical trial must have relevant professional qualification, training and experience, in order to discharge the tasks associated with testing in compliance with the rules of Good Clinical Practice.

(2) The clinical testing of a medicinal product shall take place under the guidance of a physician or a doctor of dental medicine with a recognised medical specialisation in the respective area, who shall be aware of the available preclinical and/or clinical data about the product and the study risks and procedures.
(3) A physician with suitable qualifications or a doctor of dental medicine shall be responsible for the medical care provided to test subjects during the clinical trial, and for making medical decisions.
Article 87. (1) Clinical testing may be carried out in in-patient care establishments, dispensaries and diagnostic consultative centres that have obtained a positive accreditation evaluation of overall operations and of operations carried out in separate structures of the treatment establishment associated with clinical testing in accordance with the Medical-Treatment Facilities Act.
(2) A clinical trial may only be carried out in a treatment establishment where, in compliance with Article 103, an Ethics Committee exists, set up under Article 103 and entered in the BDA register.
(3) The head of the treatment establishment in which a medicinal product is to be tested shall give consent for the participation of the chief researcher and for the conducting of the trial.
Article 88. (1) Clinical testing on humans shall be carried out for:
1. medicinal products not authorised for use in the Republic of Bulgaria;
2. medicinal products that have been authorised for use in the Republic of Bulgaria when tested for an unauthorised indication, for a pharmaceutical form other than the authorised one, in a group of patients who have not been studied so far or for obtaining additional information.
(3) Medicinal products authorised for use in the Republic of Bulgaria, within the meaning of Paragraph 1, item 2, shall be those that have obtained authorisation for use in compliance with this Act or Regulation (EC) No. 726/2004 of the European Parliament and of the Council.
Article 89. (1) Clinical testing on humans shall be carried out with medicinal products that have been manufactured, maintained and stored in accordance with the rules of Good Manufacturing Practice for medicinal products under development and research.
(2) The rules of Good Manufacturing Practice for medicinal products under development and research shall be specified in the Ordinance under Article 152.
(3) A medicinal product that has been subjected to pharmacological and toxicological studies in accordance with the requirements of Good Laboratory Practice may be proposed for clinical testing.
Article 90. A clinical trial may commence and shall be carried out where:
1. the expected therapeutic benefits for trial subjects, for present and future patients and the benefits for health care justify the foreseeable risks;
2. the physical and mental integrity of the trial subject, his right to privacy and personal data protection, in accordance with the Personal Data Protection Act, are guaranteed.
3. an insurance or compensation covering researcher or sponsor liability has been envisaged.
Article 91. The sponsor and the chief researcher shall make an insurance covering their liability for material and immaterial damage caused to subjects during or on the occasion of clinical testing.
Article 92. (1) The sponsor shall be liable in case of health deterioration or of causing death during or on the occasion of clinical testing, where the trial is carried out in accordance with the requirements and procedures based on the protocol approved by the Ethics Committee.
(2) The chief researcher shall be liable in case of health deterioration or of causing death during or on the occasion of clinical testing when the requirements and procedures based on the protocol approved by the Ethics Committee have not been observed.
Article 93. (1) The sponsor of a clinical trial shall be a person established on the territory of a Member State.
(2) The sponsor and the researcher may be the same person.
Article 94. The sponsor shall ensure the tested medicinal product/s and all articles required for its administration free of charge.
Article 95. (1) The sponsor shall prepare the labelling of the tested medicinal product in compliance with the requirements set out in the rules of Good Manufacturing Practice in respect to medicinal products under development and research.
(2) Requirements to data appearing on the packaging of medicinal products destined for testing shall be specified in the Ordinance under Article 170.
Article 96. (1) Clinical testing of medicinal products shall only be admitted on an individual who is:

1. informed, in a preliminary conference with a physician, i.e., a member of the research team, of the purposes, risks and inconveniencies of testing, and of the terms under which it is to be carried out;
2. informed of his right to withdraw from testing at any time, without any negative consequences for him;
2. has personally given consent in writing to take part, having been made aware of the nature, significance, effects and possible risks of the clinical testing.
(2) Where the individual cannot write, informed consent for the participation in a clinical trial shall be given orally in the presence of at least one independent witness who shall certify in writing that the individual has personally given informed consent for taking part in the clinical trial.
(3) A fully capacitated individual, understanding the nature, implications, significance and possible risks of the clinical trial, may only give informed consent under Paragraph 1, item 3 and Paragraph 2. The informed consent for participation in a clinical trial may be withdrawn at any time.
(4) The informed consent under Paragraph 1, item 3 shall be given, for incapacitated adults, by their statutory representatives. The consent given by the statutory representative must represent the presumed will of the subject and may be withdrawn at any time without negative consequences for the subject.
(5) In thecases under Article 162, Paragraph 3 of the Health Act, informed consent shall be given by a person appointed by the court.
(6) Incapacitated adults shall be provided with information about the trial, the possible risks and benefits, which shall correspond to their ability of understanding.
(7) The express wish of an incapacitated adult to refuse taking part or to withdraw at any time from the clinical trial must be taken into account by the researcher and, where necessary, by the chief researcher.
Article 97. (1) Clinical trial on a minor shall be carried out after obtaining written informed consent from both parents or from the legal guardians of the individual, subject to Article 96, Paragraphs 1 and 3.
(2) The consent of the parents and legal guardians must represent the presumed will of the minor and may be withdrawn at any time without negative consequences for him.
(3) The express wish of the child to refuse taking part or to withdraw at any time from the clinical trial must be taken into account by the researcher and, where necessary, by the chief researcher.
(4) Clinical trials on a minor shall be carried out after obtaining written informed consent from the individual and from both parents, or from the custodian, subject to Article 96, Paragraphs 1 and 3. Where one of the parents is unknown, deceased or deprived of parental rights or, in case of divorce no such rights have been given to him/her, the written informed consent shall be given by the minor and by the parent exercising parental rights.
(5) The consent of the minor, of the parents or of the custodian may be withdrawn at any time without negative consequences for the minor.
(6) The express wish of the minor to withdraw at any time from the clinical trial must be taken into account by the researcher and, if necessary, by the chief researcher.
(7) The child or minor shall be given information about the trial and about the possible risks and benefits in a way that will ensure understanding by a physician who has experience with children and minors.
Article 98. No informed consent to take part in clinical trials shall be required, where an immediate decision is required in order to save the individual's life and provided at this time no such consent may be obtained. The decision shall be made by at least two physicians not involved in the research team.
Article 99. (1) During the trial, the subject shall receive at his request additional information from a person independent from the sponsor.
(2) Written information provided to subjects of clinical trials of a medicinal product shall contain contact details of the independent person for additional information.

Section II
Clinical trials with vulnerable groups of patients

Article 100. Clinical trials on children and minors may be undertaken provided that:
1. the protocol has been approved by the relevant Ethics Committee after discussion of the clinical, moral and psycho-social aspects of childhood, in which at least two paediatricians have taken part;
2. a direct benefit is expected from the clinical trial for the group of patients that will be included in it;
3. the clinical trial is directly related to the clinical condition of the suffering child or minor;

4. the medicinal product tested is intended to be used for diagnosis, treatment or prevention of diseases that are specific to children and minors;
5. the trial is intended to be carried out on children and minors;
6. the purpose of the trial is to verify data obtained from clinical trials on individuals that are able to give informed consent or data obtained through other research methods;
7. the results obtained from clinical trials on adults and their interpretation may not also be considered valid for children and young persons;
8. the trial is planned in a way to minimise pain, inconvenience, fear and other foreseeable risks associated with the disease, and the level of risk and physical pain have been predefined and are constantly controlled during testing;
9. the study has been planned and is carried out in accordance with the guidelines of the European Medicines Agency;
10. no financial or other incentives are provided, other than compensation.

Article 101. (1) Clinical trials on individuals under Article 96, Paragraphs 4 and 5, who are not able to give informed consent, shall be carried out in accordance with the requirements of Article 90.

(2) Other than the requirements under Paragraph 1, the participation of adults who are not able to give informed consent in clinical trials shall be allowed, provided that:
1. the respective Ethics Committee, involving specialists with competence in respect to the disease concerned or to the group of patients, has approved the protocol after discussing the clinical, moral and psycho-social aspects of relevance to the particular disease and to the group of patients;
2. it may be expected that taking the medicinal product tested would bring benefits exceeding the risks or that risks have been fully eliminated;
3. the purpose of the trial is to check data obtained through clinical trials on humans who are able to give informed consent or of data obtained through other research methods;
4. the trial is directly connected to a life-threatening or disabling disease of which the adult person concerned who is not able to give informed consent suffers;
5. the clinical trials have been planned so that pain, inconvenience, fear and other foreseeable risks associated with the disease have been reduced to a minimum and the level of risk and the degree of physical pain have been set in advance and are constantly monitored during the trial;
6. no financial and other incentives are provided, except for compensation.

Article 102. No clinical trials of a medicinal product may be conducted on pregnant and breast-feeding women, unless the medicinal product concerned is required for their treatment and may not be tested on any other group of patients.

Section III
Ethics Committees

Article 103. (1) An Ethics Committee on multi-centre trials shall be set up with the Minister of Health and its composition shall be specified by an order thereby issued.

(2) Ethics committees shall be set up with treatment establishments in which clinical trials are conducted, whose composition shall be specified by the head of the respective treatment establishment.

(3) The Bulgarian Drugs Agency shall keep and maintain a register of the ethics committees.

(4) The register of the treatment establishments with which ethics committees have been set up shall be posted on the Bulgarian Drugs Agency website.

Article 104. (1) The committees under Article 103, Paragraphs 1 and 2, shall be composed of 7 to 12 members, having the qualifications and experience required to examine and evaluate the scientific, medical and ethical aspects of the proposed clinical trial.

(2) The committees under Paragraph 1 shall comprise no less than two members, having no medical background, representing both genders and being financially and administratively independent of the treatment establishment in which the clinical trial takes place.

(3) The committees under Paragraph 1 may use the services of external experts for the needs of their work.

(4) While conducting clinical trials on children and minors, in order to get additional support for its operations, the respective ethics committee with the treatment establishment shall mandatorily use the services of external experts.

Article 105. (1) The term of office of the members of the ethics committees under Article 103, Paragraphs 1 and 2, shall be four years.

(2) Every two years half of the ethics committees' composition shall be renewed.
(3) No ethics committee member may be appointed to the same committee for more than two consecutive terms of office.
Article 106. (1) The ethics committees under Article 103, Paragraphs 1 and 2, shall produce written standard operational procedures in compliance with the rules of Good Clinical Practice within a month of being set up, thereby fixing the terms and conditions of their work.
(2) The standard operational procedures of the ethics committees shall be approved by the Bulgarian Drugs Agency Executive Director.
(3) The ethics committees shall conduct sessions behind closed doors. Where necessary, the chairperson of the ethics committee may invite the sponsor or chief researcher to take part therein.
(4) Only those members of the ethics committees who do not participate directly in a specific trial and are administratively and financially independent of the sponsor and chief researcher may vote and take part in deliberations.
(5) In order to certify the circumstances under Paragraph 4, members of the ethics committees shall sign a statement of conflict of interests.
Article 107. (1) Central Ethics Committee shall be set up with the Council of Ministers.
(2) The Central Ethics Committee shall consist of 9 members, representing both genders, and it shall mandatorily comprise physicians, doctors of dental medicine, a psychologist, a theologist and a lawyer.
(3) The composition of the Committee shall be stipulated by decision of the Council of Ministers at the proposal of the Minister of Health for a period of 4 years.
(4) The Central Ethics Committee shall draft an opinion on deontological and ethical issues in the area of clinical trials when it has been approached by the ethics committees under Article 103, Paragraphs 1 and 2, by the BDA or by the sponsor.
(5) The Central Ethics Committee shall provide methodological guidance to the ethics committees under Article 103, Paragraphs 1 and 2.
(6) The sessions of the Central Ethics Committee shall be conducted behind closed doors. Where necessary, the chairperson of the Central Ethics Committee may invite the sponsor or chief researcher to take part therein.
(7) The Council of Ministers, at the proposal of the Minister of Health, shall specify the terms and conditions of work of the Central Ethics Committee by issuing Rules to this effect.
Article 108. (1) No member of the Central Ethics Committee may be appointed to the same committees for more than two consecutive terms of office. The term of office shall have 4-year duration.
(2) Every two years the composition of a half of the Central Ethics Committee shall be renewed.

Section IV
Authorisation to conduct clinical trials

Article 109. A clinical trial may begin when the following conditions are fulfilled:
1. the respective ethics committee has given a positive opinion, and
2. the BDA Executive Director has issued a written authorisation when one of the tested medicinal products is:
a) a medicinal product for a gene therapy;
b) a medicinal product for somatic cell therapy;
c) a medicinal product containing genetically modified organisms;
d) a high-technology medicinal product, as specified in the Appendix to Regulation (EC) No. 726/2004 of the European Parliament and of the Council;
e) a medicinal product containing a biologically active substance(s) of human or animal origin or containing biological components of human or animal origin or such components are used in its manufacturing, or
3. the sponsor failed to notify the BDA in writing within the period set by law that trials may not take place in respect to medicinal products outside those under item 2.
Article 110. (1) In order to obtain an opinion, the chief or coordinating researcher and the sponsor shall submit to the respective ethics committee under Article 103:
1. administrative documentation;
2. information about subjects;
3. documentation concerning the trial protocol;
4. documentation about the medicinal product tested;

5. documentation about the technical requirements and the staff;
6. data about funding and the administrative organisation of trials.
(2) The content, the format and the requirements to the documentation under Paragraph 1 shall be specified in the Ordinance under Article 82, Paragraph 3.
Article 111. (1) The ethics committee shall draft an opinion, taking the following into account:
1. the significance of the clinical trial;
2. the positive evaluation of the ratio between the expected benefits and the risks in accordance with Article 90, item 1, and the extent to which the conclusions are justified;
3. the clinical trial protocol;
4. the extent to which the chief researcher and the research team are suitable to conduct the clinical trial;
5. the researcher's brochure;
6. the availability of the necessary equipment and its quality;
7. the consistency and completeness of written information to be provided and the procedure for obtaining informed consent, as well as the extent to which the trial on humans incapable of giving informed consent is justified in the cases under Articles 100 and 101;
8. the foreseen compensation or restitution in case of damages or death that may result from the clinical trial;
9. the insurance covering researcher and sponsor liability;
10. where necessary, the terms and conditions of remunerating or compensating researchers and subjects in the clinical trial and the elements of the contract between the sponsor and the treatment establishment;
11. the terms and conditions of recruiting subjects.
(2) The ethics committee shall:
1. give a positive opinion;
2. provide a motivated refusal, or
3. require a modification of part of the documentation as a condition for obtaining a positive opinion.
Article 112. (1) Within a period of 60 days of filing an application, the ethics committee concerned shall rule, issuing an opinion, which it shall send to the applicant and to the BDA.
(2) Where the clinical trial includes a medicinal product for gene therapy or for somatic cell therapy, or a medicinal product containing genetically modified organisms, the term under Paragraph 1 shall be extended up to 30 days.
(3) The term for drafting an opinion shall be 180 days where the examination of a clinical trial involving medicinal product for gene therapy or for somatic cell therapy or a medicinal product containing genetically modified organisms requires consulting a committee of experts specifically set up to this effect by order of the BDA Director.
Article 113. (1) When evaluating the documentation, the ethics committee may require, on a one-off basis, the applicant to provide additional documentation. The periods under Article 112 shall be suspended until the requested documentation has been submitted.
(2) The procedure for examination of the study shall terminate where, within 60 days of receiving a request for additional information, the sponsor fails to submit the documentation requested by the committee.
Article 114. (1) Where the trial is to take place in more than one centre on the territory of the Republic of Bulgaria, an application shall be filed with the ethics committee for multi-centre trials under Article 103, Paragraph 1.
(2) Where the trial is to take place in only one centre on the territory of the Republic of Bulgaria, an application may be filed with the respective ethics committee under Article 103, Paragraphs 1 or 2 at the choice of the applicant.
(3) The opinion of the ethics committee under 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 under Article 103 is negative, the sponsor may, within a period of 90 days of the date of notification, appeal its decision before the Central Ethics Committee.
(2) Where the negative opinion of the respective ethics committee under Article 103 has been drafted without taking account of the opinion of the expert committee under Article 112, Paragraph 3, the

sponsor may, within 14 days of the date of notification, request in writing from the committee to reconsider its opinion.
(3) The expert committee under Article 112, Paragraph 3, within 60 days of the date of receiving the written application from the sponsor, shall rule on the negative opinion of the respective ethics committee, contesting or supporting it, of which it shall notify the latter in writing. The ethics committee shall come up with a final opinion, which it shall send to the sponsor.
(4) Where the expert committee under Article 112, Paragraph 3 grants support to the negative opinion, the sponsor, within 14 days of the date of notification, may appeal 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 sponsor shall submit to the Bulgarian Drugs Agency a model-based application for the conducting of a clinical trial.
(2) Where the applicant for a clinical trial is not a sponsor, the application shall be accompanied by documentation certifying that the person has been authorised by the sponsor.
(3) Where the sponsor is not registered as a natural or legal person on the territory of the Republic of Bulgaria, the application shall be accompanied by a document specifying the data about his authorised representative on the territory of the Republic of Bulgaria.
(4) The following shall be attached to the application:
1. administrative documents;
2. information about subjects;
3. documentation about the trial protocol;
4. documentation about a tested medicinal product(s);
5. documentation about the technical requirements and about the staff;
6. documentation about the funding and the administrative organisation of the trial.
(5) The content, the format and the requirements to the documentation under Paragraph 4 shall be specified in the Ordinance under Article 82, Paragraph 3.
Article 117. (1) When evaluating the documentation under Article 116, the Bulgarian Drugs Agency may obtain, on a one-off basis, additional documentation from the applicant.
(2) The periods under Articles 118, 119 and 120 shall be suspended until the requested documentation has been submitted.
Article 118. (1) Within 60 days of the date of submission of the application for a clinical trial of medicinal products under Article 109, item 3, the Bulgarian Drugs Agency shall notify the applicant in writing that the trial:
1. may be conducted on the territory of the Republic of Bulgaria, or
2. may not be conducted, specifying the reasons therefor.
(2) In cases under Paragraph 1, item 2, the sponsor may, within a period of 30 days, submit to the Bulgarian Drugs Agency an application modified in compliance with the reasons set out, or submit the required information in compliance with the Bulgarian Drugs Agency requirements.
(3) Within a period of 30 days of the date of submission of the modified application or of the additional information under Paragraph 2, the BDA shall notify the applicant in writing that:
1. the trial may be conducted on the territory of the Republic of Bulgaria, or
2. refuse the clinical trial to be conducted, stating the reasons for this.
(4) A refusal under Paragraph 3, item 2 shall be subject to appeal under the Administrative Procedure Code.
(5) A clinical trial may begin, if within the period under Paragraph 1 the Bulgarian Drugs Agency has not issued a notification refusing to approve the clinical trial.
(6) If the applicant fails to submit an application under Paragraph 2 within the specified period, the procedure shall terminate and the clinical trail shall not take place.
Article 119. (1) Within a period of 60 days of the date of submission of the application for a clinical trial involving medicinal products under Article 109, item 2, the Bulgarian Drugs Agency Executive Director shall:
1. issue an authorisation for conducting the clinical trial, or
2. a motivated refusal to issue an authorisation.

(2) The refusal under Paragraph 1, item 2, shall be subject to appeal under the Administrative Procedure Code.

Article 120. (1) In the cases of medicinal products under Article 109, item 2, a) – c), the period under Article 119, Paragraph 1 for the issuance of an authorisation by the Bulgarian Drugs Agency to conduct a clinical trial, may be extended by 30 days.

(2) In case the Bulgarian Drugs Agency consults the expert committee under Article 112, Paragraph 3, which is to evaluate the safety of medicinal products under Paragraph 1, the period extended under Paragraph 1 may be extended by another 90 days.

Article 121. The BDA Executive Director shall refuse to issue an authorisation for conducting a clinical trial of medicinal products for gene therapy where a risk exists that the genome of the reproductive cells of the trial subject could be modified.

Article 122. (1) In case of a multi-centre trial in the Republic of Bulgaria and in a third country, the Bulgarian Drugs Agency shall require from the sponsor to submit a declaration that he would allow access for inspection by BDA representatives for the purpose of establishing compliance with the requirements and principles of Good Clinical Practice and of Good Manufacturing Practice.

(2) Where the sponsor fails to submit the declaration under Paragraph 1, the Bulgarian Drugs Agency shall not examine the application filed.

Article 123. The sponsor shall declare that the documentation filed with the Bulgarian Drugs Agency and with the ethics committee contains the same information.

Article 124. (1) Procedures at the ethics committee and at the Bulgarian Drugs Agency may take place simultaneously or consecutively, at the sponsor's choice.

(2) The period under Article 118, Paragraph 1 for the examination of the documentation shall not be suspended in the event no decision has been reached by the ethics committee.

Article 125. A clinical trial shall be conducted in compliance with the protocol that has obtained a positive opinion from the respective ethics committee under Article 103, and subject to the terms specified in the documentation filed.

Section V
Changes

Article 126. (1) The sponsor may introduce changes, other than significant ones under Article 127, Paragraph 2, to the clinical trial protocol at any time.

(2) In the cases under Paragraph 1, the sponsor shall keep the documentation related to the changes and shall submit it to the Bulgarian Drugs Agency and to the ethics committee upon request.

Article 127. (1) A change in the way a clinical trial is conducted could be requested by the Bulgarian Drugs Agency whenever necessary, in order to guarantee the safety of subjects, the scientific value of the trial and/or compliance with the rules of Good Clinical Practice.

(2) A significant change in the way a study is conducted shall be any change in the protocol and/or in the information and the documentation under Articles 110 and 116 that affects:

1. the safety or the physical and mental integrity of the subjects;
2. the scientific value of the study;
3. the conducting or the organisation of the study;
4. the quality or the safety of one of the medicinal products tested.

Article 128. (1) The sponsor may apply significant changes planned in the trial protocol and in the documentation under Articles 110 and 116, where:

1. the respective ethics committee has given a written positive opinion;
2. the BDA Executive Director has issued a written authorisation for this in respect to clinical trials involving medicinal products under Article 109, item 2, or
3. within the period specified by law, the sponsor has not been notified by the Bulgarian Drugs Agency that the proposed changes in the clinical trial involving medicinal products under Article 109, item 3 have not been accepted.

(2) The provision of Paragraph 1 shall not apply to changes in the approved protocol which are required in order to protect the subjects from imminent danger when new information is discovered pertaining to the conduct of the trial, or to the development of the tested medicinal product.

(3) In the cases under Paragraph 2, the sponsor shall immediately notify the commission under Paragraph 1, item 1 and the Bulgarian Drugs Agency of the available new information, of the measures taken and of the changes introduced in the protocol.

Article 129. (1) When planning significant changes in the clinical trial and the documentation under Articles 110 and 116, the sponsor shall file a written application, based on a model, with the BDA and with the respective ethics committee.
(2) The application shall be accompanied by documentation required to justify the changes and certifying that after applying the change, the evaluation of the ratio between the benefits and the risks under Article 90, item 1 shall be kept.
(3) The requirements to the application and the documentation about the change shall be specified in the Ordinance under Article 82, Paragraph 3.
Article 130. (1) Within a period of up to 35 days of receiving an application for change, the ethics committee shall notify the applicant of its resolution, issuing:
1. a positive opinion of the requested changes, or
2. a motivated refusal of changes in the clinical trial.
(2) Within a period of up to 35 days of the date of receiving an application, subject to positive opinion of the ethics committee, the BDA shall:
1. approve the changes in the clinical trial involving medicinal products under Article 109, item 2, or
2. fail to approve the changes, expressly submitting reasons therefor.
(3) If, within a period of 35 days of submitting the documentation about the change in respect to clinical trials involving medicinal products under Article 109, item 3, the applicant fails to receive a notification of refusal, the proposed changes may be made.
Article 131. (1) In the cases under Article 130, Paragraph 2, item 2, the sponsor may submit a modification into the proposed changes, in line with the reasons, 14 days prior to applying the changes at the latest.
(2) Within a period of 14 days of the date of receiving the changed documentation under Paragraph 1, the BDA shall issue a change to the authorisation for a clinical trial involving medicinal products under Article 109, item 2, or a refusal.
(3) A refusal under Paragraph 2 shall not be subject to appeal.

Section VI
Suspension of the clinical trial

Article 132. (1) The sponsor or the researcher may undertake urgent measures in order to protect the subjects of the clinical trial against any suddenly appearing risks to their safety and health.
(2) In the cases under Paragraph 1, the sponsor shall immediately notify the Bulgarian Drugs Agency and the respective ethics committee of the action undertaken and of their causes.
Article 133. (1) When the trial is conducted under terms other than those specified upon issuance of the authorisation, or information is available that the scientific validity of the study is discredited, or there is a risk to the safety of the subjects, the Bulgarian Drugs Agency may provisionally suspend the trial or terminate it.
(2) The termination may be imposed on a particular centre or on all centres, for a multi-centre clinical trial on the territory of the Republic of Bulgaria.
(3) In case of termination of the clinical trial in all centres on the territory of the Republic of Bulgaria, the Bulgarian Drugs Agency, prior to taking action under Paragraph 1, shall notify in writing the sponsor and the chief or coordinating researcher.
(4) Within 7 days of receiving the notification, the sponsor and/or the chief researcher may give an opinion on the measures taken by the Bulgarian Drugs Agency.
(5) The provision of Paragraph 3 shall not apply where there is immediate risk to the health and safety of trial subjects.
Article 134. In the cases under Article 133, Paragraph 1, the Bulgarian Drugs Agency shall immediately notify the respective ethics committee, the regulatory bodies of all Member States, the European Medicines Agency and the European Commission of the measures taken and the reasons for this.

Section VII
Monitoring safety

Article 135. (1) The chief researcher shall immediately notify the sponsors, verbally or in writing, of any serious adverse event that has occurred in the course of the clinical trial with a subject in the centre of which he is in charge.
(2) After the notification under Paragraph 1, a detailed report in writing shall be submitted.

(3) When a notification under Paragraph 1 or a report under Paragraph 2 is made, the trial subject shall be identified by a unique code specified in the trial protocol.
(4) The provisions of Paragraphs 1 and 2 shall not apply where it has been expressly noted in the clinical trial protocol or the researcher brochure that no urgent notification is required of a specific serious adverse event.
(5) The researcher shall report to the sponsor all adverse events or laboratory deviations specified in the protocol as critical to safety, within the period and in the format compliant to the requirements of the protocol.
Article 136. When the outcome of an adverse event during the conducting of a clinical trial is lethal, the researcher shall be obligated to provide the sponsor and the ethics committee with all additional information requested.
Article 137. The sponsor shall keep detailed records of all serious adverse events that have been provided to him by researchers, and upon request shall make these available to the BDA or to the regulatory bodies of Member States in which the trial takes place, in the case of a multi-centre trial.
Article 138. (1) The sponsor shall notify the BDA, the regulatory bodies of all Member States in which a trial takes place, in the case of a multi-centre trial, and the ethics committee, respectively, of any suspected unexpected serious adverse reaction that has occurred in the course of a clinical trial and has resulted in death or has proven to be life-threatening, within 7 days at the latest of receiving the information about it.
(2) The sponsor shall provide the bodies under Paragraph 1 with additional information about the case within 8 days of the date on which a notification was sent.
(3) The sponsor shall notify the bodies under Paragraph 1 of all suspected unexpected serious adverse reactions other than those specified in Paragraph 1 that have occurred in the course of the clinical trial, 15 days at the latest from receiving the information about their occurrence.
Article 139. (1) The sponsor may fulfil his duties under Article 138, Paragraphs 1 and 3, submitting notifications to the European database of adverse reactions.
(2) (Amended, *SG* No. 71/2008, effective 12.08.2008) When a clinical trial also takes place outside the Member States, the sponsor shall submit notifications of suspected unexpected adverse reactions to the European database of adverse reactions.
(3) The format and the content of the notifications of adverse reactions shall be specified in the Ordinance under Article 191, Paragraph 1.
(4) The sponsor shall inform the researchers carrying out the clinical trial with a medicinal product of any suspected unexpected adverse reaction associated with the tested medicinal product, irrespective of its origin.
Article 140. (1) Once a year the sponsor shall submit to the Bulgarian Drugs Agency and to the respective ethics committee a list of all suspected serious adverse reactions that have occurred within the past period and a report on the safety of trial subjects.
(2) The format and content of the reports shall be specified in the Ordinance under Article 191, Paragraph 1.
Article 141. (1) The Bulgarian Drugs Agency shall record all information provided in compliance with Article 138, Paragraphs 1 and 3, about the suspected unexpected serious adverse reactions caused by medicinal products tested.
(2) The Bulgarian Drugs Agency shall immediately introduce the information under Paragraph 1 into the European database of adverse reactions.

Section VIII
Notification of completion of the clinical trial

Article 142. (1) The sponsor shall notify the Bulgarian Drugs Agency and the respective ethics committee in writing of the termination of the trial on the territory of the Republic of Bulgaria.
(2) The notification shall be filed within 90 days of the termination of the study in the format specified in the Ordinance under Article 82, Paragraph 3.
(3) Unless otherwise specified in the protocol approved by the respective ethics committee, the last visit of a subject shall be considered as the termination of the trial.
(4) Where a trial terminates early, the sponsor shall notify the Bulgarian Drugs Agency and the respective ethics committee within up to 15 days of making a decision, stating the reasons for it.

Article 143. The sponsor shall present the Bulgarian Drugs Agency and the respective ethics committee with a final report on the clinical trial.

Article 144. (1) The Bulgarian Drugs Agency shall input data in the European clinical trials database about each clinical trial on the territory of the Republic of Bulgaria, i.e., the application filed, the decision of the ethics committee, the authorisation for conducting a trial, any significant changes, termination of the study and data about inspections carried out.

(2) Upon request by another Member State, by the European Medicines Agency or the European Commission, the Bulgarian Drugs Agency shall provide additional information other than the one entered in the European clinical trials database.

(3) In case it fails to fulfil its obligations under Paragraph 1, the Bulgarian Drugs Agency shall observe the published guidelines of the European Commission.

Section IX
Non-intervention study

Article 145. (1) A non-intervention study shall be conducted with the use of medicinal products authorised for use in the Republic of Bulgaria when they are tested for additional information about the product prescribed in the usual way, complying with the terms specified in the authorisation for use.

(2) The sponsor shall submit with the respective ethics committee and with the Bulgarian Drugs Agency documentation on the conducting of a non-intervention study, as specified in the Ordinance under Article 82, Paragraph 3.

(3) The conducting of a non-intervention study may begin, if the candidate does not receive express refusal by the Bulgarian Drugs Agency Director within one week of filing an application and the documents under Paragraph 2 with the Bulgarian Drugs Agency.

Chapter Five
AUTHORISATION FOR MANUFACTURING AND IMPORTING MEDICINAL PRODUCTS

Section I
Manufacturing

Article 146. (1) The manufacturing of all types of medicinal products within the meaning of this Act, of active substances used as raw materials and of medicinal products intended for clinical trial may be carried out on the territory of the Republic of Bulgaria only by natural and legal persons registered as traders on the territory of Member States, who have obtained an authorisation for manufacturing, issued by the BDA Director.

(2) A manufacturing authorisation shall also be required in cases where products under Paragraph 1 are only intended for exportation.

(3) (Amended, *SG* No. 71/2008, effective 12.08.2008) A manufacturing authorisation shall also be required for persons who simultaneously or separately carry out one of the following operations: complete or partial manufacturing, difference processes of preparation for packaging, packaging, repackaging, labelling, quality control and releasing of batches of medicinal products and of medicinal products intended for clinical trials.

(4) (Repealed, *SG* No. 71/2008, effective 12.08.2008)

(5) No manufacturing authorisation shall be required where the process of preparation for packaging, mixing or packaging takes place in accordance with an official or magisterial formulation in a pharmacy.

Article 147. The Bulgarian Drugs Agency shall send to the European Medicines Agency a copy of the authorisations issued under Article 146 to be entered into the EU database.

Article 148. In order to obtain a manufacturing authorisation, the person under Article 146 should have:

1. suitably qualified staff, depending on the specificity of the medicinal products and pharmaceutical forms manufactured;
2. at any point in time, at least one qualified individual meeting the conditions of Article 159;
3. premises for manufacturing, controlling and storing medicinal products having the required technical equipment and control laboratories.

Article 149. Heads of production and control over the quality of medicinal products at the manufacturing undertaking shall be individuals:

1. with an educational and qualification degree of "master" in the specialised area of "pharmacy", "chemistry" or "biology" and at least two years of practical experience in pharmaceutical manufacturing;

2. meeting the requirements under item 1 and having a recognised additional specialisation in radiobiology or radiochemistry with regard to radiopharmaceuticals or medicinal products subject to ionising radiation;
3. having a recognised specialisation in clinical haematology, medical microbiology, virology or immunology with regard to manufacturing immunological medicinal products, i.e., vaccines, toxins, serums, biotechnological products and medicinal products obtained from human plasma or human blood.

Article 150. (1) A person under Article 146 shall submit with the Bulgarian Drugs Agency an application based on a model approved by the Agency Director.
(2) The following shall also be submitted by the applicant together with the application under Paragraph 1:
1. a diploma of higher education, a document of acquired specialisation, a document evidencing the record of service, a criminal record certificate and a labour contract – for persons under Article 148, item 2 and Article 149;
2. copies of contracts for entrusting the manufacturing and/or control of the products for whose manufacturing an application is made in the cases under Article 151;
3. (Amended, *SG* No. 71/2008, effective 12.08.2008) An up-to-date certificate of recordation in the commercial register or a document evidencing an up-to-date registration;
4. a list of the medicinal products, formulations and active substances to be manufactured;
5. drawings of manufacturing, control and storage premises, and a dossier for the production facility;
6. an environmental impact assessment when medicinal products are manufactured in cases provided for under the Environmental Protection Act;
7. an authorisation from the Nuclear Regulation Agency when the application concerns the manufacturing of radio pharmaceuticals or of medicinal products subjected to ionising radiation during manufacturing;
8. an authorisation to use manufacturing, control and storage premises issued in compliance with the Spatial Development Act, or another substitute document;
9. a conclusion from RIPCPH following on-site inspection;
10. a document evidencing the payment of a fee at the amount specified in the Tariff under Article 21, Paragraph 2.
(3) The requirements of the Narcotic Substances and Precursors Control Act shall also be observed when narcotic substances and pharmaceutical forms containing these substances are manufactured.

Article 151. When some stages of the manufacturing or control trials during the production process are carried out, by virtue of a contract, in another site on the territory of the Republic of Bulgaria or outside it, the persons under Article 146 shall be obligated to indicate the location of this site and to submit a copy of the contract, specifying the duties of each of the parties with regard to the compliance with the requirements of Good Manufacturing Practice in respect to medicinal products, as well as the obligations of the qualified person under Article 148, item 2.

Article 152. The conditions for issuing a manufacturing authorisation and the principles and requirements of Good Manufacturing Practice for all types of medicinal products, for medicinal products for clinical trial and for active substances shall be provided for in an Ordinance of the Minister of Health.

Article 153. (1) When an application under Article 150 is received, the Bulgarian Drugs Agency shall evaluate the documentation filed and shall conduct an on-site inspection of the manufacturing, control and storage sites, also including the cases under Article 151, in order to establish the level of compliance of the submitted documentation with the manufacturing, control and storage conditions applicable to raw materials used in manufacturing and the latter's conformity to the requirements of Good Manufacturing Practice.
(2) The costs of the on-site inspection under Paragraph 1 shall be borne by the applicant.
(3) In order to have an on-site inspection under Paragraph 1 carried out, the applicant shall pay a fee at the amount specified in the Tariff under Article 21, Paragraph 2.

Article 154. (1) When the Bulgarian Drugs Agency finds incompleteness of the submitted documentation and/or incompliance of the content of the submitted documentation with the state of affairs on site or with the requirements to the qualification of staff, it shall notify the applicant in writing and shall issue written instructions.

(2) In the cases under Paragraph 1, the period under Article 155, Paragraph 1 shall be suspended until the site or the documentation is brought in line with the requirements.

Article 155. (1) The BDA Executive Director, within a period of 90 days of submission of the application under Article 150, shall:

1. issue a manufacturing authorisation, or
2. come up with a motivated refusal.

(2) A manufacturing authorisation shall only be issued in respect to the medicinal products and formulations, active substances and medicinal products intended for clinical trials indicated in the application and in respect to the premises in which manufacturing, control and storage is to take place.

(3) The acts under Paragraph 1 shall be served on the applicant.

(4) A manufacturing authorisation shall not be limited in time.

(5) A refusal under Paragraph 1, item 2 shall be subject to appeal under the Administrative Procedure Code.

Article 156. (1) The holder of a manufacturing authorisation shall file an application in case there is a change in:

1. the person under Article 148, item 2;
2. the persons under Article 149;
3. the manufacturing equipment;
4. the location or restructuring of one of the manufacturing, control or storage sites;
5. manufacturing operations;
6. the active substances, medicinal products and formulations manufactured;
7. the court registration.

(2) Documents relating to the change shall be attached to the application under Paragraph 1, as specified in the Ordinance under Article 152.

(3) A manufacturing authorisation shall be terminated in case its holder terminates operation, of which he shall be obligated to notify the Bulgarian Drugs Agency.

Article 157. (1) When the authorisation for admission of the change is issued, the provisions of Articles 150 and 151 shall apply, the period for its delivery being no longer than:

1. 14 days, in the cases under Article 156, Paragraph 1, items 1, 2, and 7;
2. 90 days, in the cases under Article 156, Paragraph 1, items 3, 4, 5 and 6.

(2) Where the changes under Article 156, Paragraph 1, items 3, 4, 5, and 6 may not be evaluated on the basis of documents, the Bulgarian Drugs Agency shall conduct an on-site inspection. In these cases the period under Paragraph 1, item 2 shall be suspended until completion of the inspection.

(3) The on-site inspection costs under Paragraph 2 shall be borne by the applicant.

(4) In order to have an on-site inspection conducted under Paragraph 2, the applicant shall pay the fee stipulated in the Tariff under Article 21, Paragraph 2.

Article 158. (1) The Bulgarian Drugs Agency shall keep a register under Article 19, Paragraph 1, item 1of the manufacturing licenses issued, which shall contain:

1. the number and date of the manufacturing authorisation;
2. the name, seat and business address of the person who has obtained a manufacturing authorisation;
3. the address of the manufacturing, control and storage premises for the drugs;
4. the active substances, medicinal products and formulations for which authorisation is obtained;
5. the names of persons under Article 148, item 2;
6. the names of persons under Article 149;
7. the date of deletion from the register of the manufacturing authorisation and the grounds to do so.

(2) Data from the register of issued manufacturing licenses shall be posted on the Bulgarian Drugs Agency website.

(3) Upon request from the European Commission or a regulatory body of a Member State, the BDA shall provide information about a manufacturing authorisation it has issued.

Article 159. (1) The holder of a manufacturing authorisation shall hire under labour contract at least one qualified person under Article 148, item 2, who shall be permanently available to him.

(2) The qualified person under Paragraph 1 must meet the following requirements:

1. have a master's degree in medicine, pharmacy, chemistry, biotechnology or biology;
2. have at least two years of practical experience in pharmaceutical production and/or in performing qualitative and quantitative analysis of medicinal products and active substances.

(3) When the holder of a manufacturing authorisation for a medicinal product meets the requirements of Paragraph 2, he may discharge the obligations of a qualified person.
(4) The qualified person shall issue a certificate of release for each batch, certifying that the batch of medicinal products has been manufactured and controlled in compliance with the requirements of the authorisation for use under this Act.
(5) The qualified person shall issue a certificate of release for each batch, certifying that the batch of medicinal products intended for clinical trials has been manufactured and controlled in compliance with the requirements of Good Manufacturing Practice, with the production dossier for the product and the information provided under Article 110, Paragraph 1, item 4.
(6) The qualified person shall keep a register of the issued certificates of release for each batch of the medicinal product concerned.
(7) Data on the register under Paragraph 6 shall be stored for at least 5 years after the last entry and shall be presented upon request to the control bodies.
(8) When penal administrative proceedings are instituted on account of violations committed in the discharge of the qualified person's duties, the BDA shall order the holder of the manufacturing authorisation to temporarily relieve from office the qualified person.
(9) The criteria and requirements to the qualifications and education of persons under Article 148, item 2, shall be specified in the Ordinance under Article 152.

Article 160. (1) The holder of a manufacturing authorisation shall:
1. ensure the conducting of manufacturing operations in compliance with the requirements of Good Manufacturing Practice and in compliance with the information under Article 27, Paragraph 1, items 7 and 8, approved by the BDA, and in cases of medicinal products for clinical trials, in compliance with the information under Article 110, Paragraph 1, item 4, provided to the BDA by the sponsor;
2. use as starting materials only active substances manufactured in compliance with the requirements of Good Manufacturing Practice;
3. ensure the permanent presence of qualified staff for manufacturing and control in accordance with the requirements of the Ordinance under Article 152;
4. only have available medicinal products with authorisation for use or medicinal products intended for trials, in compliance with the requirements of this Act;
5. notify control bodies in advance of each change under Article 156;
6. notify immediately the control bodies in case the qualified person under Article 148, item 2 has been replaced;
7. ensure at any time access by control bodies to the premises and documentation;
8. provide the necessary conditions to the qualified person under Article 148, item 2, in order to allow him to proceed with his duties.
(2) The holder of a manufacturing authorisation shall store the mock-ups and the documentation concerning the medicinal products, active substances and medicinal products intended for clinical trials manufactured by him, subject to the terms and conditions specified in the Ordinance under Article 152.
(3) In the case of a medicinal product intended for clinical trial, the holder of a manufacturing authorisation shall guarantee that all production operations shall be carried out in accordance with the information provided by the sponsor to the Bulgarian Drugs Agency as per the Ordinance under Article 82, Paragraph 3.
(4) The documentation concerning any concluded transaction shall be kept for 5 years and shall specify the date, name of medicinal product, the amount supplied, the name and address of the recipient and the batch number.
(5) The holder of a manufacturing authorisation shall ensure and maintain a system for the blocking and withdrawal from the market of medicinal products that have demonstrated lack of compliance with quality requirements.
(6) The holder of a manufacturing authorisation shall be obligated to block and withdraw from the market the medicinal products that have demonstrated lack of compliance with quality, efficacy and safety requirements in compliance with the Ordinance under Article 274, Paragraph 1.
(7) The holder of a manufacturing authorisation shall be obligated to update the manufacturing methods following the development of new technologies and the production of medicinal products for trial.

Section II
Importation of medicinal products and active substances

Article 161. (1) Only natural and legal persons registered as traders in accordance with the legislation of a Member State, who have obtained authorisation for importation issued by the BDA Executive Director, can import into the territory of the Republic of Bulgaria from third countries all types of medicinal products, active substances used as raw materials and medicinal products destined for clinical trials.
(2) In order to obtain authorisation for importation, the person under Paragraph 1 must have:
1. at any time, at least one qualified person meeting the requirements of Article 159, Paragraphs 2 and 9;
2. a quality control laboratory in accordance with the requirements of the Ordinance under Article 152 and premises for the storage of medicinal products, active substances and excipients and of medicinal products for clinical trials, having the necessary technical equipment subject to the requirements of the Ordinance under Article 198.
Article 162. (1) In order to obtain authorisation for importation, the person under Article 161, Paragraph 1 shall file with the Bulgarian Drugs Agency an application based on a model approved by the BDA Director.
(2) The following shall be attached to the application under Paragraph 1:
1. (Amended, *SG* No. 71/2008, effective 12.08.2008) an up-to-date certificate of entry in the commercial register or a document of an up-to-date registration;
2. a list of the active substances, medicinal products and forms to be imported;
3. (Supplemented, *SG* No. 71/2008, effective 12.08.2008) a copy of the manufacturing authorisation issued by the regulatory body of the exporting state and a certificate verifying the compliance of the conditions for the manufacturing, control and storage with standards that are at least equivalent to the standards of Good Manufacturing Practice;
4. documents certifying the circumstances under Article 159, Paragraphs 1 and 2 with regard to the qualified person;
5. data about the address of the laboratory on the territory of the Republic of Bulgaria that will carry out a full quantitative and qualitative analysis at least of the active substances and of all other tests and inspections substantiating the quality of each imported batch of medicinal products, in compliance with the requirements of the authorisation for use in pursuance hereof, as well as the address of the storage premises;
6. a contract specifying the duties of each party with regard to the observation of the principles of Good Manufacturing Practice, by the contractor, and the way in which the qualified person under Article 161, Paragraph 2, item 1 shall discharge his obligations, in cases where the person under Article 161, Paragraph 1 has no laboratory of his own;
7. a document evidencing the payment of a fee specified in the Tariff under Article 21, Paragraph 2.
(3) (New, *SG* No. 71/2008, effective 12.08.2008) When the application under Paragraph 1 is received, the BDA shall assess the documentation filed and shall perform an on-site inspection of the control laboratory and of the premises for storage of medicinal products and of medicinal products intended for clinical trials, with a view to determining whether they are in compliance with the requirements of the Good Manufacturing Practice and of the Good Distribution Practice.
(4) (Renumbered from Paragraph 3, *SG* No. 71/2008, effective 12.08.2008) Where manufacturing premises are located in a third country with which the European Community has entered an agreement for the mutual recognition of certificates of Good Manufacturing Practice, the persons under Article 161, Paragraph 1 shall attach to their application the address of all premises for the manufacturing of medicinal products, active substances or medicinal products intended for clinical trials, the name, seat and business address of the person who has obtained a manufacturing authorisation, a certificate of the compliance of manufacturing, control and storage conditions with standards that are equivalent to those approved under the requirements of Good Manufacturing Practice, and the name of the qualified person.
(5) (Renumbered from Paragraph 4, amended, *SG* No. 71/2008, effective 12.08.2008) In cases other than those under Paragraph 4, the Bulgarian Drugs Agency, where necessary, shall conduct an on-site inspection to establish compliance of the documentation with the manufacturing, control and storage conditions for medicinal products in the exporting state. When compliance is established with Good Manufacturing Practice, the Bulgarian Drugs Agency shall issue a certificate.
(6) (Renumbered from Paragraph 5, amended, *SG* No. 71/2008, effective 12.08.2008) The costs of the on-site inspection under Paragraph 5 shall be borne by the importer.

(7) (Renumbered from Paragraph 6, amended, *SG* No. 71/2008, effective 12.08.2008) In order to have an on-site inspection under Paragraph 3 or under Paragraph 5 conducted, the applicant shall pay a fee at the amount specified in the Tariff under Article 21, Paragraph 2.

Article 163. (1) The qualified person under Article 161, Paragraph 2, item 1 shall issue a certificate for the release of each batch, evidencing that the batch of a medicinal product imported from a third country, irrespective of whether the product was manufactured or not in another Member State, prior to being placed on the territory of the Republic of Bulgaria, has been subjected to a full qualitative and quantitative analysis, at least of the active substances, and that all necessary trials and inspection, in compliance with the requirements for issuing an authorisation for use in pursuance hereof, have been carried out.

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

(3) Where the batch of a medicinal product is imported from a third country with which the European Community has entered an agreement for the mutual recognition of certificates of Good Manufacturing Practice, a qualified person shall issue a certificate for release of the batch on the basis of the documentation that accompanies the said batch, without having to carry out control trials on the territory of the Republic of Bulgaria.

(4) The qualified person under Paragraph 1 shall issue a certificate of release for each imported batch to the effect that the batch of a medicinal product on the territory of the Republic of Bulgaria, which is intended for clinical trials, has been manufactured and controlled in compliance with standards that are equivalent to Good Manufacturing Practice, to the product's manufacturing dossier and that in respect to every batch of medicinal products all necessary quality analyses and tests have been carried out in accordance with the information provided to the BDA by the sponsor as per the Ordinance under Article 82, Paragraph 3.

(5) The qualified person under Paragraph 1 shall issue a certificate of release in respect to every batch of a medicinal product used for the sake of comparison in a clinical trial on the territory of the Republic of Bulgaria, which is imported from a third country and is not accompanied by a document certifying that it has been manufactured and controlled in compliance with standards that are equivalent to Good Manufacturing Practice, including the cases in which for this medicinal product an authorisation for use has been issued.

(6) (Amended, *SG* No. 71/2008, effective 12.08.2008) No control trials shall be required on the territory of the Republic of Bulgaria when the requirements under Paragraph 4 or 5 have been complied with in another Member State and the medicinal product intended for clinical trials is accompanied by a certificate of release of the batch issued by another qualified person.

(7) The qualified person under Paragraph 1 shall store the documentation in respect to every batch of a medicinal product for at least 5 years and shall, upon request, submit it to the control bodies.

(8) The holder of an authorisation for importation shall ensure and maintain a system for blocking and market withdrawal of medicinal products that have shown lack of compliance with quality requirements.

(9) The holder of an authorisation for importation must block and withdraw from the market medicinal products that have shown lack of compliance with the requirements to safety and efficacy as per the Ordinance under Article 274, Paragraph 1.

(10) The provisions of Article 160, Paragraph 1, items 4, 5, and 7 shall also apply with respect to the holders of an authorisation for importation.

(11) The holder of an authorisation for importation shall provide the qualified person under Article 161, Paragraph 2, item 1 with the necessary conditions for the discharge of his duties and shall immediately notify the control bodies when he is replaced.

(12) When penal administrative proceedings are instituted for violations committed while the qualified person is discharging his duties, the Bulgarian Drugs Agency shall order the holder of the authorisation for importation to temporarily relieve from office the qualified person.

Article 164. (1) The BDA Executive Director shall issue an importation authorisation within a period of 30 days of the date of submission of the application under Article 162 or a motivated refusal.

(2) The refusal under Paragraph 1 shall be subject to appeal under the Administrative Procedure Code.

(3) The authorisation for importation shall only be issued in respect to medicinal products, the forms of their active substances and in respect to the medicinal products intended for clinical trials indicated in the application, as well as in respect to the premises in which control and storage is to take place.
(4) An authorisation for importation shall not be limited in time.
Article 165. (1) The holder of an authorisation for importation from a third country shall file an application with the Bulgarian Drugs Agency in case the following are changed:
1. the person under Article 161, Paragraph 2, item 1;
2. the active substances, the medicinal products and the forms in respect to which the authorisation for importation has been issued;
3. the address of the laboratory under Article 161, Paragraph 2, item 2;
4. the court registration of the trader.
(2) Documents relating to the change as specified in the Ordinance under Article 152 shall be attached to the application under Paragraph 1.
Article 166. (1) The provisions of Article 164 shall apply to the issuance of the authorisation, the term for this being:
1. in cases under Article 165, Paragraph 1, items 1, 2, and 4 – up to 14 days;
2. in cases under Article 165, Paragraph 1, item 3 – up to 30 days.
(2) When the change under Article 165, Paragraph 1, item 3 may not be assessed on the basis of documents, the Bulgarian Drugs Agency shall conduct an on-site inspection. In such cases the term under Paragraph 1, item 2 shall stop running until the completion of the inspection.
(3) The costs of the on-site inspection under Paragraph 2 shall be borne by the applicant.
(4) In order to have an on-site inspection under Paragraph 2 carried out, the applicant shall pay a fee at the amount specified in the Tariff under Article 21, Paragraph 2.
Article 167. (1) The Bulgarian Drugs Agency shall keep a register under Article 19, Paragraph 1, item 2 of the authorisations for importation issued, which shall contain:
1. the number and the date of the authorisation for importation;
2. the name, seat and business address of the person who has obtained an authorisation for importation;
3. the address of the control and storage premises for medicinal products;
4. the active substances, the medicinal products and formulations for which authorisation has been obtained;
5. the name of the person under Article 161, Paragraph 2, item 1;
6. the date of deletion from the register of the date of the authorisation for importation and the grounds for this.
(2) Register data shall be posted on the Bulgarian Drugs Agency website.

Chapter Six
MEDICINAL PRODUCTS PACKAGING AND BROCHURES

Article 168. (1) The packaging of a medicinal product shall consist of immediate and/or outer packaging and of a patient brochure.
(2) The outer packaging of medicinal products containing the substances listed in Appendix 2 to Article 3, Paragraph 2 of the Narcotic Substances and Precursors Control Act shall be marked by two diagonal red bands and the outer packaging of medicinal products containing substances in Appendix No. 3 to Article 3, Paragraph 2 of the Narcotic Substances and Precursors Control Act – by two blue bands. The packaging shall mandatorily bear an indication that a medicinal product is only dispensed by special medical prescription.
(3) The outer packaging and the medicinal products brochure may contain symbols or pictogrammes intended to illustrate the information contained in them, in order to make them easier for patients to assimilate.
(4) The outer packaging and the transport containers of medicinal products containing radionuclides must be marked in accordance with the requirements for the safe transportation of radioactive material of the International Atomic Energy Agency.
(5) When a medicinal product is allowed for use on the territory of the Republic of Bulgaria, the outer packaging shall be marked for separate collection and recycling in accordance with the Waste Management Act and the instruments for its enforcement.

(6) When a medicinal product is allowed for use, its name on the outer packaging, the pharmaceutical form and the content of the active substance per dosing unit shall also be printed in Braille.
(7) The requirements of Paragraph 6 shall not apply to vaccines and medicinal products in hospital packaging.
Article 169. (1) The information on packaging and brochures for a medicinal product must be in full compliance with data on the product summary approved by the Bulgarian Drugs Agency upon issuance of the authorisation for use, and must meet the requirements specified in the Ordinance under Article 170.
(2) Information on packaging and in the brochure may be in several languages, one mandatorily being Bulgarian. The content of the information in different languages must be identical.
(3) The name of the medicinal product shall be mandatorily written in the Bulgarian language and the international non-patent name of the medicinal substance shall be printed in accordance with the WHO Anatomic Therapeutic Chemical Classification System. The name and address of the holder of an authorisation for use may be printed in Latin.
(4) The information on packaging and in brochures must be in a language that the patient understands, be easy to read and non-erasable.
Article 170. The requirements to packaging and brochures of medicinal products shall be specified in an Ordinance of the Minister of Health.

Chapter Seven
CLASSIFICATION OF MEDICINAL PRODUCTS

Article 171. (1) Depending on the manner in which medicinal products are dispensed for use, they shall be classified as follows:
1. medicinal products dispensed for use by prescription;
2. medicinal products dispensed for use without prescription.
(2) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) The regime for the dispensation of medicinal products shall be determined by the Bulgarian Drugs Agency in the authorisation for use/certificate of registration or by the authorisation for parallel import of the medicinal product on the territory of the republic of Bulgaria.
(3) The person under Article 26, Paragraph 1 shall specify the regime for dispensation of medicinal products in the application for authorisation for use/certificate of registration, for changing an authorisation for use or upon renewal thereof.
Article 172. Medicinal products under Article 171, Paragraph 1, item 1 shall fall in the following categories:
1. medicinal products of limited prescription intended for use only in some specialised areas;
2. medicinal products making the object of special prescription;
3. medicinal products for one-off or multiple dispensation by a single prescription.
Article 173. Medicinal products meeting the following requirements shall be dispensed by prescription:
1. they may constitute a direct or indirect threat to human health, even if used by the rules, if administered without medical supervision;
2. they often are widely administered incorrectly and, as a result, may constitute a threat to human health;
3. they contain substances whose activity and/or adverse reactions require subsequent additional study;
4. they are usually prescribed by a doctor for parenteral administration.
Article 174. Medicinal products shall be subject to special medical prescription when they meet any of the following conditions:
1. they contain narcotic substances, within the meaning of the Narcotic Substances and Precursors Control Act, at amounts admitted for use;
2. if used incorrectly, they may create considerable risk of abuse, resulting in drug dependence, or be used for illegal purposes;
3. they contain new medicinal substances whose characteristics are sufficiently well known and, for this reason, to a preventative purpose, they may be categorised as item 2 medicinal products.
Article 175. Medicinal products shall be subject to limited medical prescription if they meet any of the following conditions:
1. they are limited for use only in hospitals because of limited experience of use or in the interest of public health;

2. they are intended for the treatment of medical conditions that may only be diagnosed in treatment establishments, even though they may be administered and the course of treatment may be monitored in other medical establishments as well;
3. they are intended for outpatient treatment, but their use may cause serious adverse reactions requiring a prescription by a specialist and supervision during treatment.

Article 176. (1) The Bulgarian Drugs Agency may approve the regime of dispensation of a medicinal product requested by the applicant under Article 26, Paragraph 1, based on a judgement of:
1. the minimum single dose, the maximum daily dose, the amount of active substance per dosing unit, the pharmaceutical form, the specific type of immediate packaging of the product, and/or
2. other specific conditions for use.
(2) The Bulgarian Drugs Agency may indicate the exact category of the medicinal product under Article 172, but in accordance with the criteria under Article 174 and Article 175 it shall determine whether the medicinal product shall be classified as a product dispensed only by medical prescription.

Article 177. Medicinal products that do not meet the requirements under Articles 173, 174 and 175 and the criteria specified in the Ordinance under Article 178, shall be dispensed without medical prescription.

Article 178. The criteria for the classification of medicinal products and the requirements to the documentation for introducing a change in the classification shall be specified in an Ordinance of the Minister of Health.

Article 179. (1) The Bulgarian Drugs Agency shall prepare and post on its website a list of medicinal products that are dispensed by medical prescription on the territory of the Republic of Bulgaria.
(2) The list under Paragraph 1 shall be updated annually.

Article 180. In the presence of new data about a medicinal product, for which an authorisation for use has been issued or a certificate of registration, the BDA shall reconsider and, if necessary, amend the classification in accordance with the requirements of Article 173 and the criteria specified in the Ordinance under Article 178.

Article 181. In cases when a change in the classification of a medicinal product is allowed based on considerable preclinical and clinical trials, no subsequent applicant or holder of an authorisation for use may refer, within a period of one year following the date of the authorisation for change issued by a regulatory body of a Member State, to the classification of the same substance when filing an application for change.

Article 182. The Bulgarian Drugs Agency shall notify the European Commission and the regulatory bodies of other Member States on an annual basis of the changes that have occurred in the list under Article 179.

Chapter Eight
MONITORING DRUG SAFETY

Article 183. Medical specialists shall be obligated to immediately inform the holder of an authorisation for use and the Bulgarian Drugs Agency about any suspected serious or unexpected adverse reaction, notwithstanding whether the medicinal product has been used or not in compliance with the approved product summary.

Article 184. (1) The Bulgarian Drugs Agency shall set up and maintain a system for monitoring the safety of medicinal products placed on the market.
(2) The system under Paragraph 1 shall record in a database all incoming notifications of adverse reactions from medicinal products authorised for use, including any information about the abuse thereof or their use which is not in compliance with the BDA-approved product summary, about the scientific analysis of collected data and about the measures provided for in this Act that have been taken to reduce the risk.
(3) The Bulgarian Drugs Agency shall electronically provide the information, as collected through this system, about any suspected serious adverse reactions observed on the territory of the Republic of Bulgaria to the regulatory bodies of other Member States and to the European Medicines Agency, which shall then be entered into the database set up under Regulation (EC) No. 726/2004 of the European Parliament and of the Council, not later than 15 days from receiving it.
(4) The Bulgarian Drugs Agency shall provide the notifications of suspected serious adverse reactions observed on the territory of the Republic of Bulgaria to the holder of an authorisation for use of the respective product within a period of 15 days from the date of receiving such notification.

(5) The Bulgarian Drugs Agency shall post on its website the manuals for monitoring the safety of medicinal products published by the European Commission and by the European Medicinal Agency.

Article 185. The holder of an authorisation for use shall be obligated to set up and maintain a system for monitoring and evaluation of the safety of medicinal products, thereby guaranteeing its responsibility for medicinal products placed on the market and its readiness to take immediate action where needed.

Article 186. (1) The holder of an authorisation for use shall appoint a qualified person for drug safety established on the territory of a Member State.

(2) Data about the person under Paragraph 1, his name, professional background, address, telephone and fax numbers shall be provided to the BDA together with the application for an authorisation for use.

(3) The holder of an authorisation for use shall notify the Bulgarian Drugs Agency of any change in the data under Paragraph 2.

Article 187. The qualified person under Article 186, Paragraph 1 shall be responsible for:

1. recording and analysing all notifications of suspected adverse reactions of which the holder of an authorisation for use under Article 188 has become aware;
2. filing urgent reports with the Bulgarian Drugs Agency of notifications of adverse reactions and of regular safety reports under Articles 189 and 190;
3. the immediate submission, upon request by the Bulgarian Drugs Agency, of additional information required to evaluate the benefit/risk ratio of the use of a medicinal product, including data about the sales or level of prescription of the medicinal product;
4. providing the Bulgarian Drugs Agency with any new information, irrespective of its source, which is relevant to the evaluation of the benefit/risk ratio of the use of a medicinal product, including information from post-marketing studies of the product safety.

Article 188. (1) The holder of an authorisation for use shall be obligated, acting on his duties under Article 185, to record all notifications of suspected adverse reactions observed on the territory of the European Union or in third countries.

(2) Notifications under Paragraph 1 must be accessible for reviewing, inspection and evaluation in the presence of at least one person under Article 186, Paragraph 1.

Article 189. The holder of an authorisation for use shall file with the Bulgarian Drugs Agency a report within a period of 15 days of the date of receiving a notification of an adverse reaction in the following cases:

1. in the event of notifications from medical specialists of a suspected adverse reaction observed on the territory of the Republic of Bulgaria;
2. in the event of other notifications of serious adverse reactions observed on the territory of the Republic of Bulgaria, meeting the criteria specified in the Ordinance under Article 191, Paragraph 1 of which he has been informed;
3. in the event of notification of suspected serious and of unexpected adverse reactions, as well as in all cases of suspected transmission of infectious agents through a medicinal product, observed in third counties, in accordance with the requirements of the Ordinance under Article 191, Paragraph 1;
4. in the event of notifications of suspected serious adverse reactions observed in other affected Member States, in the cases under Article 76.

Article 190. (1) Apart from cases under Article 189 and when no other requirements have been imposed as a condition for authorising use, the holder of an authorisation for use shall be obligated to provide the Bulgarian Drugs Agency with regular reports on safety, containing all notifications of adverse reactions and an evaluation of the benefit/risk ratio of the use of the medicinal products, immediately upon request by the Bulgarian Drugs Agency or every 6 months from the date of the authorisation for use until the date of release on the market under Article 54, Paragraph 1.

(2) The holder of an authorisation for use, when no other requirements have been imposed as a condition to authorise use, shall be obligated to submit regular reports to the BDA on safety, which shall contain an evaluation of the benefit/risk ratio of the use of the medicinal product, immediately upon request by the Agency, or:

1. every 6 months during the first two years after the date of placing the medicinal product on the market;
2. once a year during the next two years;
3. once every three years after the fourth year following the date of placing the medicinal product on the market.

(3) After issuance of an authorisation for use, its holder may request a change in the periods under Paragraphs 1 and 2 for the submission of regular safety reports in pursuance hereof.

Article 191. (1) The requirements to the collection, validation and provision of information about adverse reactions and to the content and format of reports under Articles 189 and 190 shall be specified in an Ordinance of the Minister of Health.

(2) When discharging their duties under this Chapter, the holders of licenses for use shall also take into consideration the requirements of manuals published by the European Medicines Agency and the European Commission, and they shall also use the internationally accepted medical terminology.

Article 192. (1) The holder of an authorisation for use may not provide the public with information associated with safety data about a medicinal product authorised for use without prior coordination with the BDA.

(2) The information under Paragraph 1 must be objective and not misleading.

Article 193. (1) In the cases where, as a result of the evaluation of data about drug safety, the BDA decides that an authorisation for use must be temporarily suspended, withdrawn or changed, it shall inform its holder, the other Member States and the European Medicines Agency with a view to obtaining an official opinion from the respective committee to the European Commission.

(2) Where urgent measures must be taken to protect public health, the BDA may temporarily suspend the authorisation for use of a medicinal product, notifying the European Medicines Agency, the European Commission and the other Member States within up to one business day.

(3) The Bulgarian Drugs Agency shall be obligated to take the provisional and/or final measures recommended by the European Commission.

Article 194. The provisions of this Chapter shall not apply to homeopathic medicinal products under Article 35.

Chapter Nine
WHOLESALE TRADE IN MEDICINAL PRODUCTS

(Title amended, *SG* No. 71/2008, effective 12.08.2008)

(Section I. Wholesale trade in medicinal products)

(Title repealed, *SG* No. 71/2008, effective 12.08.2008)

Article 195. (1) Natural and legal persons holding an authorisation for this type of operations, issued by a regulatory body in the respective Member State, may carry out wholesale trade in medicinal products.

(2) Where the person under Paragraph 1 has warehouse facilities on the territory of the Republic of Bulgaria, he may carry out wholesale trade in medicinal products after obtaining an authorisation from the BDA Executive Director.

Article 196. (1) The manufacturer of medicinal products, within the meaning of this Act, may only carry out wholesale trade in the medicinal products for which he holds a manufacturing authorisation.

(2) The importer of medicinal products, within the meaning of this Act, may only carry out wholesale trade in the medicinal products for which he holds an authorisation for importation.

Article 197. Persons under Article 195 must have:

1. suitable premises, equipment and installations, and suitable transportation vehicles ensuring the right storage, distribution and transportation of medicinal products in compliance with the requirements of Good Distribution Practice;
2. qualified staff and a responsible master of pharmacy with at least two years of service record in the area of specialisation, whose duties shall be specified in the Ordinance under Article 198.

Article 198. The principles and requirements of Good Distribution Practice shall be specified in an Ordinance of the Minister of Health.

Article 199. (1) The persons under Article 195, Paragraph 2 shall file with the Bulgarian Drugs Agency:

1. an application specifying the name, seat and business address of the trader; the address and a description of the premises and installations for the storage of medicinal products;
2. an up-to-date certificate of registration in the commercial register;
3. the name, a certificate of criminal record, a diploma of higher education and a document of service record of the responsible master of pharmacy under Article 197, item 2, and a copy of his labour contract;

4. an authorisation for the use of storage premises under Article 197, item 1, issued in compliance with the Spatial Development Act or another substitute document;
5. a development project for the premises under Article 197, item 1, approved in compliance with the Spatial Development Act;
6. a document certifying the legal grounds for the use of premises;
7. a conclusion from the RIPCPH, following an on-site inspection for the compliance with health requirements in the premises for wholesale trade in accordance with the Ordinance under Article 198;
8. a document evidencing the payment of a fee at the amount set in the Tariff under Article 21, Paragraph 2.
(2) The persons under Article 195, Paragraph 1 shall file an application with the Bulgarian Drugs Agency together with:
1. a copy of the authorisation for wholesale trade, issued by a regulatory body in a Member State;
2. the name and address of the contact person on the territory of the Republic of Bulgaria;
3. the address of storage premises for medicinal products on the territory of the Member States.
(3) In the case of wholesale trade in narcotic substances and in pharmaceutical forms containing these, the requirements of the Narcotic Substances and Precursors Control Act shall also apply.
(4) In the case of wholesale trade in radiopharmaceuticals, an opinion of the Nuclear Regulation Agency shall also be submitted.
Article 200. The Bulgarian Drugs Agency shall evaluate the documentation and conduct an on-site inspection of the sites specified in the application with a view to establishing their compliance with the requirements of Good Distribution Practice.
Article 201. (1) The Bulgarian Drugs Agency shall notify the applicant in writing where it finds incompleteness of the submitted documentation.
(2) In the cases under Paragraph 1 the period under Article 202, Paragraph 1 shall be suspended.
Article 202. (1) Within a period of 90 days of the date of submission of the application under Article 199, Paragraph 1, the BDA Executive Director shall issue an authorisation for wholesale trade or a motivated refusal.
(2) A refusal under Paragraph 1 shall be subject to appeal under the Administrative Procedure Code.
Article 203. Within a period of 15 days of the date of submission of the documentation under Article 199, Paragraph 2, the Bulgarian Drugs Agency Executive Director shall issue a certificate of registration for wholesale trade on the territory of the Republic of Bulgaria to the person under Article 195, Paragraph 1.
Article 204. (1) An authorisation for wholesale trade in medicinal products shall not be limited in time.
(2) An authorisation under Article 202 or a certificate under Article 203 shall terminate where its holder so requests in writing from the BDA Executive Director.
(3) The person under Article 195 shall be obligated to notify the BDA in writing within 7 days of terminating its operations for wholesale trade in medicinal products. In these cases the BDA Executive Director shall terminate the authorisations/certificates of wholesale trade in medicinal products that have been issued.
Article 205. (1) The Bulgarian Drugs Agency shall keep a register of the authorisations issued under Article 202, Paragraph 1 for wholesale trade in medicinal products, which shall contain the following:
1. the number and date of the authorisation;
2. the name, seat and business address of the person who has obtained the authorisation;
3. the address of the premises for storage of medicinal products;
4. data on the responsible master of pharmacy under Article 197, item 2;
5. a list of the drugs containing narcotic substances, of radiopharmaceuticals, immunological medicinal products and medicinal products obtained from human plasma and human blood;
6. the date of deletion of the authorisation from the register and the grounds to do so;
7. comments about any of the recorded circumstances.
(2) The Bulgarian Drugs Agency shall keep a register of the certificates issued under Article 203 for wholesale trade in medicinal products, which shall contain:
1. the number and date of the certificate;
2. the number of the authorisation for wholesale trade in medicinal products and the issuing body;
3. the name, seat and business address of the person who has obtained the certificate;
4. data on the person under Article 199, Paragraph 2, item 2;

5. the date of deletion of the certificate from the register and the grounds to do so;
6. any comments about the recorded circumstances.
(3) Data from the register shall be posted on the Bulgarian Drugs Agency website.
Article 206. (1) When circumstances pertaining to the issued authorisation for wholesale trade have changed, the holder thereof shall file an application with the Bulgarian Drugs Agency in compliance with Article 199, attaching thereto documentation relating to such changes.
(2) An authorisation for change shall be issued under the terms and conditions of Articles 200-202. Where storage premises have been changed, the period under Article 202 shall apply, the period in all other cases being 14 days.
Article 207. (1) The holder of an authorisation for wholesale trade carrying out his operations on the territory of the Republic of Bulgaria shall be obligated to:
1. provide access at any time by the control bodies to the storage premises for medicinal products;
2. trade only in medicinal products allowed under the present Act;
3. trade in medicinal products whose packaging and brochures are in compliance with the authorisation for use issued, under the terms and conditions of the present Act, the shelf life of which has not expired;
4. supply medicinal products only from manufacturers, importers or wholesale traders who have obtained licenses for these operations under the present Act;
5. supply medicinal products to other holders of wholesale authorisations, pharmacies and drugstores opened under the present Act;
5a. (New, *SG* No. 71/2008, effective 12.08.2008) supply medicinal products to treatment establishments for their own needs;
6. supply medicinal products to physicians and doctors of dental medicines when there is no pharmacy in the respective populated area, under the terms and conditions specified in an Ordinance of the Minister of Health;
7. keep a system to trace the movement of received and expedited medicinal products that shall contain:
a) the date of receipt and submission;
b) the name of the medicinal product;
c) the batch number and the number of the certificate for release of the batch, issued by the qualified person under Article 148, item 2 or by the qualified person under Article 161, Paragraph 2, item 1 and the number of the certificate for release of the batch, issued by the Bulgarian Drugs Agency in cases under Articles 69 and 70;
d) the amount received or supplied;
e) the name and address of the person from whom the medicinal product has been received or to whom it has been supplied;
8. store documentation about purchases and/or sales of all medicinal products;
9. observe the requirements of Good Distribution Practice specified in the Ordinance under Article 198.
(2) The documentation under Paragraph 1, items 7 and 8 shall be kept for at least 5 years and shall be provided, upon request, to the control bodies.
Article 208. (Supplemented, *SG* No. 71/2008, effective 12.08.2008) The provisions of Article 207, Paragraph 1, items 2-9, and Paragraph 2 and Article 209a, shall also apply to wholesale traders under Article 203, as well as to importers and manufacturers who trade in medicinal products manufactured by them.
Article 209. The special requirements of other laws shall also apply to the wholesale trade in medicinal products containing narcotic substances or obtained from blood, in immunological products and in radiopharmaceuticals.
Article 209a. (New, *SG* No. 71/2008, effective 12.08.2008) (1) Wholesale traders in medicinal products may supply medicinal products to:
1. other wholesale traders in medicinal products;
2. pharmacies and drugstores;
3. the Ministry of Defence and the Ministry of Interior for their own needs, with the exception of their institutional treatment establishments, as well as to the State Reserve and Wartime Reserves State Agency;
4. the Ministry of Health, notably:

a) vaccines, toxins and sera needed for the implementation of the Immunisation Calendar of the Republic of Bulgaria, as well as for emergency epidemic situations;
b) medicinal products intended for the treatment of diseases, which are paid for under the Health Act, as well as for securing the implementation of national programme in the health care sphere;
(2) Physicians and doctors of dental medicine in populated areas where there is no pharmacy may obtain supplies of medicinal products from wholesale traders in compliance with the provisions of the Ordinance under Article 207, Paragraph 1, item 6.
Article 210. (1) The manufacturers, importers and wholesale traders in medicinal products may provide samples of medicinal products authorised for use to:
1. physicians and doctors of dental medicine;
2. higher medical schools and medical colleges;
3. other manufacturers and wholesale traders in medicinal products.
(2) In the cases under Paragraph, 1 the packaging of the medicinal products shall bear the inscription "sample."
(3) No more than two samples of the same pharmaceutical form in the smallest existent packaging may be provided in one calendar year to persons under Paragraph 1, item 1, and to higher medical schools and medical colleges – only the amounts required for training purposes.
(4) The manufacturers, importers and wholesale traders in medicinal products shall keep a record of all persons provided with samples, of the amounts and time of supplies and, upon request, shall submit these data to the control bodies.
Article 211. (1) Wholesale traders must have a system for blocking and withdrawing medicinal products from the market, which have demonstrated not to be compliant with quality, safety and efficacy requirements.
(2) The holder of a wholesale trade authorisation shall be obligated to block and withdraw from the market medicinal products that have demonstrated lack of compliance with quality, safety and efficacy requirements, in compliance with the procedure specified in the Ordinance under Article 274, Paragraph 1.
Article 212. (1) The BDA Executive Director shall notify the European Commission, the regulatory bodies of other Member States and the European Medicines Agency of the authorisations for wholesale trade issued, of the authorisations suspended provisionally or withdrawn and of the reasons for this.
(2) When the BDA Executive Director finds that a person under Article 195, Paragraph 1 does not discharge his duties under Article 207, Paragraph 1, items 2-9, he shall notify the regulatory body of the Member State that had issued the wholesale trade authorisation and the European Commission.
(3) When the regulatory body under Paragraph 2 suspends provisionally or withdraws the wholesale trade authorisation of a person under Article 195, Paragraph 1, it shall notify the BDA Executive Director and the European Commission.

Chapter Nine "a"

(Title amended, *SG* No. 71/2008**, effective 12.08.2008**)

PARALLEL IMPORTATION OF MEDICINAL PRODUCTS

Article 213. (Amended, *SG* No. 71/2008, effective 12.08.2008) A natural or legal person registered under the Commerce Act, under the legislation of a Member State, after obtaining authorisation for parallel importation, issued by the BDA Executive Director, may carry out parallel importation of medicinal products on the territory of the Republic of Bulgaria.
Article 214. (1) A medicinal product authorised for use in another Member State may be imported in parallel on the territory of the Republic of Bulgaria when it is identical or similar to a medicinal product authorised for use in the Republic of Bulgaria in pursuance hereof.
(2) (Amended, *SG* No. 71/2008, effective 12.08.2008) For the purposes of Paragraph 1, a medicinal product shall be identical or similar if it has identical quantitative and qualitative composition with respect to the active substance/s, if it is offered in the same primary packaging, under the same name, with a similar graphic design of the packaging.
Article 215. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) In order to obtain an authorisation for parallel importation of a medicinal product on the territory of the Republic of Bulgaria, the person under Article 213 shall file an application with the BDA Executive Director, indicating the Member State from which parallel importation is to be made.
(2) The following data and documents shall be attached to the application:

1. the name, pharmaceutical form and amount of active substance per dosing unit of the medicinal product authorised for use in the Republic of Bulgaria;
2. the name, pharmaceutical form and amount of active substance per dosing unit of the medicinal product intended for parallel importation;
3. the name of the holder of the authorisation for use and of the manufacturer, if other than the holder of the authorisation for use;
4. the number of the authorisation for use of the medicinal product in the Republic of Bulgaria and the number of the authorisation for use of the medicinal product in the Member State from which parallel import is to be effected;
5. a declaration establishing the circumstances under Article 217, item 1;
6. a copy of the patient brochure and a sample of the medicinal product as it is sold in the Member State from which parallel import is to be effected, a translation of the brochure content into Bulgarian, accompanied by a declaration that the translation corresponds to the original brochure;
7. a proposed patient brochure for the medicinal product subject to parallel import, accompanied by a declaration that the brochure content is identical with the brochure content of the medicinal product authorised for use in the Republic of Bulgaria, with the exception of the following data:
a) the name and business address of the person carrying out parallel importation;
b) the name of the manufacturer, where different for the two products;
c) period of stability when different for the two products;
d) excipients when different for the two products;
8. in case of repackaging:
a) (Amended, *SG* No. 71/2008, effective 12.08.2008) a sample of the product in the form in which it is to be released on the market in Bulgaria;
b) a copy of the contract between the person carrying out parallel importation and the persons carrying out partial manufacturing operations, i.e., packaging, labelling, etc.;
c) a certificate of Good Manufacturing Practice when the processes of repackaging are carried out outside the territory of the Republic of Bulgaria;
d) if carried out by the person under Article 213, a copy of the manufacturing authorisation issued by the regulatory body of the Member State in which repackaging takes place;
9. a document evidencing the payment of a fee at the amount specified in the Tariff under Article 21, Paragraph 2.
(3) (Amended, *SG* No. 71/2008, effective 12.08.2008) Where differences exist between the medicinal product for parallel import and the product authorised for use on the territory of the Republic of Bulgaria (in terms of the composition of excipients or others), the person under Paragraph 1 shall submit evidence that these do not have any impact on the therapeutic qualities of the medicinal product for parallel import.
(4) In the cases under Paragraph 3, the person under Paragraph 1 shall indicate the differences on the packaging and in the patient brochure of the medicinal product subject to parallel import.
(5) Where the person under Article 213 performs repackaging and/or labelling of the medicinal product in Bulgarian on the territory of the Republic of Bulgaria, he must hold a manufacturing authorisation issued by the BDA Executive Director.
(6) The product subject to parallel import shall be used under the terms of the issued authorisation for use of the medicinal product on the territory of the Republic of Bulgaria.
Article 216. (1) An authorisation for parallel importation on the territory of the Republic of Bulgaria shall be issued within 45 days of the date of submission of the documentation to the Bulgarian Drugs Agency.
(2) When the Bulgarian Drugs Agency requires additional documentation from the applicant, the period under Paragraph 1 shall be suspended until receipt of the requested documentation.
(3) When the Bulgarian Drugs Agency requires from the regulatory body of the Member State from which parallel importation is carried out information relating to the issuance of the authorisation for use of the imported medicinal product, the period under Paragraph 1 shall be extended by 45 days.
(4) in the event that the Bulgarian Drugs Agency does not receive the requested documentation in the period under Paragraph 3, the procedure for issuance of an authorisation for parallel importation on the territory of the Republic of Bulgaria shall be terminated.

(5) Authorisations issued for parallel importation on the territory of the Republic of Bulgaria shall be posted on the Bulgarian Drugs Agency website.
(6) The authorisation for parallel importation shall be valid for 5 years. A new authorisation shall be issued in compliance with Article 215.
(7) The authorisation for parallel importation shall not terminate automatically when the holder of the authorisation for the use of the medicinal product placed on the market on the territory of the Republic of Bulgaria withdraws it for reasons unrelated to a threat to the health of the population.
Article 217. The holder of an authorisation for parallel importation shall be obligated to:
1. notify the holder of the authorisation for use of the medicinal product placed on the market on the territory of the Republic of Bulgaria of his intentions to carry out parallel importation and, upon request, to provide a sample of the medicinal product subject to parallel import;
2. store for a period of 5 years the following documentation: the name and address of the person to whom the medicinal product subject to parallel imported has been supplied, the date of submission, the amount supplied and the batch number;
3. submit to the Bulgarian Drugs Agency:
a) an updated patient brochure of the product subject to parallel import in compliance with the changes made in the issued authorisation for use of the medicinal product authorised in the Republic of Bulgaria;
b) (Amended, *SG* No. 71/2008, effective 12.08.2008) A declaration that the content of the brochure under a) is identical to the content of the product brochure authorised for use in the Republic of Bulgaria with the exception of data under Article 215, Paragraph 2, item 7, a) – d);
4. record and report to the holder of the authorisation for use and to the Bulgarian Drugs Agency all notifications of suspected adverse reactions to the imported medicinal product.

Chapter Ten
RETAIL TRADE IN MEDICINAL PRODUCTS

Article 218. Retail trade in medicinal products shall only be carried out in pharmacies and drugstores in pursuance hereof, with the exception of the cases under Article 232, Paragraph 2.
Article 219. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) A pharmacy shall be a medical establishment in which the following operations shall take place: storage, preparation, packaging, control, consultations, dispensation, with or without medical prescription, of medicinal products authorised for use in the Republic of Bulgaria, of medical products, as well as of food supplements, of cosmetic and sanitary products on a list specified by the Minister of Health.
(2) The structure, work procedures and arrangements of pharmacies, the nomenclature of medicinal products, as well as the list under Paragraph 1, shall be specified in an Ordinance of the Minister of Health.
(3) (Amended, *SG* No. 71/2008, effective 12.08.2008) Pharmacies may offer food supplements without registering in compliance with the Foodstuffs Act.
Article 220. (1) The operations under Article 219, Paragraph 1 shall be carried out by a master of pharmacy.
(2) (Supplemented, *SG* No. 71/2008, , effective 12.08.2008) A master of pharmacy shall be obligated to comply with a medical prescription by a doctor, also in respect to pharmaceutical forms prepared under magisterial and official formulations in compliance with the procedure specified in the Ordinance under Article 221, Paragraph 1.
(3) An assistant pharmacist may carry out all operations under Article 219, Paragraph 1 in the presence and under the control of a master of pharmacy, with the exception of: dispensation of medicinal products under medical prescription, control and consultations.
Article 221. (1) (Previous Article 221, *SG* No. 71/2008, effective 12.08.2008) The Minister of Health shall designate in an Ordinance medical specialists who may issue prescriptions, the procedure for prescribing medicinal products, the period of execution, the cases and the procedure when a master of pharmacy may refuse to execute a medical prescription.
(2) (New, *SG* No. 71/2008, effective 12.08.2008) Bulgarian citizens and foreign nationals residing permanently or temporarily in the country, when travelling outside the Republic of Bulgaria, may carry or take out medicinal products needed for their treatment in compliance with the provisions of the Ordinance under Paragraph 1.

(3) (New, *SG* No. 71/2008, effective 12.08.2008) Persons passing in transit or residing temporarily on the territory of the Republic of Bulgaria may possess medicinal products intended solely for their treatment in quantities stipulated in the Ordinance under Paragraph 1.

Article 222. (1) (Declared unconstitutional by the Constitutional Court of the Republic of Bulgaria – *SG* No. 65/2008, amended, *SG* No. 71/2008, effective 26.07.July 2008) A natural or legal person registered as trader under the Bulgarian legislation or under the legislation of a Member State, who has signed a labour contract or a contract for management of a pharmacy with a master of pharmacy, and in the cases provided under the law – with an assistant pharmacist, shall be entitled to carry out retail trade in medicinal products, whereby one person may open not more than 4 pharmacies on the territory of the Republic of Bulgaria.

(2) (New, *SG* No. 71/2008, effective 27.07.2008) Where the person under Paragraph 1 is a master of pharmacy and is the manager of the pharmacy, he shall not be required to present a labour contract or a contract for management of the pharmacy.

(3) (Renumbered from Paragraph 2, amended, *SG* No. 71/2008, effective 27.07.2008) The master of pharmacy under Paragraph 1 shall be the head of the pharmacy and shall mandatorily work in it.

(4) (Renumbered from Paragraph 3, *SG* No. 71/2008, effective 27.07.2008) The following shall have the right to open a pharmacy for their own needs:

1. treatment establishments, under Article 5 of the Treatment Establishments Act, which provide in-patient care;
2. treatment establishments for in-patient care;
3. dispensaries;
4. hospices with in-patient facilities under Article 10, item 5 of the Treatment Establishments Act.

(5) (Repealed, renumbered from Paragraph 4, *SG* No. 71/2008, effective 27.07.2008) Pharmacies of treatment establishments for outpatient care with the Ministry of Defence and the Ministry of Interior may be headed by an assistant pharmacist at the proposal of the respective institution, provided an authorisation to this effect has been issued by the Minister of Health.

Article 223. (1) A master of pharmacy or an assistant pharmacist may only head one pharmacy and he shall mandatorily work in it.

(2) A master of pharmacy or an assistant pharmacist, who is the head of a pharmacy, may not be hired to work under a contract with a sole proprietor or commercial company the objectives of which are the manufacturing, importation, wholesale trade or retail trade in medicinal products, or work anywhere else.

(3) A person under Paragraph 1 who holds an authorisation for retail trade in medicinal products may not be the owner or take part in commercial companies whose objectives are the manufacturing, importation, wholesale or retail trade in medicinal products, including the cases of companies belonging to related parties within the meaning of the Commerce Act.

Article 224. The head of a pharmacy must:

1. be a master of pharmacy, or assistant pharmacist in the cases provided for by law;
2. not be deprived of the right to exercise the profession;
3. not be convicted for criminal offences associated with the practising of his profession or for criminal offences against property and the economy, or for intentional criminal offences against the person;
4. have at least one year of experience as a master of pharmacy.

Article 225. (Amended, *SG* No. 71/2008, effective 27.07.2008) (1) A person under Article 222, Paragraph 1, who has signed a labour contract or a contract for management of a pharmacy with an assistant pharmacist or a master of pharmacy with less than one year's experience, shall be entitled to carry out retail trade in medicinal products in a populated area on the territory.

(2) An assistant-pharmacist who has obtained an authorisation for retail trade in medicinal products under Paragraph 1, shall be the head of pharmacy and shall mandatorily work in it.

Article 226. (1) Pharmacies for the sale of medicinal products to the citizens may be opened on the territory of outpatient treatment establishments.

(2) No pharmacies for the sale of medicinal products to the citizens may be opened on the territory of medical establishments under Article 21, Paragraph 2 Health Act, of in-patient care establishments and of treatment establishments under Article 10 of the Treatment Establishments Act.

Article 227. The requirements to the locations and to the premises of pharmacies shall be specified in the Ordinance under Article 219, Paragraph 2.

Article 228. (Amended, *SG* No. 71/2008, effective 27.07.2008) (1) An authorisation for retail trade in medicinal products in a pharmacy shall be issued by the Minister of Health or by a Deputy Minister of Health authorised by him upon submission of a model-based application, to which the following shall be attached:

1. an up-to-date certificate of entry in the commercial register, accordingly a document of up-to-date registration, or a certified transcript of a similar document of a Member State of the persons under Article 222, Paragraph 3;
2. a labour contract or a contract for management of a pharmacy, signed with a master of pharmacy or with an assistant pharmacist;
3. a copy of the legal document on the constituting of the persons under Article 222, Paragraph 4;
4. documents certifying compliance with the requirements under Article 224;
5. criminal conviction record of the master of pharmacy or of the assistant-pharmacist designated as head of pharmacy;
6. a medical certificate for the master of pharmacy or the assistant-pharmacist designated as head of pharmacy;
7. a certificate of entry on the register of the respective Regional College of the Bulgarian Pharmacist Union for master of pharmacy who is the head of the pharmacy;
8. a document for fee paid in an amount stipulated in the Tariff under Article 21, Paragraph 2.

(2) Pharmacies under Article 222, Paragraphs 4 and 5 shall be opened and closed down at the request of the person representing the treatment establishment.

(3) The requirements of the Narcotic Substances and Precursors Control Act shall also apply to the opening of a pharmacy where medicinal products containing narcotic substances are to be dispensed and sold.

(4) The application and the documents under Paragraph 1 shall be filed with the respective RIPCPH, which shall draft the hygiene conclusion within a period of 14 days.

(5) The Regional Inspectorate for the Protection and Control of Public Health shall send the documents under Paragraph 4 to the Ministry of Health within three days of the issuing of the hygiene conclusion.

Article 229. (1) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) The Higher Pharmacy Council shall submit a motivated proposal to the Minister of Health or to a Deputy Minister authorised by him for the issuance of an authorisation, or a refusal to carry out retail trade in medicinal products in a pharmacy.

(2) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) Within one month of receiving the documentation under Article 228, Paragraph 4, the Minister of Health shall issue an authorisation for retail trade in medicinal products in a pharmacy or a motivated refusal for the issuance of an authorisation. The authorisation or the refusal shall be served on the person who has filed an application.

(3) Where discrepancies or incompleteness are found in the submitted documentation, the Higher Pharmacy Council shall notify the applicant in writing and shall give instructions for their removal. In these cases the period under Paragraph 2 shall be suspended from the date of notification until removal of the deficiencies.

(4) (New, *SG* No. 71/2008, effective 12.08.2008) In the event that within 60 days from the date of the notification under Paragraph 3 the applicant has failed to eliminate the identified non-compliances or incompletenesses, the procedure of issuing an authorisation for retail trade in medicinal products or of amending the authorisation issued shall be terminated.

(5) (Renumbered from Paragraph 4, *SG* No. 71/2008, effective 12.08.2008) The refusal of the Minister of Health to issue an authorisation shall be subject to appeal under the Administrative Procedure Code.

Article 230. (1) The Minister of Health shall keep a register of authorisations issued for retail trade in medicinal products under Article 229, Paragraph 2, that shall contain:

1. the number and date of the authorisation;
2. (Supplemented, *SG* No. 71/2008, effective 12.08.2008) the name, type of trader, seat and business address of the person that has been granted authorisation;
3. the name, personal data and the address of the head of the pharmacy;
4. the address of the pharmacy;

5. the operations to be carried out in the pharmacy;
6. the date of termination of the authorisation and of deletion from the register and the grounds to do so;
7. comments with regard to any of the registered circumstances.
(2) Register data shall be published on the website of the Ministry of Health.
Article 231. (1) In case circumstances entered on the register under Article 230, Paragraph 1, items 2-5 have changed, the person who has been granted an authorisation for retail trade in medicinal products shall file an application in compliance with Article 228, Paragraph 1, attaching thereto the documents pertaining to any such changes.
(2) Upon issuance of the authorisation admitting the changes under Paragraph 1, the provisions of Article 229 shall apply.
Article 232. (1) Physicians and doctors of dental medicine may store medicinal products according to a list specified by the Minister of Health.
(2) Where there is no pharmacy in a populated area, the persons under Paragraph 1 may store and sell medicinal products only in the event that they have obtained an authorisation to this effect in compliance with a procedure specified in an Ordinance of the Minister of Health.
Article 233. The head of pharmacy shall incur liability for the operations specified in Article 219, Paragraph 1.
Article 234. (1) The sale of medicinal products from automated machines shall be prohibited, except for medicinal products specified on a list included in the Ordinance under Article 219, Paragraph 2.
(2) Automated machines under Paragraph 1 may only be owned by persons under Article 222 and Article 238, Paragraph 2.
(3) The sale of second-hand medicinal products shall be prohibited.
(4) The sale of medicinal products on the Internet dispensed by medical prescription shall be prohibited.
Article 235. (1) An authorisation for retail trade in medicinal products under Article 229, Paragraph 2 shall be terminated upon termination of the operations of persons under Articles 222 and 225.
(2) The Minister of Health shall terminate an authorisation for retail trade in medicinal products:
1. at the request of the person who has been granted an authorisation for retail trade;
2. where it has been found that the head of pharmacy does not meet the requirements specified in Articles 224 and 225.
(3) Within 14 days of terminating the operations under Paragraph 1, the persons under Articles 222 and 225 shall notify thereof the Minister of Health in writing.
Article 236. (1) A pharmacy may not be closed for more than 30 days in the same calendar year on account of the absence of its head.
(2) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) Where the head of pharmacy is prevented from discharging his duties due to being on leave because of temporary inability to work, pregnancy, childbirth, adoption or child care, the pharmacy may operate for a term of not more than two years under the management of another master of pharmacy or assistant-pharmacist, correspondingly, in the cases under Article 225, who meets the requirements of Article 224. An authorisation shall be issued in these cases by the Minister of Health or by a Deputy Minister authorised by him..
(3) The authorisation under Paragraph 2 shall be issued for a term of up to 30 days.
Article 237. Upon termination of operations by the person who has been granted an authorisation to open a pharmacy, medicinal products may be sold to persons who have been granted an authorisation for wholesale trade in medicinal products.
Article 238. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) Medicinal products dispensed without medical prescription may be sold in a drugstore. Products and commodities of significance to human health, specified in the Ordinance under Article 243, and medical articles, may also be sold in a drugstore.
(2) (Amended, SG No. 71/2008, effective 12.08.2008) All natural and legal persons registered under the Commerce Act, under the legislation of a Member State shall have the right of carrying out retail trade in medicinal products by opening a drugstore.
(3) (Amended, SG No. 71/2008, effective 12.08.2008) The head of a drugstore must be a medical specialist who:
1. has not been deprived of the right to practise his profession;

2. has not been convicted for crimes connected with the practising of his profession, for criminal offences against property and the economy, or for deliberate criminal offences against the person;
3. has at least one year of professional experience.

Article 239. (1) Drugstores shall be opened following registration with the Bulgarian Drugs Agency.
(2) Persons under Article 238, Paragraph 2 shall file an application for registration with the Bulgarian Drugs Agency, to which the following documents shall be attached:
1. an up-to-date certificate of entry on the commercial register;
2. a document evidencing education and a certificate of criminal record for the person designated as head of the drugstore;
3. a medical certificate for the person under item 2;
4. an authorisation for the use of premises or another substitute document issued in compliance with the Spatial Development Act;
5. a hygiene conclusion from the respective RIPCPH;
6. a document evidencing the payment of a state fee at the amount specified in the Tariff under Article 21, Paragraph 2.

Article 240. (1) Within a period of 30 days of receiving the documentation under Article 239, Paragraph 2, the BDA Executive Director shall issue a certificate of registration of the drugstore or a motivated refusal to do so.
(2) The refusal of the Executive Director under Paragraph 1 shall be subject to appeal under the Administrative Procedure Code.

Article 241. (1) The Bulgarian Drugs Agency shall keep a register of drugstores that shall contain:
1. the number and date of the issued certificate;
2. the seat and business address of the person who has been granted a certificate of drugstore registration;
3. the name, personal data and address of the head of drugstore;
4. the drugstore address;
5. the date of termination of the registration and the grounds for it;
6. comments about any of the registered circumstances.
(2) Register data shall be posted on the Bulgarian Drugs Agency website.

Article 242. In case the drugstore or head's address have changed, the person who has been granted the certificate of its opening shall file an application in compliance with Article 239, Paragraph 2 and documents pertaining to any such change.

Article 243. The terms and conditions of the drugstore work arrangements shall be specified in an Ordinance of the Minister of Health.

Chapter Eleven
ADVERTISEMENT OF MEDICINAL PRODUCTS

Article 244. (1) Any form of information, presentation, promotion or proposals with the aim of encouraging the prescription, sale or use of medicinal products shall be considered as advertisement thereof, including the following:
1. advertisement intended for the population;
2. advertisement intended for medical specialists;
3. visits by medical trade representatives to medical specialists;
4. provision of sample medicinal products;
5. sponsorship of promotional meetings and scientific congresses attended by medical specialists, including the coverage of their travel and accommodation in the respective country in which the event takes place.
(2) The following shall not be considered advertisement of medicinal products:
1. text appearing on the outer packaging approved during the licensing procedure for use;
2. correspondence concerning a specific issue or problems pertaining to a particular medicinal product;
3. information and instructions with regard to changes in packaging, warnings about adverse reactions as part of general measures for the safety of a medicinal product, trade catalogues and pricelists, provided they do not include data of advertisement nature with regard to the medicinal product concerned;
4. statements concerning human health or diseases when they do not, directly or indirectly, suggest a course of treatment, the prevention or diagnosis involving the use of medicinal products;

5. campaigns conducted by the Ministry of Health for the vaccination of the population, if material associated with them contains no data about a particular medicinal product.

Article 245. (1) The holder of the authorisation for use shall be obligated to set up a scientific unit for the distribution of information about the medicinal products for which he has been granted an authorisation for use in pursuance hereof.

(2) The holder of an authorisation for use shall be obligated to:

1. guarantee that the advertisement of a medicinal product has been presented to the population or to medical specialists in a manner compliant with the requirements of this Chapter and with the authorisation for advertisement issued by the Bulgarian Drugs Agency;
2. have data and material available from all advertisement campaigns undertaken as part of its operations, including information about the groups for which the advertisement is intended, about the manner of its implementation and about the date on which the advertisement campaign is to be launched;
3. guarantee training for medical commercial representatives;
4. implement with accuracy and within the set timelines the instructions of officials controlling advertisement action.

(3) medical commercial representatives must report to the scientific units under Paragraph 1 any information about the use of medicinal products they advertise, especially as regards information about adverse reactions notified to them by medical specialists.

Article 245a. (New, *SG* No. 71/2008, effective 12.08.2008) Advertisement shall be allowed only for medicinal products for which an authorisation for use has been issued under the present Act.

Article 246. (1) The content of the advertisement must correspond to data from the medicinal product summary approved during licensing for use and present only indications specified during the licensing for use.

(2) The advertisement of a medicinal product must only suggest its correct use, objectively presenting its therapeutic indications, without exaggerating possibilities for treatment, prevention or diagnosis using the medicinal product concerned.

(3) The advertisement must not contain misleading information.

(4) (New, *SG* No. 71/2008, effective 12.08.2008) The advertisement may not contain an offer and/or promise of a gift and/or another material or nonmaterial benefit.

(5) (New, *SG* No. 71/2008, effective 12.08.2008) A medical specialist or a person claiming to be a medical specialist may not engage in direct or indirect advertising of medicinal products in the printed and/or electronic media, as well as on the Internet.

Article 247. Only the advertisement to the population of medicinal products dispensed without medical prescription shall be admitted.

Article 248. (Supplemented, *SG* No. 71/2008, effective 12.08.2008) Apart from the cases under Article 247, vaccination advertisement campaigns shall be admitted, carried out by holders of authorisation for use, subject to the requirements of Article 251 and following a procedure stipulated in the Ordinance under Article 249.

Article 248a. (New, *SG* No. 71/2008, effective 12.08.2008) Advertising on the Internet shall be prohibited for medicinal products dispensed with a medical prescription, with the exception of vaccination advertising campaigns conducted in compliance with Article 248 and approved by the competent authorities.

Article 249. The requirements to the advertisement of medicinal products shall be specified in an Ordinance of the Minister of Health.

Article 250. An application for authorisation of the advertisement of a medicinal product shall be filed by a holder of an authorisation for use of the medicinal product concerned or by a person thereby authorised.

Article 251. (1) In order to be granted advertisement authorisation, the person under Article 250 shall file with the Bulgarian Drugs Agency an application based on a model approved by the Agency Executive Director to be accompanied by:

1. a project for the advertisement;
2. a notarised power of attorney from the holder of an authorisation for use, where the application is filed by another person;
3. the literary sources of quotations, tables or other material used, if any;

4. a document evidencing the payment of a fee at the amount specified in the Tariff under Article 21, Paragraph 2.
(2) Advertisement projects under Paragraph 1, item 1 must be clear, with a text, if any, that is easy to understand and allow evaluating all of its elements: text and illustrations.
(3) An Advertisement Expert Council shall be set up with the Bulgarian Drugs Agency. Its composition shall include physicians and specialists with practical experience in the field of advertisement. The BDA Executive Director shall by order determine the composition of the Council, including a representative of the for Professional Ethics Committee of the Bulgarian Union of Physicians, of the Bulgarian Dentists' Union and of the Bulgarian Pharmacy Union, the amount of remuneration of its members and he shall approve Rules on the Terms and Conditions of its Work. Representatives of patient organisations may also be included in the composition of the Council.
(4) The Council under Paragraph 3 shall execute an expert assessment of the project for advertisement and come up with an opinion for the BDA Executive Director.
(5) Where the advertisement is found to be incompliant with the requirements hereof, within 7 days of the date of submission of the application under Paragraph 1, the BDA shall give written instructions for the removal of incompliance within a month of the date of notification. The period for ruling shall start running on the day of notification until removal of incompliance.
(6) In case the applicant fails to act on the instructions within a month of the date of notification under Paragraph 5, the authorisation procedure shall be terminated.
Article 252. (1) Within a month of submission of the documentation under Article 251, Paragraph 1, based on the opinion under Article 251, Paragraph 4, the BDA Executive Director shall by order authorise the advertisement or issue a motivated refusal, of which the holder of the authorisation for use shall be notified.
(2) The refusal of the Executive Director shall be subject to appeal under the Administrative Procedure Code.
Article 253. (1) The authorisation for advertisement issued under Article 252, Paragraph 1 shall refer to a specific medicinal product within the term of validity of its authorisation for use.
(2) Where changes have been made in the authorisation for use of a medicinal product, resulting in changes in an authorised advertisement for the product, the holder of an authorisation for use shall file with the BDA an application for change.
Article 254. In case the authorised advertisement has changed, the person under Article 250 shall file an application in compliance with Article 251.
Article 255. (1) The distribution of sample medicinal products containing narcotic substances within the meaning of the Narcotic Substances and Precursors Control Act shall be prohibited.
(2) Direct provision of sample medicinal products by medical commercial representatives under Article 244, Paragraph 1, item 3 to the population shall be prohibited.
Article 256. Sample medicinal products shall be provided to medical specialists under the terms and conditions specified in the Ordinance under Article 249.
Article 257. (1) Medical commercial representatives under Article 244, Paragraph 1, item 3 must have been trained through arrangements made by the holder of the authorisation for use who has appointed them, they must have scientific knowledge and be able to provide accurate maximally complete information about the medicinal product they present.
(2) At each visit medical commercial representatives must have available a product summary, data about the prices of the medicinal product, the terms of payment, and provide these upon request.
(3) When medicinal products are presented to medical specialists, the medical commercial representatives may not offer gifts or any other material or nonmaterial benefits.

Chapter Twelve
PRICES OF MEDICINAL PRODUCTS

Article 258. (1) The State shall regulate the prices of medicinal products included on the Positive Drug List under Article 262, Paragraph 4 and paid by public means in accordance with the lowest reference prices from the Member States.
(2) The State shall regulate the ceiling prices of medicinal products dispensed without medical prescription outside those under Paragraph 1.
(3) The State shall register the maximum retail prices of medicinal products dispensed without medical prescription.

Article 259. (1) At the proposal of the Minister of Health, the Council of Ministers shall set up a Commission for the Prices of Medicinal Products shall and determine its composition.
(2) Representatives of the Ministry of Health, the Ministry of Finance, the Ministry of Economy and Energy, and of the Ministry of Labour and Social Policy, of the National Health Insurance Fund and of the BDA shall mandatorily be included in the Commission for the Prices of Medicinal Products.
(3) The members of the Commission for the Prices of Medicinal Products shall have a 4-year term of office.
(4) A person who is member of the Commission for the Prices of Medicinal Products may not be member of the commissions under Article 261 and Article 265 at the same time.
(5) Every two years half of the composition of the Commission under Paragraph 1 shall be renewed.
(6) The terms and conditions for the work of the Commission for the Prices of Medicinal Products shall be specified in an Ordinance of the Council of Ministers.
(7) The Commission under Paragraph 1 shall meet at least once a month.
(8) An Information and Analysis Unit shall be set up with the Commission for the Prices of Medicinal Products. The Unit shall collect, analyse and provide the Commission with information about the prices of medicinal products in the Member States under a procedure specified in the Ordinance under Paragraph 6.
(9) The Commission for the Prices of Medicinal Products shall keep a website on which it shall post information about its operations.
Article 260. (1) At the proposal of the Minister of Health, the Council of Ministers shall specify in an Ordinance the rules and conditions for price regulation of medicinal products under Article 258, Paragraph 1, for regulation of ceiling prices for medicinal products under Article 258, Paragraph 2, allowed for use by medical prescription, in case of retail sales, as well as the terms and conditions for retail trade registration of the prices of medicinal products dispensed without medical prescription.
(2) The Commission for the Prices of Medicinal Products shall rule within a period of up to:
1. 45 days, in respect to medicinal products under Article 258, Paragraphs 1 and 2;
2. 30 days, in respect to medicinal products under Article 258, Paragraph 3.
(3) The period under Paragraph 2 shall start running on the date of submission of the application in compliance with the Ordinance under Paragraph 1.
(4) The Ministry of Health shall collect a fee at the amount specified in the Tariff under Article 21, Paragraph 2 for filing an application for the formation, registration of or change in the formed or registered price of a medicinal product.
Article 261. (1) A Commission for the Positive Drug List shall be set up with the Council of Ministers.
(2) The Commission for the Positive Drug List shall examine and make decisions on applications for the inclusion in, change and/or exclusion of medicinal products from the Positive Drug List of the Republic of Bulgaria.
(3) Members of the Commission for the Positive Drug List shall have a 4-year term of office.
(4) Every two years half the composition of the Commission under Paragraph 1 shall be renewed.
(5) The composition of the Commission for the Positive Drug List shall be determined by the Council of Ministers at the proposal of the Minister of Health.
(6) (Amended, *SG* No. 71/2008, effective 12.08.2008) The Commission for the Positive Drug List shall consist of 11 members and shall comprise three representatives from the Ministry of Health, one representative from the Ministry of Labour and Social Policy, two representatives from the National Health Insurance Fund, two representative from the Bulgarian Drugs Agency, one representative from the Ministry of Finance, and one representative each from the Bulgarian Union of Physicians and from the Bulgarian Dentists Union.
(7) Medical specialists, lawyers and economists with academic achievements and/or practical experience in the field of medicinal products and in the respective areas of their application may be appointed as members of the Commission for the Positive Drug List.
(8) A person who is member of the Commission for the Positive Drug List may not be member of the Commission under Articles 259 and 265 at the same time.
(9) Records of proceedings from the session of the Commission under Paragraph 1 shall be posted on its website.
Article 262. (1) The positive drug list shall include medicinal products dispensed by medical prescription, required to cover the health needs of the population and paid out with means from the

NHIF budget, the national budget, outside the scope of mandatory health insurance, and from the budget of treatment establishments under Article 6 of the Medical-Treatment Facilities Actand from the budget of treatment establishments with state and/or municipal interest under Articles 9 and 10 of the Medical-Treatment Facilities Act.
(2) The positive drug list shall be a list of medicinal products drafted according to pharmacological classes with the respective international non-patent names, with the respective daily dose defined, a price under Article 258, Paragraph 1, a daily dose reference value, a price calculated on the basis of a reference value and a level of payment.
(3) A treatment course and a corresponding reference value shall be determined for medicinal products for which no daily dose has been defined.
(4) The positive drug list shall include medicinal products:
1. intended for the treatment of diseases paid in compliance with the Health Insurance Act;
2. paid from the budget of the treatment establishments under Article 5 of the Medical Treatment Facilities Act and from the budget of treatment establishments with state and/or municipal interest under Articles 9 and 10 of the Medical Treatment Facilities Act;
3. intended for the treatment of diseases outside the scope of the Health Insurance Act, paid in compliance with Article 82, Paragraph 1, item 8 of the Health Act;
4. intended for the treatment of rare diseases, AIDS and infectious diseases.
(5) The level of payment for medicinal products under Paragraph 4, item 1 shall be determined in accordance with the NHIF budget for the respective year.
(6) (New, *SG* No. 71/2008, effective 12.08.2008) The National Health Insurance Fund shall reimburse the medicinal products under Paragraph 4, item 1 in compliance with the Ordinance under Article 45, Paragraph 8 of the Health Insurance Act.
(7) (Renumbered from Paragraph 6, *SG* No. 71/2008, effective 12.08.2008) The Ministry of Health shall collect a fee at the amount specified in the Tariff under Article 21, Paragraph 2 for filing an application for inclusion or for changing a medicinal product included on the list under Paragraph 1.
Article 263. (1) Medicinal products on the positive drug list shall be selected in accordance with evidence for efficacy, therapeutic efficiency, and safety, and the analysis of pharmacological and economic indicators.
(2) The period for inclusion of medicinal products on the Positive Drug List shall be 90 days from the date of submission of an application pursuant to the Ordinance under Article 264.
Article 264. At the proposal of the Minister of Health, the Council of Minister shall specify in an Ordinance the terms, rules and criteria for inclusion, changes and/or exclusion of medicinal products on/from the Positive Drug List, as well as the terms and conditions of work of the Commission for the Positive Drug List.
Article 265. (1) The Council of Ministers shall set up a Transparency Commission.
(2) The composition of the Transparency Commission shall be determined by the Council of Ministers at the proposal of the Minister of Health. Representatives of the Ministry of Health, the BDA, the NHIF, the Bulgarian Union of Physicians, the Bulgarian Dentists' Union, the Bulgarian Union of Pharmacists, and of patient and pharmaceutical industry organisations shall be mandatorily included in the Commission.
(3) A member of the Transparency Commission may not be a member of the Commissions under Articles 259 and 261 at the same time.
(4) The Council of Ministers shall specify by Rules the terms and conditions of work of the Transparency Commission.
Article 266. (1) The Transparency Commission shall be a body before which the decisions of the commissions under Article 259, Paragraph 1 and Article 261, Paragraph 1 may be appealed.
(2) Decisions of the Transparency Commission shall be made by a majority of two-thirds of its composition.
(3) Decisions under Paragraph 2 shall be subject to appeal under the Administrative Procedure Code, the appeal thereof not suspending their execution.

Chapter Thirteen
STATE CONTROL OF MEDICINAL PRODUCTS

Article 267. (1) The Ministry of Health shall head the state control of medicinal products. Immediate direction shall be provided by the Chief State Health Inspector, the BDA Executive Director and by RIPCPH Directors, who shall be state inspectors controlling medicinal products.

(2) The Bulgarian Drugs Agency and the RIPCPH shall be state control bodies for medicinal products.
(3) Immediate control shall be exercised by officials – inspectors and experts designated by orders of the BDA Director or of the respective RIPCPH Director.
(4) When discharging their control functions, the bodies under Paragraph 1 may request assistance from the bodies of the Ministry of Interior.
Article 268. (1) The Bulgarian Drugs Agency shall exercise control over:
1. compliance of premises, installations and conditions for the manufacturing, control of and trade in medicinal products and the observation of requirements of Good Manufacturing Practice for medicinal products and of Good Distribution Practice;
2. operations of manufacturers, importers, the holder of an authorisation for use, of wholesale traders in medicinal products, of pharmacies and drugstores;
3. the quality, safety and efficacy of medicinal products;
4. the clinical trials of medicinal products and the observation of requirements of Good Clinical Practice;
5. the information about drugs in relation to their licensing for use and advertisement;
6. the system for drug safety of the holders of an authorisation for use.
(2) The Regional Inspectorates for the Protection and Control of Public Health shall exercise control over the premises, installations and conditions of storage and over the trade in medicinal products, as well as over the operations of wholesale traders, pharmacies and drugstores located on the territory of the respective region.
(3) Development projects for the construction of new and/or the reconstruction of existent sites associated with the manufacturing of medicinal products shall be coordinated with the BDA in accordance with the rules of Good Manufacturing Practice for medicinal products.
Article 269. (1) Control under Article 267 shall be performed through inspections and laboratory tests.
(2) Inspections and laboratory tests under Paragraph 1 shall be performed:
1. in relation to the issuance of licenses for use, manufacturing, of authorisations for importation and of certificates in compliance with this Act;
2. in relation to performing supervision of the market of medicinal products;
3. upon request of the European Commission, the European Medicines Agency or of a competent body in another Member State;
4. upon request of a manufacturer, importer or a holder of an authorisation for use outside the cases under item 1.
(3) The Bulgarian Drugs Agency shall perform inspections as part of the certification procedure in relation to the monographs of the European Pharmacopoeia.
(4) The Bulgarian Drugs Agency shall perform inspections of medicinal product manufacturers established in third countries in relation to an application they have filed to obtain an authorisation for use or an authorisation of importation.
(5) When compliance with the conditions and requirements of Good Manufacturing Practice is found as a result of the inspection, the Bulgarian Drugs Agency shall issue a certificate of Good Manufacturing Practice within a period of 90 days from conducting such inspection.
(6) The Bulgarian Drugs Agency shall notify the European Medicines Agency of any certificates of Good Manufacturing Practice it has issued.
(7) Where an inspection finds non-compliance of the actual conditions with the requirements of Good Manufacturing Practice, the BDA shall notify the European Medicines Agency thereof.
Article 270. (1) The officials under Article 267, Paragraph 3 shall have the right, within their competence:
1. to access all documents directly or indirectly associated with a violation of this Act or of the legislation of Member States transposing the requirements of Directive 2001/83/EC of the European Parliament and of the Council on the endorsing of a Community Code relating to medicinal products for human use, last amended by Directive 2004/27/EC of the European Parliament and of the Council, irrespective of the document format;
2. to order any person to provide information about the violation under item 1, which he is aware of;
3. to inspect, at any time, the sites subject to control and to obtain, inspect and make copies of all documents pertaining to the overall operation of the controlled site;
4. to take samples of medicinal products, of active substances and excipients for laboratory testing;

5. to inspect the premises, records and documents of the holders of licenses for use or persons whom the holder of an authorisation for use has entrusted the implementation of operations under Chapter Eight;
6. to draw up acts establishing the presence of administrative violations.
(2) The officials under Article 267, Paragraph 3 shall draw up a report of the inspection they have conducted that will then be provided to the inspected manufacturer or holder of an authorisation for use of a medicinal product.
(3) The BDA Executive Director or the respective RIPCPH Director, depending on the hierarchical system of the official who has found the violation, shall have the right to:
1. order in writing the offender to cease and desist the violation under Paragraph 1, item 1;
2. require the offender to declare that he would cease and desist the violation under Paragraph 1, item 1 and, if necessary, require him to publicly disclose the declaration;
3. order the termination or prohibition of any violation under Paragraph 1, item 1 and, where necessary, publicly disclose the order of termination or prohibition of the violation.
Article 271. (1) The Regional Inspectorates for the Protection and Control of Public Health shall have the right to:
1. stay construction operations and issue prescriptions when they find violations of hygiene standards and requirements in the process of construction; in case of illegal construction of sites and installations for the manufacturing, storage and sale of medicinal products, they shall notify the National Control of Construction Directorate or the municipal technical service;
2. prohibit putting into operation and suspend the operation of sites and installations when requirements and hygiene standards have been violated in the manufacturing, storage and sale of medicinal products until the violations have been removed;
3. (Amended, *SG* No. 71/2008, effective 12.08.2008) prohibit medicinal products in the presence of documented information about: non-compliance with quality requirements; medicinal products imported or manufactured in violation of this Act; medicinal products offered in packaging with brochures that do not comply with the requirements of this Act, and send samples thereof to the Bulgarian Drugs Agency
4. give conclusions with regard to the compliance of controlled sites with statutory requirements;
5. issue orders, prescriptions and instructions within their competence that shall be binding on all persons on the territory of the respective region.
(2) Compulsory administrative measures under Paragraph 1 or under Article 270, Paragraph 3 shall be imposed by order of the RIPCPH Director.
(3) Orders under Paragraph 2 shall be subject to appeal under the Administrative Procedure Code, whereby their appeal shall not stay their enforcement.
Article 272. (1) The Bulgarian Drugs Agency shall:
1. prohibit putting into operation and suspend the operations of sites and installations when the rules of Good Manufacturing Practice of medicinal products are violated, until such violations have been removed;
2. prohibit the manufacturing, importation, exportation and trade in medicinal products which directly or indirectly threaten the health of humans, and order their destruction, processing or use for other purposes;
3. provisionally suspend the operation of sites for wholesale and retail trade in medicinal products when the conditions under which the respective authorisation or authorisation have been issued;
4. prohibit medicinal products in the presence of recorded information about: incompliance with quality, efficiency and safety requirements; medicinal products imported or manufactured in violation of this Act, as well as medicinal products offered in packaging with brochures that do not meet the requirements hereof; where necessary, order their withdrawal from pharmacies and drugstores, from wholesale trade warehouses, from manufacturers and treatment establishments and notify the Ministry of Health thereof;
5. suspend clinical trials in the presence of established violations until their removal or order the termination thereof;
5a. (New, *SG* No. 71/2008, effective 12.08.2008) issue orders for the blocking, withdrawal and destruction of counterfeit medicinal products and of medicinal products of undetermined origin;
6. issue orders, prescriptions and instructions within its competence that shall be binding on all persons.

(2) Compulsory administrative measures under Paragraph 1 and under Article 270, Paragraph 3 shall be imposed by order of the BDA Director.
(3) The orders under Paragraph 2 shall be subject to appeal under the Administrative Procedure Code, whereby the appeal shall not stay their enforcement.
Article 273. (1) The terms and conditions for taking samples, conducting trials and tests and the payment for them shall be specified in an Ordinance of the Minister of Health.
(2) When the outcomes of laboratory tests are contested, these shall be repeated. Repeated tests shall be conducted upon written request by the interested party, submitted within 7 days of the date of receipt of the result of the initial test.
(3) Repeated tests under Paragraph 2 shall be conducted by experts designated by the BDA Executive Director, who have not been involved in the initial testing, in the presence of an authorised representative of the interested party.
Article 274. (1) The terms and conditions for blocking and withdrawing from the market of medicinal products that have demonstrated non-compliance with quality, safety and efficacy requirements shall be specified in an Ordinance of the Minister of Health.
(2) The terms and conditions for the destruction, processing or use for other purposes of medicinal products shall be specified in an Ordinance of the Minister of Health.
Article 275. (1) When exercising control, the Bulgarian Drugs Agency shall take all necessary measures in order to ensure the right validation of manufacturing and refinement of medicinal products obtained from human blood or human plasma, the sustainability of batch quality and in order to guarantee, within technological constraints, the absence of a specific virus contamination.
(2) The manufacturers shall notify the Bulgarian Drugs Agency of the method used to reduce or eliminate pathogenic viruses, which may be transmitted through medicinal products obtained from human blood or human plasma.
(3) The Bulgarian Drugs Agency shall test and send for testing to another official laboratory for control of medicinal products in the Republic of Bulgaria or in another Member State samples of bulk product/not poured into bottles and/or of a medicinal product intended for trial either in the course of evaluating the application for an authorisation for use under Article 46, Paragraph 1, item 2, or after issuing an authorisation for use.
Article 276. The BDA Executive Director shall temporarily suspend, withdraw, terminate or amend an authorisation for use of a medicinal product/registration by order, where it is found that:
1. there is an inadmissible adverse reaction in case of correct use, or
2. there is no therapeutic efficacy (there shall be no therapeutic efficacy where it is found that the therapeutic results announced during licensing for use cannot be obtained), or
3. the benefit/risk ratio is unfavourable with correct use, or
4. the quantitative and qualitative composition of the medicinal product do not correspond to those declared during licensing for use, or
5. the data from the dossier under Articles 27-32 are untrue, or
6. (Amended, *SG* No. 71/2008, effective 12.08.2008) the data from the dossier under Articles 27-32 have not been completed or have not been changed in accordance with the requirements of Chapter Three, Section VI, or
7. control trials are not conducted in accordance with the methods indicated in Article 27, Paragraph 1, item 8, or
8. the data on the packaging and/or in the brochure do not correspond to those approved when the authorisation for use was issued;
9. (New, *SG* No. 71/2008, effective 12.08.2008) the holder of the authorisation for use has not fulfilled his obligations under Article 45, Paragraph 1 of Regulation (EC) No. 1901/2006.
Article 277. (1) The BDA Executive Director, irrespective of the measures under Article 276, shall prohibit by order the supply of medicinal products concerned and shall order their prohibition and withdrawal from the market when:
1. there is an inadmissible adverse reaction in case of correct use, or
2. there is no therapeutic efficacy, or
3. the benefit/risk ratio is unfavourable in case of correct use, or
4. the quantitative and qualitative composition of the medicinal product concerned does not correspond to those declared during licensing for use, or

5. no control of the medicinal product and/or of the ingredients and at the intermediate stages of the manufacturing process has been exercised, or the requirements under which the manufacturing authorisation has been issued are not implemented.
(2) The BDA Executive Director may impose a prohibition under Paragraph 1 in respect only of specific batches of the medicinal product.
Article 278. (1) The BDA Executive Director shall, by order, temporarily suspend or withdraw the authorisation for use of a class or of all medicinal products for which the requirements under which a manufacturing authorisation has been issued are not observed in respect to the place of manufacturing.
(2) By order, the BDA Executive Director may take, other than the measures under Article 276, a provisional suspension of importation of a class or of all medicinal products from third countries, or withdraw the authorisation for importation of a class or of all medicinal products when they do not comply with the requirements of Chapter Five.
(3) By order, the BDA Executive Director may take, other than the measures under Article 276, a provisional suspension or the withdrawal of a manufacturing authorisation for a class or for all medicinal products that do not comply with the requirements of Chapter Five.
Article 279. (1) The orders under Articles 276, 277 or 278 shall be served on the holder of an authorisation for use, the manufacturer or the importer.
(2) The orders under Paragraph 1 shall be subject to appeal under the Administrative Procedure Code, whereby their appeal shall not stay their enforcement.
Article 280. (1) When a violation of the provisions of Chapter Eleven has been found, or of the Ordinance under Article 249, the BDA Executive Director shall order the suspension of distribution or of the advertisement.
(2) By virtue of the order under Paragraph 1, the BDA Director may obligate the advertiser to publish or distribute, in coordination with the Bulgarian Drugs Agency, a disclaimer of the allegations contained in the advertisement through the same means, in the same format and volume.
(3) The order under Paragraph 2 shall be subject to appeal under the Administrative Procedure Code.

Chapter Fourteen
PENAL ADMINISTRATIVE PROVISIONS

Article 281. (1) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) Anyone manufacturing, importing, selling, storing or allowing for use in the Republic of Bulgaria medicinal products that have not been authorised for use, outside the cases under Articles 8, 9, and 10, unless subject to a more serious sanction, as well as counterfeit medicinal products or medicinal products of undetermined origin, shall be sanctioned by fine of BGN 25,000 to BGN 50,000.
(2) The same sanction shall be imposed on persons manufacturing, importing, selling or allowing the use, in the Republic of Bulgaria, of medicinal products that do not comply with the requirements of the effective pharmacopoeia and fail to meet the conditions stipulated during their licensing for use.
(3) When the violations under Paragraphs 1 and 2 relate to medicinal products not authorised for use containing narcotic substances or when they have been committed for a second time, unless the acts constitute criminal offences, the authorisation issued in pursuance hereof shall be withdrawn.
(4) Medical specialists who manufacture, sell or allow the use of medicinal products that have not been authorised shall be barred from exercising the profession for a term of 6 months to 2 years.
(5) The sanction under Paragraph 4 shall be imposed by order of the Minister of Health at the proposal of the BDA Executive Director.
Article 282. (1) Anyone selling medicinal products in packaging or with patient brochures that do not comply with the requirements of this Act, shall be sanctioned by a fine of BGN 750 to BGN 1,500 and in case of repeating the same violation – by a fine of BGN 1,500 to BGN 3,000.
(2) Anyone selling medicinal products without patient brochures shall be sanctioned by a fine of BGN 750 to BGN 1,500, and in case of repeating the same violation – by a fine of BGN 1,500 to BGN 3,000.
Article 283. (1) Anyone importing, trading in or allowing the use of medicinal products whose shelf life has expired, shall be sanctioned by fine of BGN 10,000 to BGN 20,000.
(2) Anyone breaking the immediate/outer packaging or selling/allowing the use of medicinal products whose immediate/outer packaging has been broken, shall be sanctioned by a fine of BGN 750 to BGN 1,500 and in case of repeating the same violation – by a fine of BGN 1,500 to BGN 3,000.
Article 284. (1) Anyone manufacturing, importing or conducting wholesale trade in medicinal products or selling such products without the requisite authorisation be sanctioned by a fine of BGN 50,000.

(2) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) Anyone manufacturing, importing or conducting wholesale trade in medicinal products, or selling medicinal products in violation of the issued authorisation or authorisation, or selling, storing or providing counterfeit medicinal products, as well as medicinal products of undetermined origin, shall be sanctioned by a fine of BGN 25,000 to BGN 50,000.
(3) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) In the cases under Paragraphs 1 and 2, the bodies of state control shall suspend by order the operation of the site concerned.
(4) The order under Paragraph 3 shall be subject to appeal under the Administrative Procedure Code, whereby the appeal shall not stay its enforcement.

Article 285. (1) Anyone trading in medicinal products without a certificate of batch release shall be sanctioned by a fine of BGN 5,000 to BGN 10,000, and in case of repeating the same violation – by a fine of BGN 10,000 to BGN 20,000.
(2) A wholesale trader supplying drugstores with medicinal products outside the lists approved by the Minister of Health shall be sanctioned by a pecuniary sanction of BGN 2,500 to BGN 5,000 and in case of repeating the same violation – by a fine of BGN 5,000 to BGN 10,000.
(3) A qualified person who has allowed the sale of batches of medicinal products without a certificate of release of each separate batch shall be sanctioned by a fine of BGN 2,500 to BGN 5,000.

Article 286. (1) For clinical trials conducted in violation hereof, unless the act constitutes a criminal offence, the guilty persons who have allowed or committed this violation shall be imposed a fine of BGN 5,000 to BGN 10,000 and in case of allowing or committing the same violation for a second time – a fine of BGN 10,000 to BGN 20,000.
(2) Medical specialists who have allowed or committed violations under Paragraph 1 may also be imposed the sanction of "disbarment from exercising the profession" for a period of 6 months to two years.
(3) The measure under Paragraph 2 shall be imposed by the Minister of Health at the proposal of the BDA Executive Director.

Article 287. (1) (Supplemented, *SG* No. 71/2008, effective 12.08.2008) Anyone conducting retail trade in medicinal products without an authorisation/certificate for this or who works in violation of the authorisation/certificate issued to him shall be sanctioned by a fine, or accordingly by a property sanction of BGN 5,000 to BGN 10,000.
(2) The sanction under Paragraph 1 shall also be imposed on persons conducting retail trade in a pharmacy or drugstore after termination of the effects of the authorisation/permit.
(3) (Amended, *SG* No. 71/2008, effective 12.08.2008) Anyone selling in a drugstore medicinal products dispensed with a medical prescription or products of significance to human health, outside those stipulated in the Ordinance under Article 243, shall be sanctioned by the fine under Paragraph 1, and in case of repeating the same violation, the certificate of registration of the drugstore shall be withdrawn.
(4) In the cases under Paragraphs 1 and 2, the state control bodies for medicinal products shall suspend by order the operation of the site concerned.
(5) The order under Paragraph 4 shall be subject to appeal under the Administrative Procedure Code, whereby the appeal shall not stay its enforcement.
(6) (Repealed, *SG* No. 71/2008, effective 12.08.2008)

Article 287a. (New, *SG* No. 71/2008, effective 12.08.2008) (1) A medical specialist working with persons engaged in retail trade in medicinal products, without having an authorisation/certificate for that, shall be sanctioned with a fine of BGN 2,500 to BGN 5,000.
(2) The sanction under Paragraph 1 shall also be imposed on persons under Paragraph 1 working in a pharmacy or drugstore after the termination of the validity of its authorisation/certificate.
(3) In the event that more than two violations under Paragraphs 1 and 2 have been found, the Minister of Health may deprive the medical specialist of the right to practice his profession for a period of up to two years.

Article 288. (1) A retail trader in medicinal products who has allowed the operations under Article 219 to be carried out by an incompetent person shall be sanctioned by a pecuniary sanction of BGN 5,000 to BGN 10,000, and in the event of repeating the same violation, the authorisation for retail trade shall be withdrawn.
(2) In the cases under Paragraph 1, the state control bodies shall suspend the operation of the site by order.

Article 289. Anyone selling medicinal products at prices other than those formed in pursuance hereof shall be sanctioned by fine of BGN 5,000 to BGN 10,000, and in the event of repeating the same violation, by a fine of BGN 6,000 to BGN 12,000.

Article 290. (1) (Amended, *SG* No. 71/2008, effective 12.08.2008) Anyone advertising medicinal products not authorised for use in pursuance hereof shall be sanctioned by fine of BGN 10,000 to BGN 20,000.

(2) (New, *SG* No. 71/2008, effective 12.08.2008) Anyone advertising a product by ascribing to it and/or suggesting properties connected with the prevention, diagnosis or treatment of human diseases shall be sanctioned by fine of BGN 10,000 to BGN 20,000.

(3) (Renumbered from Paragraph 2, amended, *SG* No. 71/2008, effective 12.08.2008) Anyone advertising medicinal products in violation hereof shall be sanctioned by fine of BGN 10,000 to BGN 20,000.

(4) (Renumbered from Paragraph 3, amended, *SG* No. 71/2008, effective 12.08.2008) The sanctions under Paragraph 2 shall also be imposed on persons who have allowed the broadcasting, publication and distribution of advertisement.

Article 290a. (New, *SG* No. 71/2008, effective 12.08.2008) A medical specialist or a person claiming to be a medical specialist, who engages in direct or indirect advertising of medicinal products in the printed and/or electronic media, as well as on the Internet, shall be sanctioned with a fine of BGN 1,000 to BGN 5,000, and in the event of repeated offence – a fine of BGN 3,000 to BGN 10,000.

Article 291. (1) When the violations under Articles 281-287, Article 289, Article 290, Article 292 and Article 294 have been committed by legal persons or sole proprietors, pecuniary sanctions at an amount no lesser than triple the amount of the envisaged minimums for the respective fines and not larger than the triple amount of the envisaged maximum amounts of the respective fines shall be imposed.

(2) For violations of Article 289, the pecuniary sanction shall be nine times the amount of the sum taken in excess, where the latter exceeds the maximum amount of the sanction under Paragraph 1.

(3) The imposition of a pecuniary sanction shall not exclude the imposition of a fine to the delinquent officials.

(4) The imposition of pecuniary sanctions shall not exclude the imposition of measures envisaged with regard to the competency of medical specialists and qualified persons.

Article 292. (1) Anyone failing to implement an order, prescription or instruction of the state control bodies under this Act, outside the cases under Article 270, Paragraph 1, item 2 or Paragraph 3, shall be sanctioned by fine of BGN 1,500 to BGN 3,000.

(2) For failure to implement an order under Article 270, Paragraph 1, item 2 or Paragraph 3, the guilty persons shall be sanctioned by fine of BGN 500 to BGN 1,000.

Article 293. (1) In the cases under Article 281, Paragraphs 1-3, Article 283, Paragraph 1, as well as in the event of failure to observe the conditions under which the authorisation for retail trade in medicinal products in a pharmacy has been issued, the Minister of Health shall issue an order for its withdrawal.

(2) For failure to observe the conditions under which the authorisations/licenses/certificates for manufacturing, importation, parallel importation, wholesale trade in medicinal products or for the registration of a drugstore, as well as in the cases under Article 281, Paragraphs 1-3, Article 283, Paragraph 1 and Article 287, Paragraph 3, the BDA Executive Director shall issue an order for their withdrawal.

(3) In case of failure to discharge notification duties under Article 204, Paragraph 3 for termination of operations by a wholesale trader in medicinal products, the BDA Executive Director shall issue an order for withdrawal of the issued authorisation.

(4) In case of failure to discharge the duties of notification under Article 235, Paragraph 3 for termination of operations by the holder of an authorisation for retail trade in medicinal products, the Minister of Health shall issue an order for withdrawal the authorisation issued.

(5) The orders under Paragraphs 1-4 shall be subject to appeal under the Administrative Procedure Code, whereby the appeal shall not stay their enforcement.

Article 294. Anyone violating the provisions of this Act or the Ordinances for its implementation, outside the cases under Articles 281-293, shall be sanctioned by a fine of BGN 1,000 to BGN 3,000 and in case of repeating the same violation – by a fine of BGN 3,000 to BGN 5,000.

Article 295. (1) The presence of violations under this Act shall be established by acts drafted by BDA or RIPCPH state inspectors.

(2) The presence of violations under Article 289 shall be established by officials designated by the Minister of Health.
(3) Penal decrees shall be issued by the Minister of Health, the Chief State Health Inspector, by the BDA Executive Director or the Directors of RIPCPH, depending on the hierarchical system of the official who has found the presence of a violation.
Article 296. The drafting of acts, the issuance, appeal from and the execution of penal decrees shall be carried out in compliance with the Administrative Violations and Sanctions Act.
Article 297. In the cases under Articles 281, 282, 283, 284, 285 and 287 the sanctioning body shall also order seizure to the benefit of the state of medicinal products making the object of violation, subject to the terms and conditions specified in an Ordinance of the Minister of Health.

ADDITIONAL PROVISIONS

§ 1. For the purposes of this Act:
1. **"Active substance"** shall be any substance (ingredient) intended for use as a pharmacologically active ingredient of the pharmaceutical form concerned.
2. **"Bioequivalence"** shall be present where medicinal products are pharmaceutically equivalent or pharmaceutical alternatives, and if their bioavailability after administration in the same molar dose is similar to the extent that their effect in terms of efficacy and safety is substantively similar.
3. **"Bioavailability"** shall be the speed and level at which the active substance or its therapeutically active part are absorbed from the pharmaceutical form and become available at the location of activity. When the medicinal substance is intended to have a systemic therapeutic effect, bioavailability shall mean the speed and level at which the medicinal substance or its therapeutically active part are released from the pharmaceutical form and pass into the general circulation.
4. **"Researcher brochure"** shall be the overall clinical and non-clinical data about the tested medicinal product(s) that are relevant to the trial of the product or products on humans.
5. **"Valid documentation"** shall be the documentation which, in terms of content and completeness, meets the requirements specified in a particular procedure hereof.
6. **"A substance whose use is well established in medical practice"** shall be a substance to which the following criteria may apply:
a) The period for substantiating well established use in medical practice is not less than 10 years from the date of the first systematised and documented use of the substance as a medicinal product in the European Union or in the European Economic Area;
b) The quantitative aspects of the use of the substance, taking into account its level of use in medical practice, its level of use in terms of geographical spread and its level of monitoring through the system of safety, including the studies carried out prior to marketing and thereafter and the published scientific literature concerning epidemiological studies and, in particular, comparative epidemiological studies;
c) A high level of scientific interest in the use of the substance (i.e. based on the number of scientific publications) and uniformity of scientific evaluations within academic circles.
7. **"Outer packaging"** shall be the packaging not entering immediately in contact with the medicinal product.
8. **"Sponsor"** shall be a natural or legal person, institution or organisation responsible for the start, managing and/or funding of a clinical trial.
9. **"Generic medicinal product"** shall be a medicinal product of the same qualitative and quantitative composition in terms of its active substances and of the same pharmaceutical form as its reference medicinal product, and its bioequivalence with the reference medicinal product has been substantiated through suitable bioavailability tests. The various oral pharmaceutical forms of immediate release shall be considered as the same pharmaceutical form. The various salts, esthers, ethers, isomers, isomer mixtures, complexes or derivatives of an active substance shall be considered as the same active substance, unless they vary significantly in their safety and/or efficacy.
10. **"Chief researcher"** shall be the physician or doctor of dental medicine designated by the sponsor who is charge of the overall the clinical trial in compliance with the approved protocol and manual of Good Clinical Practice, and of the work of the researchers.
11. **"Defined daily dose"** shall be the average daily maintenance dose of a medicinal product, which is administered to adults for the main therapeutic indication of the respective medicinal product.
12. **"Good Clinical Practice"** shall be all internationally recognised ethical and scientific requirements to quality that are observed in the planning, conducting, accounting for and reporting on clinical trials.

13. **"Good Laboratory Practice"** shall be a system of internationally recognised rules on the conditions for planning, the processes of organisation, conducting, monitoring and recording laboratory trials.
14. **"Good Manufacturing Practice"** shall be a system of internationally recognised business rules covering all aspects of manufacturing, i.e., staff, premises, installations, material, documentation, quality control, and which is intended to ensure safety, efficacy and compliance with specifications.
15. (Supplemented, *SG* No. 71/2008, effective 12.08.2008) **"Member State"** shall be a Member State of the European Union or a state signatory to the Agreement on the European Economic Area.
16. **"Label"** shall be the information appearing on the immediate or outer packaging of a medicinal product.
17. **"Immunological medicinal product"** shall be a medicinal product containing vaccines, toxins, serums or allergens. Agents used to create active immunity or to establish a state of immunity or to cause passive immunity shall be in the scope of vaccines, toxins and serums. Allergens shall be medicinal products intended to identify or stimulate a specific targeted change in the immunological response to an allergic agent.
18. **"Bioequivalence study"** shall be a clinical trial aimed at proving that two medicinal products are bioequivalent when these are pharmaceutically equivalent or pharmaceutical alternatives and when their bioavailability, following administration at the same molar dose, is similar to an extent that is a condition of equivalent efficacy and safety.
19. **"Bioavailability study"** shall be a clinical trial aimed at demonstrating what the speed and level are at which the active substance or its therapeutically significant part in the tested medicinal product reach the systemic blood circulation from the respective pharmaceutical form.
20. **"Tested medicinal product"** shall be the pharmaceutical form of an active substance or placebo which is tested or used for comparison in a clinical trial, including products for a which an authorisation for use has been issued, but are used for a non-authorised indication with a view to receiving additional information about the authorised formulation, or have been constituted as a set (in a pharmaceutical form or in a packaging) other than the authorised formulation.
21. **"Researcher"** shall be the physician or doctor of dental medicine designated by the sponsor and by the chief researcher, who carries out in practice the clinical trial under the guidance of the chief researcher in accordance with the approved protocol and the manual of Good Clinical Practice for the conduct of the clinical trial in the research centre. When a clinical trial is carried out by a team, the researcher shall be head in charge of it and shall be referred to as chief researcher.
22. **"Informed consent"** shall be a statement of any person capable of giving consent or, in case the person is not capable of doing so, of his statutory representative, which must be in writing, dated and signed, concerning the participation in a clinical trial and taken in complete freedom after due notification with regard to its nature, significance, effects and risks, and recorded in a suitable way.
23. **"Kit"** shall be any substance, which prior to being used is usually dissolved, suspended, diluted or combined with radionuclides, as a result of which the ready radioactive medicinal product is obtained.
24. **"Clinical trial of a medicinal product"** shall be any study on humans intended to discover or confirm the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products tested, and/or to determine the adverse reactions to one or more medicinal products tested, and/or to study the absorption, distribution, metabolism and excretion of one or more medicinal products tested for the purpose of establishing their safety and/or efficacy.
25. **"Clinical advantage"** shall be a significant therapeutic or diagnostic advantage of a medicinal product compared to another medicinal product that has already been authorised for use.
26. **"Coordinating researcher"** shall be a researcher appointed to the purpose of coordinating researchers from different centres involved in a multi-centre trial.
27. **"Patient brochure"** shall be a brochure containing information for the user, accompanying a medicinal product.
27a. (New, *SG* No. 71/2008, effective 12.08.2008) **"Medicinal product for high-technological therapy"** shall be a medicinal product defined in Article 3 of Regulation (EC) No. 1394/2007 of the European Parliament and of the Council of 13 November 2007 concerning medicinal products for modern therapy and for amendment of Directive 2001/83/EC and of Regulation (EC) No. 726/2004.
28. **"Medicinal product obtained from human plasma or from human blood"** shall be a medicinal product manufactured from human blood ingredients, using a method that involves an

industrial process. Albumin, immunoglobulin, coagulating factors and antiproteases, solutions of plasma proteins, other plasma fractions or combinations thereof shall fall within the above.
29. **"A medicinal product intended for treatment, prevention and diagnosis of rare diseases"** shall be the product which:
a) is intended for the diagnosis, prevention or treatment of life-threatening diseases or chronic diseases with a progressive course affecting no more than 5 out of 10,000 people on the territory of the country, or
b) is intended for the diagnosis, prevention or treatment of life-threatening diseases and of chronic conditions that seriously damage health (diseases with a high share of disease-related inability to work and disability), evidence being attached that the sale of the product does not provide a satisfactory level of return that would justify the required investment in scientific research and development operations without further incentives for the author of the product, and
c) when there is no satisfactory method for diagnosis, prevention or treatment of the respective condition or, if one exists, the proposed medicinal product has significantly more advantages than the former and it yields significantly more benefit for the those affected by said condition.
30. **"Pharmaceutical form"** shall be a structure that is suitable for administration and contains the active substance(s), including or not any excipients, obtained through the use of certain technological operations ensuring the desired treatment effect and stability during storage within the set shelf-life.
31. (Amended, *SG* No. 71/2008, effective 12.08.2008) **"A person established on the territory of a Member State or of an EEA country"** shall be a legal subject registered under the civil or commercial legislation of a Member State, which has been created by virtue of a legislative instrument, having a seat and a business address in a Member State or in a country under the Agreement on the European Economic Area.
32. **"Magistral preparation"** shall be a prescription for a medicinal product prepared in a pharmacy by prescription of a medical specialist following an approved formulation, which is intended for a particular patient.
33. **"International non-patent name"** shall be the recommended name of the active substances, approved and published by the WHO.
34. **"Medical specialists"** shall be physicians, doctors of dental medicine, masters of pharmacy, nurses, midwives, medical laboratory analysts, medical auxiliaries and assistant pharmacists.
35. **"Medical commercial representative"** shall be a person that has undergone special training, having scientific knowledge for the provision of accurate and full information about the medicinal product which he advertises.
36. **"Multi-centre clinical trial"** shall be a clinical trial carried out with the use of a single protocol, but in more than one centre and by more than one researcher. Research centres may be located on the territory of the same Member State, of more than one Member States and/or in Member States and third countries.
37. **"The name of a medicinal product"** shall be the name given to a product, which may be:
a) a freely chosen name (trade name);
b) a generally accepted one, used together with the trademark or the name of the manufacturer;
c) a scientific name, used together with the trademark or the name of the manufacturer.
38. **"Scientific literature"** shall be a publication(s) of the results from scientific research in specialised international medical publications.
39. **"New active substance"** shall be:
a) a chemical, biological or radiopharmaceutical substance, which has not been allowed for use as a medicinal product in the European Union;
b) an isomer, a mixture of isomers, a complex or derivative or a salt of a chemical substance, which has been authorised for use as a medicinal products in the European Union, but varies in terms of safety and efficacy from the previous authorised substance;
c) a biological substance which has been authorised for use as a medicinal product in the European Union, but has a different molecular structure and a different origin compared to the raw material, or it has been obtained through a different production process;
d) a radiopharmaceutical substance whose radionuclides or molecular ties (or ligands) that have not been authorised as a medicinal product in the European Union or the mechanism for connecting molecules and radionuclides in pairs has not been allowed in the European Union.

40. **"Adverse event"** shall be any unfavourable change in the health condition observed with the administration of a medicinal product to a patient or subject of a clinical trial, which is not necessarily causally associated with the course of treatment.
41. **"Adverse reaction"** shall be any undesired and unexpected response to a medicinal product, which is manifested upon administration of the product at doses usually used for treatment, prevention or diagnosis of a disease in humans or for the restitution, correction or modification of a physiological function. In the case of a clinical trial – any adverse and unforeseen response to a tested medicinal product, irrespective of the administered dose. The types of adverse reactions shall be:
a) **"unexpected"** – an adverse reaction that has not been mentioned in the product summary or whose nature, severity or outcome do not correspond to those mentioned in the product summary; in the case of a clinical trial, a reaction shall be adverse if its nature, severity or outcome do not correspond to the information about the tested medicinal product, specified in the researcher brochure;
b) **"suspected"** – an adverse reaction, of which the notifier or holder of an authorisation for use suspects a possible causal connection with the medicinal product administered;
c) **"serious"** – any unfavourable effect on the health condition, which has become the reason for a lethal outcome, for an imminent threat to life, hospitalisation or extension of the term thereof, for significant or lasting injuries, disability or congenital abnormalities;
d) a combination of reactions under a), b) and c).
42. **"A common name"** shall be the international non-patent name of the medicinal or auxiliary substance (INN) recommended by WHO; if none exists, the name in the European Pharmacopoeia shall be used and if missing there as well – another pharmacopoeian name; when no pharmacopoeian name is available, the usual accepted name shall be used.
43. **"Batch"** shall be a set amount of the drug, manufactured in accordance with the established reproducible technological scheme, ensuring the required level of batch homogeneity as regards the required control indicators.
44. **"Maintenance of the authorisation for use of a medicinal product"** shall cover all necessary operations in view of maintaining the up-to-date registration status of a medicinal product, including the monitoring of medicinal safety.
45. **"Benefit"** shall be a positive outcome/therapeutic efficacy of a medicinal product for a particular patient, groups of patients or the public. The quantitative evaluation of the expected benefit shall include an approximate calculation of the probability of a positive outcome.
46. **"Auxiliary substance"** shall be a substance complying to a particular specification, with particular qualitative characteristics, which is included in the composition of the pharmaceutical form and confers upon it a structure, stability and regulates its effects.
47. **"Post-marketing study"** shall be any study performed of the use of a medicinal product within the approved product summary in the period following its licensing for use.
48. **"Post-marketing study of safety"** shall be a pharmacological and epidemiological study or a clinical trial carried out in conformity with the conditions of the authorisation for use for the purpose of identifying or performing a quantitative evaluation of the risks associated with the use of the product in clinical practice.
49. **"A potentially serious threat to the health of the population"** shall exist where there is high likelihood that the use of a medicinal product may cause irremovable, unredeemable and irreversible negative consequences. The evaluation process shall identify the threat of causing damage to the health of the population and its actual exposure in the event of extensive use of the product concerned. Serious risk to health in the context of use of a particular medicinal product may be assessed under the following conditions:
a) efficacy – data submitted on the therapeutic efficacy with regard to the proposed indication(s), to the proposed target group(s) of patients and to the proposed dosage, specified in the draft patient brochure shall not fully substantiate, from a scientific perspective, claims for efficacy;
b) safety – the evaluation of data from preclinical toxicity/pharmacological safety and clinical safety may not convincingly substantiate the conclusion that all potential safety aspects with regard to the target group(s) of patients have been accurately and exhaustively reflected in the proposed patient brochure or that the absolute level of risk is unacceptable;
c) quality – the proposed manner of production and the control methods may not guarantee the lack of significant defects in product quality that may have an impact on product safety and/or efficacy;

d) the benefit/risk ratio – the evaluation of the ratio of benefits to risk is unfavourable, bearing in mind the nature of the identified risk(s) and the potential benefit with regard to the proposed indication(s) and the target group(s) of patients.

50. **"Representative of the person under Article 26, Paragraph 1 or of the holder of an authorisation for use"** shall be a person established on the territory of the Republic of Bulgaria and designated by the person under Article 26, Paragraph 1 or by the holder of an authorisation for use to represent him before the regulatory bodies on the territory of the Republic of Bulgaria.

51. **"An acceptable level of safety"** shall be available when the data submitted are taken at a statistically significant safety in clinical trials carried out in conformity with the Good Clinical Practice.

52. **"The manufacturing of a medicinal product"** shall constitute all operations for the provision of the materials, their processing during the production process, including packaging and labelling, quality control, batch release, storage, dispatching and the control operations thereto related.

53. **"A clinical trial protocol"** shall be a document describing the objective(s), the project, the methodology, the statistical processing and the organisation of a trial. The protocol shall also include any and all subsequent modifications and supplements thereto.

54. **"Market placement/release"** shall be the distribution of a medicinal product for trade on the territory of the Republic of Bulgaria outside the immediate control of the holder of an authorisation for use.

55. **"Immediate packaging"** shall be the packaging which comes into immediate contact with the medicinal product.

56. **"Radiopharmaceutical"** shall be a medicinal product which contains, when ready for use, one or more radionuclides (radioactive isotopes) included therein for a medical purpose.

57. **"Radionuclide generator"** shall be any system, including a fixed maternal radionuclide, of which a daughter radionuclide is obtained separated by elution or by other methods, and used in a radiopharmaceutical.

58. **"Radionuclide precursor"** shall be any other radionuclide manufactured for the radioactive marking of another substance, immediately prior to its introduction into a patient's body.

59. **"A herbal medicinal product"** shall be a medicinal product containing, as medicinal substances, one or more herbal substances, or one or more herbal preparations, or one or more herbal substances in combination with one or more herbal preparations.

60. **"Herbal substances"** shall mainly be plants or parts thereof, algae, fungi, lichens, that are entire, broken or cut down and are used unprocessed, usually desiccated, but sometimes fresh as well. Certain exudates that have not been subjected to any specific processing also belong to herbal substances. Herbal substances must have a specific botanical scientific name for the plants of which they originate in accordance with the bionominal system (genus, species, variety and author).

61. **"Herbal preparation"** shall be a product obtained after extraction, distillation, squeezing, fractioning, refinement, concentration or fermentation of a herbal substance. The herbal preparation may also take the form of ground or pulverised herbal substances, tinctures, extracts, ether oils, processed herbal fluids/juices.

62. **"Rare diseases"** shall be diseases characterised by an incidence not higher than 5 per 10,000 individuals.

63. **"Reference medicinal product"** shall be a medicinal product authorised in compliance with Article 23, subject to the requirements of Article 27.

64. **"Reference value of the defined daily dose"** for an international non-patent name with the respective pharmaceutical form based on the anatomic-therapeutic classification of drugs shall be the lowest value of the defined daily dose, determined on the basis of values of the defined daily dose of different medicinal products coming under the respective international non-patent name in the respective medicinal formulation based on the anatomic-therapeutic classification of drugs.

65. **"The reference value of a treatment course"** shall be the lowest value of a treatment course determined on the basis of values of treatment courses with drugs under an international non-patent name in the respective pharmaceutical form.

66. **"Risk associated with the use of a medicinal product"** shall be:

a) a risk to the patient's health or a risk to the health of the population associated with the quality, safety or efficacy of a medicinal product;

b) a risk of adverse effects on the environment.

67. **"Serious adverse event"** shall be any unfavourable change in the health condition which has become the cause of lethal outcome, an immediate threat to life, hospitalisation or extension of the term thereof, significant or lasting injuries, disability and congenital abnormalities.
68. **"A certificate of batch release"** shall be a document issued by the qualified person to the manufacturer or to the importer for each separate batch, and it shall include the requirements as per the specification, as well as all the results from tests for release of the batch concerned.
69. **"Certificate of additional protection"** shall be a document affording additional patent protection to a medicinal product for no more than 5 years of the date of expiry of the main patent.
70. **"Urgent safety restriction measures"** shall be provisional changes in the product information with regard to one or more parts of the product summary, indication, method of administration, contraindications and warning resulting from new information pertaining to the safe use of the medicinal product concerned.
71. **"Spontaneous notification"** shall be a voluntary notification sent about a suspected adverse reaction to the use of a medicinal product addressed to the holder of the authorisation for use, to bodies in charge of the supervision of medicinal products or to other organisation, which does not originate in a study or in another organised system for the collection of information.
72. **"The shelf life of a medicinal product"** shall be the period of time during which, if stored in accordance with the prescribed conditions, a medicinal product meets the requirements of the specification produced on the basis of research in the field of stability carried out on several batches of the ready formulation.
73. (Amended, *SG* No. 71/2008, effective 12.08.2008) **"A medicinal product corresponding to a herbal medicinal product"** shall be a product containing the same active substances, notwithstanding the composition of excipients, intended for the same purpose, of an equivalent amount of the medicinal substance(s) and with the same dosage and with the same or a similar route of administration as the product for which an application has been made.
74. **"Notification of an adverse reaction"** shall be information recorded about one or more suspected adverse reactions related to the use of one or more medicinal products by the same patient. In order to recognise the validity of a notification of an adverse reaction, a minimum of data shall be required for the identification of the notifying subject (his initials or address, or profession/speciality), of the patient (initials or age, or date of birth, or gender), of the adverse reaction/event and of the suspected medicinal product.
75. **"Significant change in the clinical trial protocol"** shall be any change in the protocol and/or in the information in the accompanying documentation which could affect:
a) the safety or physical or mental integrity of the subjects;
b) the scientific value of the study;
c) the conducting or organisation of the study;
d) the quality or safety of any of the medicinal products tested.
76. (Amended, *SG* No. 71/2008, effective 12.08.2008) **"Third country"** shall be a state that is not a Member State of the European Union, or is not a state signatory to the Agreement on the European Economic Area.
77. **"Wholesale trade"** shall be all operations for the acquisition, storage, supply, importation or exportation of medicinal products with the exception of the direct provision of medicinal products to the population.
78. **"Subject"** shall be the person who takes part in a clinical trial, irrespective whether he receives the tested medicinal product or the medicinal product used for comparison.
79. **"Vulnerable groups of patients"** shall be persons whose wish for participation in the clinical trial may be affected by the expectation of benefits or by a possible sanction to be imposed by hierarchical superiors in relation to the participation or refusal thereof by the person in the clinical trial. Examples of a group in a hierarchical structure shall be: medical, pharmacy, dentistry students or nurses, laboratory staff, staff in the pharmaceutical industry, army service officers or persons deprived of liberty. Other vulnerable groups shall be patients with incurable diseases, persons in senior citizens homes, unemployed individuals or beggars, emergency patients, vagrants, travellers, young persons, children and persons who are unable to give consent.

80. **"Pharmacopoeia"** shall be a collection of approved specifications and relevant requirements in relation to the manufacturing, testing, storage and marking of active substances, excipients, pharmaceutical forms, packaging material and ingredients of the medicinal product concerned.
81. **"Official formulation"** shall be a prescription for a medicinal product prepared in a pharmacy based on a formulation under the effective pharmacopoeia and intended to be provdred to patients in the same pharmacy.
81a. (New, *SG* No. 71/2008, effective 12.08.2008) **"Counterfeit medicinal product"** shall be a medicinal product with false data concerning its identity, indicated on the product, on the primary or other packaging (e.g., misleading claim about the name, composition, quantity of the active substance per dose unit or other elements), history or origin (e.g., misleading claim about the manufacturer, the state in which the product was manufactured, the state of origin or the holder of the authorisation for use). The counterfeit medicinal product may contain the correct components or other components, it may not contain an active substance, or it may contain an active substance in a quantity different from the correct one, or it may be with a forged packaging. Legitimately authorised medicinal products with deviations in the quality or products that do not comply with the requirements of the Dood Manufacturing Practice and/or of the Good Distribution Practice shall be distinguished from the counterfeit medicinal products.
82. **"Homeopathic medicinal product"** shall be a medicinal product prepared of substances referred to as homeopathic stock in accordance with the manufacturing procedures of the European Pharmacopoeia and in the absence thereof – in accordance with the national pharmacopoeia of a Member State.
83. **"The price calculated on the basis of a reference value"** shall be the price formed for each medicinal product on the Positive Drug List, calculated on the basis of the set reference value per defined daily dose or treatment course.
84. **"Centre"** shall be a unit of the medical establishment in which a clinical trial takes place.
85. **"Abuse of medicinal products"** shall be the permanent or occasional intentional excessive use of medicinal products accompanied by harmful physical or psychological effects.
§ 2. The name of the Bulgarian Drugs Agency shall be written in Latin, as follows: Bulgarian Drug Agency.
§ 3. The Council of Ministers shall specify the terms and conditions for the provision, storage and renewal of medicinal products stored by the State Reserve and Wartime Stocks State Agency.
§ 4. This Act shall implement the provisions of Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use, last amended by Directive 2004/27/EC of the European Parliament and of the Council.
§ 5. The periods for the protection of data about reference medicinal products shall apply in accordance with the provisions of Article 89 of Regulation (EC) No. 726/2004 of the European Parliament and of the Council and of Article 2 of Directive 2004/27/EC of the European Parliament and of the Council.

TRANSITIONAL AND FINAL PROVISIONS

§ 6. The Human Medicinal Drugs and Pharmacies Act (Promulgated, *SG* No. 36/1995; No. 61/1996 - Judgement No. 10 of the Constitutional Court/1996; amended, *SG* No. 38/1998, No. 30/1999, No. 10/2000, No. 37/2000 - Judgement No. 3 of the Constitutional Court/2000; amended, *SG* No. 59/2000, No. 78/2000 – Judgement No. 7 of the Constitutional Court/2000; amended, *SG* No. 41/2001, No. 107 and 120/2002; corrected, *SG* No. 2/2003; amended, *SG* No. 56, 71 and 112/2003, No. 70 and 111/2004, No. 37, 76, 85, 87, 99 and 105/2005, No. 30, 31, 34, 75 and 105/2006) shall be repealed with the exception of the provision of Article 10, Paragraph 2, which shall apply for a period of up to one year of the date of entry of this Act into force.
§ 7. (1) Authorisation for the use of medicinal products issued until the entry of this Act into force under a national procedure, which are also authorised in the Member States in compliance with the centralised procedure, shall be terminated as of 1 January 2007.
(2) Licenses for the use of medicinal products issued until the entry of this Act into force under a national procedure shall be brought in line with the requirements hereof as of the date of their renewal.
(3) Licenses for the use of medicinal products falling into the scope of Regulation (EC) No. 726/2004 of the European Parliament and of the Council and authorised for use in compliance with the repealed Human Medicinal Drugs and Pharmacies Act, being significantly similar products, not authorised for use in the European Union in compliance with the centralised procedure, shall be terminated.

(4) Medicinal products authorised for use in the EU in compliance with the centralised procedure, whose national authorisation for use has been terminated under Paragraph 1, may be sold on the territory of the Republic of Bulgaria in packaging with brochures in compliance with the terminated national authorisation for use over a period not exceeding one year of the date of termination thereof.

§ 8. (1) The approved ceiling prices and the prices registered in compliance with the repealed Human Medicinal Drugs and Pharmacies Act for medicinal products authorised for use in the EU in compliance with a centralised procedure whose national authorisation for use has been terminated under § 7, Paragraph 1, shall remain valid for a period of up to one year of the date of termination thereof.

(2) The approved ceiling prices and the prices registered under the repealed Human Medicinal Drugs and Pharmacies Act for medicinal products other than those under Paragraph 1, shall remain valid until 31 December 2007.

§ 9. (1) Applications for an authorisation for use, for renewal and change in the issued authorisation filed until the entry of this Act into force shall be examined and completed under the terms and conditions hereof.

(2) The applications and documentation filed for licensing the use of medicinal products falling within the scope of the procedure under Article 74 or Article 75 shall be brought in line with the requirements hereof within three months of the entry of this Act into force.

(3) Where, within the period under Paragraph 2, the application and the documentation under Paragraph 2 have not been brought in line with the requirements hereof, the procedure for their examination shall be terminated.

§ 10. (1) Clinical trials authorised prior to the entry of this Act into force shall be completed under the previous procedure.

(2) Applications for conducting a clinical trial on the territory of the Republic of Bulgaria shall be filed, examined and completed under the terms and conditions hereof after entry into force of the Ordinance under Article 82, Paragraph 3.

(3) Applications for changes in authorised clinical trials, filed prior to the entry of this Act into force, shall be examined and completed under the terms and conditions hereof.

§ 11. Applications for the issuance of manufacturing licenses and authorisations for wholesale trade in medicinal products filed until the entry of this Act into force shall be examined and completed under the terms and conditions hereof.

§ 12. (1) Manufacturers of drugs who have obtained a manufacturing authorisation in compliance with the repealed Human Medicinal Drugs and Pharmacies Act shall bring their manufacturing operations in line with the requirements hereof in terms of the qualified person under Article 148, item 2, within three months of the entry of this Act into force.

(2) Manufacturers found as of the entry of this Act into force shall pursue their operations on the basis of licenses issued in compliance with the repealed Human Medicinal Drugs and Pharmacies Act.

§ 13. The persons who have obtained an authorisation for wholesale trade in medicinal products in compliance with the repealed Human Medicinal Drugs and Pharmacies Act shall bring their operations in line with the requirements hereof within 12 months of entry of this Act into force.

(2) Until an authorisation for wholesale trade in medicinal products has been issued in pursuance hereof, but not later than the expiry of the period under Paragraph 1, the persons under Paragraph 1 shall pursue their operations based on the authorisation for wholesale trade in medicinal products issued in compliance with the repealed Human Medicinal Drugs and Pharmacies Act.

(3) The issuance of an authorisation for wholesale trade in medicinal products in pursuance hereof or the expiry of the term under Paragraph 1 shall terminate the authorisation for wholesale trade in drugs under the repealed Human Medicinal Drugs and Pharmacies Act.

§ 14. (1) Persons who have obtained an authorisation for wholesale trade in drugs in compliance with the repealed Human Medicinal Drugs and Pharmacies Act may import medicinal products onto the territory of the Republic of Bulgaria from third countries based on the said authorisation until obtaining an authorisation for importation in pursuance hereof, but no later than 12 months of the entry of this Act into force.

(2) Within one month of the entry of this Act into force, the persons under Paragraph 1 shall file with the Bulgarian Drugs Agency a notification of the person who shall discharge the functions of a qualified person within the meaning of Article 161, Paragraph 2, item 1.

§ 15. The term of validity of authorisations for wholesale trade in medical products issued in compliance with the repealed Human Medicinal Drugs and Pharmacies Act shall be extended *ex officio* until 31 December 2007.
§ 16. (Repealed, *SG* No. 71/2008, effective 12.08.2008).
§ 17. (1) Drugstores found until the entry of this Act into force shall carry out their operations based on certificates issued in compliance with the repealed Human Medicinal Drugs and Pharmacies Act.
(2) Applications for the issuance of certificates of registration for drugstores filed until the entry of this Act into force, shall be examined and completed under the terms and conditions hereof.
§ 18. (1) (Amended, *SG* No. 71/2008, effective 14.04.2008) The Positive Drug List under this Act shall be produced in pursuance hereof and shall enter into force on 30 January 2009.
(2) (Amended, *SG* No. 71/2008, effective 14.04.2008) Until the entry into force of the Positive Drug List under Paragraph 1, the effective Positive Drug List shall be the Positive Drug List adopted with the Ordinance for Establishing a Positive Drug List in the Republic of Bulgaria (Promulgated, *SG*, No. 113/2003; amended, No. 18/2004, No. 4/2005 and Nos. 8, 107 and 112/2007).
(3) (New, *SG* No. 71/2008, effective 14.04.2008) Until the entry into force of the List under Paragraph 1, the National Health Insurance Fund shall reimburse the medicinal products on the NHIF list of medicinal products, adopted subject to Decision No. РД-УС-04-127 of 27 December 2007 for determining the conditions that providers of medical care ought to meet, the procedure of signing contracts with them, and other conditions under Article 55, Paragraph 2, items 2, 4, 6 and 7 of the Health Insurance Act (Promulgated, *SG*, No. 5/2008; amended, No. 45/2008).
§ 19. (1) Within a period of three months of the entry of this Act into force:
1. the Council of Ministers shall amend and supplement the Organic Rules of the Bulgarian Drugs Agency, bringing it in line with this Act;
2. the Minister of Health shall issue the Ordinance under Article 82, Paragraph 3.
(2) Within a period of up to 6 months of the entry of this Act into force, the Council of Ministers shall adopt and the Minister of Health shall issue the other legislative instruments for the enforcement of this Act.
§ 20. After expiry of the first two years of the term of office of the members of Commissions under Article 103, 107, 259 and 261, half of the members whose term of office will be terminated shall be drawn by lot.
§ 21. (Amended, *SG* No. 71/2008, effective 12.08.2008) Within a period of up to two years of the entry of this Act into force, the Bulgarian Drugs Agency shall take the necessary action to have its laboratory for the control of medicinal products and active substances accredited by the European Directorate for the Quality of Medicines and Healthcare.
§ 22. (Effective 14 April 2008 – *SG* No. 31/2007) The following amendments shall be made to the Health Insurance Act (Promulgated, *SG* No. 70/1998; amended, *SG* Nos. 93 and 153/1998, Nos. 62, 65, 67, 69, 110 and 113/1999, Nos. 1, 31 and 64/2000, No. 41/2001, Nos. 1, 54, 74, 107, 112, 119 and 120/2002, Nos. 8, 50, 107 and 114/2003, Nos. 28, 38, 49, 70, 85 and 111/2004, Nos. 39, 45, 76, 99, 102, 103 and 105/2005, Nos. 17, 18, 30, 33, 34, 59, 95 and 105/2006, Nos. 11/2007, Nos. 26/2007 – Judgement No. 3/2007 of the Constitutional Court):
1. In Article 45:
a) Paragraphs 4, 5, 6, and 7 shall be repealed;
b) Paragraph 8 shall be amended as follows:
"(8) The terms and conditions for the reimbursement of medicinal products on the Positive Drug List under Article 262 of the Medicinal Products in Human Medicine Act, of medical products and of dietary food for special medical purposes shall be regulated in an Ordinance of the Minister of Health".
2. In Article 55, Paragraph 2, item 7 shall be amended as follows:
"7. The lists of medical products and dietary foods for special medical purposes and the prices up to which the NHIF shall provide full or partial reimbursement; the conditions for prescription and obtainment of drugs, medical products and dietary foods for special medical purposes."
§ 23. In the Medical-Treatment Facilities Act (Promulgated, *SG* No. 62/1999; amended, *SG* Nos. 88 and 113/1999 ; corrected, *SG* No. 114/1999; amended, *SG* Nos. 36, 65 and 108/2000; *SG* No. 51/2001 – Judgement No. 11/2001 of the Constitutional Court; amended, *SG* Nos. 28 and 62/2002, Nos. 83, 102 and 114/2003, No. 70/2004, Nos. 46, 76, 85, 88 and 105/2005, Nos. 30, 34, 59 and 105/2006) the following supplements shall be made:

1. In Article 17, a paragraph 4 shall be created:
"(4) Clinical trials may be conducted in the diagnostic and consultative centre in compliance with the Medicinal Products in Human Medicine Act."
2. In Article 26, a paragraph 4 shall be created:
"(4) Clinical trials may be conducted in dispensaries in compliance with the Medicinal Products in Human Medicine Act".
§ 24. In § 14 of the Transitional and Final Provisions to the Amendment Act to the Doctors and Dentists Professional Organisations Act (*SG*, No. 76/2005), the following amendments and supplements shall be made:
1. The existent text shall become paragraph 1 and shall be amended as follows:
"(1) Individual and group dental practices, stomatological and medical and stomatological centres registered as traders under the Commerce Act or as cooperatives under the Cooperatives Act shall bring their names in line with § 2 hereof and shall enter the change on the commercial register, the BULSTAT register and in the respective Regional Health Centre no later than 31 December 2007."
2. Paragraphs 2, 3, and 4 shall be created:
"(2) Individual dental practices that are not registered as traders under the Commerce Act shall bring their names in line with § 2 hereof and shall enter the change on the BULSTAT register and in the respective Regional Health Centre within the period under Paragraph 1."
(3) Entry of the change in the name for practices and centres under Paragraph 1 on the commercial register and on the BULSTAT register shall be made, as follows:
1. Until 1 July 2007, in compliance with the Commerce Act, the Cooperatives Act and the BULSTAT Register Act;
2. After 1 July 2007, in compliance with the Commercial Register Act.
(4) No state fees shall be owed for the registration of changes under Paragraphs 1 and 2."
§ 25. In the Patents and Utility Models Registration Act (Promulgated, *SG* No. 27/1993; amended, *SG* No. 83/1996, No. 11/1998, No. 81/1999, Nos. 45 and 66/2002, Nos. 17, 30 and 64/2006), Article 20, item 7 shall be repealed.
§ 26. Item 9 in Article 5 of the Professional Organisation of Masters of Pharmacy Act (Promulgated *SG*, No. 75/2006; amended, No. 105/2006) shall be amended as follows:
"9. Give opinions about the opening of pharmacies in accordance with Article 228, Paragraph 1, item 9 of the Medicinal Products in Human Medicine Act."
§ 27. In § 1, item 7 of the Additional Provision to the Integration of Persons with Disabilities Act (Promulgated, *SG* No. 81/2004; amended, *SG* Nos. 28, 88, 94, 103 and 105/2005, Nos. 18, 30, 33, 37, 63, 95, 97 and 108/2006) sentence two shall be amended as follows: "Medical products shall not be auxiliary equipment, devices and installations."
§ 28. In the Excise Duties and Tax Warehouses Act (Promulgated, *SG* No. 91/2005; amended, *SG* No. 105/2005, Nos. 30, 34, 63, 81, 105 and 108/2006), in Article 22, Paragraph 3, item 2 the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act."
§ 29. In the Genetically Modified Organisms Act (Promulgated, *SG* No. 27/2005; amended, *SG* No. 88 and 99/2005, No. 30/2006) in Article 2, Paragraph 2, item 3 the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act."
§ 30. In the Consumer Protection Act (Promulgated, *SG* No. 99/2005; amended, *SG* No. 30, 51, 53, 59, 105 and 108/2006) in Article 186, Paragraph 2, item 4 the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act".
§ 31. In the Health Act (Promulgated, *SG* No. 70/2004; amended, *SG* Nos. 46, 76, 85, 88, 94 and 103/2005, Nos. 18, 30, 34, 59, 71, 75, 81, 95 and 102/2006) the following amendments shall be made:
1. In Article 4, the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act."
2. In Article 21, Paragraph 3, the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act."
§ 32. In the Narcotic Substances and Precursors Control Act (Promulgated, *SG* No. 30/1999; amended, *SG* No. 63/2000, Nos. 74, 75 and 120/2002, *SG* No. 56/2003, Nos. 76, 79 and 103/2005, *SG* Nos. 30, 75, and 82/2006) the following amendments shall be made:

1. In Article 32, Paragraph 3 the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act."
2. In Article 33, Paragraph 1, item 1, the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act."
3. In Article 34, after the word "issue" the words "to a master of pharmacy" shall be deleted.
4. In Article 39, Paragraph 2 the words "Article 55, item 2 of the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "Article 197, item 2 of the Medicinal Products in Human Medicine Act."
5. Paragraph 3 in Article 44a shall be repealed.
6. In Article 44b the words "master of pharmacy" shall be deleted.
7. In § 1, item 14 of the Additional provision, the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act."

§ 33. In the Blood, Blood Donation and Blood Transfusion Act (Promulgated, *SG* No. 102/2003; amended, *SG* No. 70/2004, Nos. 30 and 65/2006) in Article 8, Paragraph 4 the words "the Human Medicinal Drugs and Pharmacies Act" shall be replaced by "the Medicinal Products in Human Medicine Act."

§ 34. In the Environmental Protection Act (Promulgated, *SG* No. 91/2002; corrected, *SG* No. 98/2002; amended, *SG* No. 86/2003, No. 70/2004, No. 74, 77, 88, 95 and 105/2005, No. 30, 65, 82, 99, 102 and 105/2006) in Article 140, the words "pharmaceutical products and medical products within the meaning of § 1, item 40 of the additional provisions to the Human Medicinal Drugs and Pharmacies Act shall be replaced by "medicinal products, within the meaning of the Medicinal Products in Human Medicine Act."

§ 35. In the Foodstuffs Act (Promulgated, *SG* No. 90/1999, amended, *SG* No. 102/2003, *SG* No. 70/2004, *SG* Nos. 87, 99 and 105/2005, *SG* Nos. 30, 31, 34, 51, 55 and 96/2006), item 4, in Article 2, Paragraph 3 shall be amended as follows:
"4. Medicinal products within the meaning of the Medicinal Products in Human Medicine Act."

§ 36. Until the entry into force of the instruments under § 19, legal instruments issued for the implementation of the repealed Human Medicinal Drugs and Pharmacies Act shall apply, insofar as they do not stand in contradiction hereto.

§ 37. This Act shall become effective on the day of its promulgation in the *State Gazette*, with the exception of § 22, which shall enter into force one year after the entry of this Act into force.
This Act was adopted by the 40th National Assembly on 30 March 2007 and the official seal thereof has been affixed hereunder.

TRANSITIONAL AND FINAL PROVISIONS to the Amendment and Suppementing Act of the Medicinal Products in Human Medicine Act
(*SG*, No. 71/2008, effective 12.08.2008)

§ 65. (1) The authorisations for use of medicinal products, issued in compliance with the repealed Drugs and Pharmacies in Human Medicine Act (Promulgated, *SG*, No. 36/1995; amended, No. 61/1996, No. 38/1998, No. 30/1999, Nos. 10, 37, 59 and 78/2000, No. 41/2001, Nos. 107 and 120/2002, Nos. 2, 56, 71 and 112/2003, Nos. 70 and 111/2004, Nos. 37, 76, 85, 87, 99 and 105/2005, Nos. 30, 31, 34, 75 and 105/2006; repealed, No. 31/2007), which fall within the scope of the repealed Regulation (EC) No. 2309/93 of the Council of 22 July 1993, which stipulates the procedure in the Community for issuing authorisations (licenses) and for exercising supervision over medicinal products used in human and veterinary medicine, and a European Agency for the Evaluation of Medicinal Products is established, but the medicinal products are not authorised for use in the other Member States under the procedure stipulated with the repealed Directive 87/22/EEC ofthw Council of 22 December 1986 concerning the harmonisation of the national measures connected with the market release of highly technological products, especially those obtained through biotechnology, or under Regulation (EC) No. 2309/93, shall be terminated.
(2) The authorisations for use of medicinal products, issued in compliance with the repealed Drugs and Pharmacies in Human Medicine Act, which fall within the scope of Regulation (EC) No. 726/2004 of the European Parliament and of the Council, but not authorised in compliance with the centralised procedure, shall be terminated.
§ 66. (1) Masters of pharmacy and assistant pharmacists who have obtained authorisation to open a pharmacy as sole traders, the treatment establishments, as well as the municipalities that had obtained

authorisation to open a pharmacy in compliance with the repealed Drugs and Pharmacies in Human Medicine Act, shall conduct their activities on the basis of the authorisations issued to them.
(2) The applications for the issuance of authorisation for retail trade in medicinal products, filed prior to the entry into force of this Act, shall be considered in compliance with its provisions.
(3) Outside the cases under Paragraph 1, the persons who had obtained authorisation to open a pharmacy prior to the entry into force of this Act, shall bring their activities in line with its requirements within one year of its entry into force.
(4) The persons under Paragraph 3 shall file an application for re-registration with the Ministry of Health, together with:
1. an application for the issuing of authorisation for retail trade in medicinal products by the persons under Article 222, Paragraph 1, following a model endorsed by the Minister of Healh;
2. up-to-date certificate of entry in the Commercial Register, or document for up-to-date registration of the person under Article 222, Paragraph 1;
3. a copy of the authorisation for the opening of a pharmacy, issued under the repealed Drugs and Pharmacies in Human Medicine Act;
4. notarised copy of the labour contract or of the contract for assigning the management to the head of the pharmacy – in the cases when this is required;
5. declaration from the persons under Article 222, Paragraph 1, that the conditions under which the authorisation for retail trade with medicinal products of the persons under Paragraph 2 was issued have been preserved;
6. document for paif one-off fee of BGN 100.
§ 67. The persons who had filed applications for re-registration under the repealed § 16 of the Transitional and Final Provisions, who are to conduct their activities in compliance with the requirements of this Act, shall file the following documents with the Ministry of Health within three months of its entry into force:
1. an application based on a model endorsed by the Minister of Health;
2. up-to-date certificate of entry in the Commercial Register, or a document for up-to-date registration, or a notarised transcript of a similar document under the national legislation of an EU Member State, or under the legislation of another state signatory to the Agreement on the European Economic Area, under Article 222, Paragraph 1;
3. a labour contract or a contract for management of the pharmacy concluded with a master of pharmacy or with an assistant pharmacist.
§ 68. (1) A master of pharmacy or an assistant pharmacist who has obtained authorisation to open a pharmacy in compliance with the repealed § 16 of the Transitional and Final Provisions, may transfer the authorisation issued to him to a person under Article 222, Paragraph 1.