THE CROATIAN PARLIAMENT

1522

Pursuant to Article 89 of the Constitution of the Republic of Croatia, I hereby issue the

DECISION

PROMULGATING THE MEDICINAL PRODUCTS ACT

I hereby promulgate the Medicinal Products Act, passed by the Croatian Parliament at its session on 14 June 2013.

Class: 011-01/13-01/136

Reg. No: 71-05-03/1-13-2

Zagreb, 18 June 2013

President
of the Republic
of Croatia
Ivo Josipović, m.
p.

MEDICINAL PRODUCTS ACT

I. GENERAL PROVISIONS

Article 1

(1) With a view to ensure efficacy, quality and safety of medicinal products as products of special importance for human health, this Act lays down the procedures for testing, placing on the market, manufacture, labelling, classification, distribution, pharmacovigilance, quality control, advertising, supply of the Croatian market with medicinal products and supervision of medicinal products, investigational medicinal products, active substances, and excipients.

(2) All gender-related references used in this Act and the regulations adopted on its basis shall be deemed to include both genders, whether they are used in the feminine or the masculine gender.

Article 2

(1) By virtue of this Act, the provisions of the following directives are transposed into the legal order of the Republic of Croatia:

1. Council Directive (89/105/EEC) of 21 December 1988 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems (OJ L 40, 11.2.1998),

2. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws and other regulations of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (OJ L 121, 1.5.2001),

3. Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or import of such products (OJ L 91/13, 9.4.2005),

4. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001),

5. Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 amending Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 33/30, 8.2.2003),

6. Commission Directive 2003/63/EC of 25 June 2003, amending Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 159, 27.6.2003),

7. Commission Directive 2003/94/EC of 16 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use (OJ L 262/22, 14.10.2003),

8. Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004, regarding traditional herbal medicinal products (OJ 136, 30.4.2004),

9. Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004, amending Directive 2001/83/EC on the Community code relating to medicinal products for human use (OJ L 136, 30.4.2004),

10. Directive 2008/29/EC of the European Parliament and of the Council of 11 March 2008, amending Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 81, 20.3.2008),

11. Directive 2009/53/EC of the European Parliament and of the Council of 18 June 2009, amending Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 168, 30.3.2009),

12. Commission Directive 2009/120/EC of 14 October 2009, amending Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 242, 15.9.2009),

13. Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 276, 21.10.2011),

14. Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 174, 1.7.2011),

15. Directive 2012/26/EU of the European Parliament and of the Council of 25 October 2012 amending Directive 2001/83/EC as regards pharmacovigilance (OJ L 299, 27.10.2012).

(2) This Act regulates implementation of the following regulations:

1. Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products (OJ L 18, 22.1.2000),

2. Commission Regulation No 847/2000 of 27 April 2000 laying down the provisions for implementation of the criteria for designation of a medicinal product as an orphan medicinal product and definitions of the concepts „similar medicinal product“ and „clinical superiority“ (OJ L 103, 28.4.2000),

3. Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004, laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing the European Medicines Agency (OJ L 136, 30.4.2004),

4. Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use (OJ L 378, 27.12.2006),

5. Regulation (EC) No 1902/2006 of the European Parliament and of the Council of 20 December 2006 amending Regulation 1901/2006 on medicinal products for paediatric use (OJ L 378, 27.12.2006),

6. Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007, amending Directive 2001/83 of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 324, 10.12.2007)

7. Commission Regulation (EC) No 658/2007 of 14 June 2007 concerning financial penalties for infringement of certain obligations in connection with marketing authorisations granted under Regulation (EC) No 726/2004 of the European Parliament and of the Council (OJ L 155, 15.6.2007),

8. Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L334/7, 12.12.2008),

9. Commission Regulation (EU) No 712/2012 of 3 August 2012 amending Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing

authorisations for medicinal products for human use and veterinary medicinal products (OJ L 209, 4.8.2012),

10. Regulation 1027/2012 of the European Parliament and of 25 October 2012 amending Regulation amending Regulation (EC) No 726/2004 as regards pharmacovigilance (OJ L 316, 14.11.2012).

Article 3

For the purposes of this Act, the following terms shall bear the following meanings:

1. *Medicinal product* shall mean:

- any substance or combination of substances presented as having properties for curing or preventing disease in human beings, or

- any substance or combination of substances which may be used or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to make a medical diagnosis,

2. *Substance* referred to in item 1 of this Article may be of the following origins:

– of human origin, e.g. human blood and human blood products,

– of animal origin, e.g. micro-organisms, animals, parts of organs, animal secretions, toxins, extracts, blood products,

– of vegetable origin, e.g. micro-organisms, plants, parts of plants, vegetable secretions, vegetable extracts,

– of chemical origin, e.g. elements, naturally occurring chemical substances and chemical products obtained by a chemical reaction,

3. *Active substance* shall mean any substance or combination of substances used in the manufacture of a medicinal product and becoming an active ingredient of the medicinal product, intended to furnish pharmacological, immunological or metabolic activity with a view to restoring, correcting or modifying physiological functions or making a medical diagnosis,

4. *Excipient* shall mean any constituent of a medicinal product other than the active substance or packaging material,

5. *Intermediate product* shall mean any product that has undergone a partial processing and is used as raw material in the successive step of a medicinal product manufacture,

6. *Magistral formula* shall mean any medicinal product prepared in a pharmacy in accordance with a medical prescription for an individual patient, in compliance with the standard formula provided in pharmaceutical reference books or pharmacopoeia,

7. *Galenic preparation* shall mean any medicinal product prepared in a pharmacy or galenic laboratory according to the current pharmacopoeia or standard formula provided in

pharmaceutical reference books, as well as in line with Good Laboratory Practice relevant to galenic laboratories,

8. *Name of the medicinal product* shall mean the name given to a medicinal product, which may be either an invented name or a common or scientific name. The common or scientific name must be followed by a trademark or the name of the marketing authorisation holder. The invented name shall be different from and shall not be liable to confusion with the common name,

9. *Common name* shall mean the international non-proprietary name (INN) recommended by the World Health Organisation, or, if one does not exist, the usual common name,

10. *Strength of the medicinal product* shall mean the content of the active substance expressed quantitatively per dosage unit, per unit of volume or weight according to the dosage form,

11. *Immunological medicinal products* shall mean vaccines, toxins, serums and allergens, namely:

a) Vaccines, toxins and serums shall cover in particular:

- agents used to produce active immunity,

- agents used to produce passive immunity,

- agents used to diagnose the state of immunity;

b) Allergen product shall mean any medicinal product which is intended to identify or induce a specific acquired alteration in the immunological response to an allergising agent.

12. *Medicinal products derived from human blood or human plasma* shall mean medicinal products based on blood constituents including, in particular, albumin, coagulating factors and immunoglobulins of human origin which are prepared industrially, taking into account the self-sufficiency principle,

13. *Radiopharmaceutical* shall mean any medicinal product which, when ready for use, contains one or more radionuclides (radioactive isotopes), intended for a medicinal purpose,

14. *Radionuclide generator* shall mean any system incorporating a fixed parent radionuclide from which a particular radionuclide is produced for fresh preparation of a radiopharmaceutical,

15. *Radionuclide in a sealed radiation source* shall mean any radioactive substance in a tightly sealed container used for external radiation treatment,

16. *Radionuclide kit* shall mean any preparation to be reconstituted or combined with radiounuclides in the final radiopharmaceutical, usually immediately prior to its administration,

17. *Radionuclide precursor* shall mean any radionuclide produced for the radiolabelling of another substance prior to administration,

18. *Homeopathic medicinal product* shall mean any medicinal product prepared from substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the EU Member States. A homeopathic medicinal product may contain a number of principles,

19. *Herbal medicinal product* shall mean any medicinal product exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations,

20. *Traditional herbal medicinal product* shall mean any herbal medicinal product the efficacy and safety of which can be recognised on the basis of its long-term traditional use, and which fulfils the conditions laid down in this Act,

21. *Herbal substances* shall mean whole or fragmented or cut plants, plant parts, algae, lichen, fungi, in a dried or fresh form, and certain exudates that have not been subjected to a specific treatment. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author),

22. *Herbal preparations* shall mean preparations obtained by subjecting herbal substances to treatments such as fractionation, extraction, fermentation, distillation, purification, concentration, pressing. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates,

23. *Risk related to the use of medicinal product* shall mean:

– any risk to the health of a patient or public health, relating to the quality, safety or efficacy of a medicinal product,

– any risk of undesirable effects on the environment,

24. *Risk-benefit balance* shall mean an evaluation of positive therapeutic effects of the medicinal product in relation to the risks as defined in item 23 of this Article,

25. *Clinical trial* shall mean any investigation in human subjects which is intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s), and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal products with the object of ascertaining its (their) safety and/or efficacy. This includes clinical trials conducted in either one site or multiple sites, whether in one or more EU Member States,

26. *Multi-centre clinical trial* shall mean a clinical trial conducted according to a single protocol but at more than one site, and therefore by more than one investigator. The trial sites may be located in a single EU Member State, in a number of EU Member States and/or in EU Member States and third countries,

27. *Non-commercial clinical trials* shall mean clinical trials conducted by researchers without the participation of the pharmaceutical industry,

28. *Non-interventional trial of a medicinal product* shall mean any study where the medicinal products are prescribed in accordance with the terms of the marketing authorisation. The

assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice, and the prescription of the medicinal product is clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures shall be applied to patients and epidemiological methods shall be used for the analysis of collected data,

29. *Investigational medicinal product* shall mean a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already authorised for marketing but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form,

30. *Clinical/non-interventional trial sponsor* shall mean a natural or legal person who takes responsibility for the initiation, management and/or financing of a clinical/non-interventional trial,

31. *Representative of the clinical/non-interventional trial sponsor* shall mean a natural or legal person established in the European Union that is authorised by the clinical/non-interventional trial sponsor seated out of the European Union,

32. *Investigator* shall mean a physician or a person with qualifications required for clinical trials i.e. the scientific background and the experience in patient care. The investigator shall be responsible for the conduct of a clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the leader responsible for the team and may be called the principal investigator,

33. *Trial site* shall mean a health-care establishment where a clinical trial is conducted,

34. *Subject* shall mean an individual who participates in a clinical trial as either a recipient of the investigational medicinal product or a control,

35. *Investigator's brochure* shall mean a compilation of the clinical and non-clinical data on the investigational medicinal product which are relevant for the clinical trial,

36. *Protocol of a clinical trial* shall mean a document that describes the objectives, design, methodology, statistical considerations and organisation of a trial. The term protocol refers to the protocol, successive versions of the protocol and protocol amendments,

37. *Informed consent* shall mean a written, signed and dated document of a trial subject given in writing, which proves the subject's free will to participate in a clinical trial, after being duly informed of its nature, significance, implications and risks, which is appropriately documented. Where a subject is not capable of giving such consent or is a minor, his legal representative or a guardian may sign an informed consent. If the subject is illiterate or unable to write, his oral consent shall be given in the presence of at least one witness, provided that he is not a member of the trial team,

38. *Good laboratory practice* shall mean a quality system governing organisational processes and conditions for planning, conducting, monitoring, archiving, recording and reporting on pre-clinical tests which are safe for human health and the environment,

39. *Good clinical practice* shall mean a set of internationally recognised ethical and scientific requirements which have to be observed in designing, conducting, recording and reporting on clinical trials,

40. *The Central Ethics Committee* shall mean an independent body consisting of healthcare professionals and non-medical members, whose responsibility is to protect the rights, safety and well-being of clinical trial subjects and to provide assurance of that protection by, among other things, expressing an opinion on the trial protocol, the suitability of investigators, the legal person on whose premises the trial is conducted, the equipment, and on the methods and documents to be used to inform trial subjects and obtain their informed consents. The minister in charge of health (hereinafter: "the Minister") shall appoint the Central Ethics Committee,

41. *Inspection of clinical trials* shall mean the act by a competent authority of conducting supervision of clinical trials, review of documents, facilities, records, quality assurance system, and any other resources related to clinical trials and that may be conducted at the trial site, at the sponsor's and/or contract research organisation's facilities, or at other legal person's facilities which the competent authority sees fit to inspect,

42. *Immediate packaging* shall mean a container or other form of packaging immediately in contact with the medicinal product,

43. *Outer packaging* shall mean the packaging into which is placed the immediate packaging,

44. *Summary of Product Characteristics* shall mean a summary of expert information on a medicinal product which has been approved through the marketing authorisation procedure and which is intended for healthcare professionals,

45. *Labelling of medicinal products* shall mean information provided on the immediate or outer packaging,

46. *Package leaflet* shall mean a leaflet containing information for the user which accompanies the medicinal product,

47. *Biological medicinal product* shall mean a product, the active substance of which is a biological substance. A biological substance is a substance that is produced by or extracted from a biological source and that needs for its characterisation and the determination of its quality a combination of physicochemical-biological testing, together with the production process and its control. Biological medicinal products shall include immunological medicinal products, medicinal products derived from human blood and human plasma, medicinal products produced by biotechnological methods and advanced therapy medicinal products,

48. *Advanced-therapy medicinal products* shall mean medicinal products for human use that are based on gene therapy, somatic-cell therapy or tissue engineering, as stipulated by Regulation (EC) No 1394/2007,

49. *Falsified medicinal product* any medicinal product which is deliberately and fraudulently mislabelled with respect to:

a) its identity, including its packaging and labelling, its name or its composition as regards any of the ingredients including excipients and the strength of those ingredients;

b) its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorisation holder, or

c) its history, including the records and documents relating to the distribution channels used.

This definition shall not apply to unintentional quality defects and to infringements of intellectual property rights,

50. *Natural person* shall mean an individual that independently and continuously engages in a business activity in accordance with a special regulation, or a person established in the European Union, who independently conducts an activity in compliance with regulations of the EU Member State concerned,

51. *Marketing authorisation holder* shall mean any natural or legal person established in the European Union that is in possession of a marketing authorisation issued by the Agency for Medicinal Products and Medical Devices or the European Commission and that is responsible for placing medicinal products on the market,

52. *Representative of the marketing authorisation holder* shall mean a natural or a legal person appointed by the marketing authorisation holder as her/his representative in the Republic of Croatia,

53. *Manufacturing authorisation* shall mean the decision issued by the competent authority confirming that the manufacturer meets the conditions imposed on facility/ies for the production of a medicinal product and/or an investigational medicinal product with respect to premises, equipment and staff, and implements the principles and guidelines of Good Manufacturing Practice,

54. *Manufacturer of a medicinal product* shall mean a natural or legal person holding the manufacturing authorisation issued by the competent authority for the production of a medicinal product and/or an investigational medicinal product,

55. *Good Manufacturing Practice* shall mean the part of the quality assurance system which ensures that medicinal products are consistently and permanently produced and controlled in accordance with the relevant quality standards and in line with their intended purpose,

56. *Qualified person for the release of a medicinal product batch* shall mean a person who meets the conditions laid down in Article 49 of Directive 2001/83/EC,

57. *Pharmacovigilance* shall mean the system consisting of activities related to identification, evaluation, understanding, prevention and response in the event of adverse reactions to medicinal products and which takes in account current scientific knowledge relating to harmful effects of the medicinal products use,

58. *Person of the marketing authorisation holder qualified for pharmacovigilance in the Republic of Croatia* shall mean a doctor of medical science specialised in clinical pharmacology, or a doctor of medical science, or a doctor of dental medicine, or a graduate pharmacist, or a master of medical biochemistry, or a doctor of veterinary medicine with two years of experience in pharmacovigilance or two years of experience in his/her profession with appropriately documented training in pharmacovigilance,

59. *Adverse reaction* shall mean any response to a medicinal product which is noxious and unintended,

60. Adverse reaction in clinical trials shall mean any noxious and unintended response to a medicinal product regardless of administered dose,

61. *Unexpected adverse reaction* shall mean an adverse reaction, the nature, severity or outcome of which is not consistent with the summary of product characteristics or the investigator's brochure for medicinal products in clinical trials,

62. *Adverse event* shall mean any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease coinciding with the administration of a medicinal product, but not necessarily in any causal relation to it,

63. *Serious adverse reaction/event* shall mean any adverse event or adverse reaction that is fatal, life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or serious disability or incapacity, including a congenital anomaly/birth defect and other medically significant conditions,

64. *Periodic safety update report (hereinafter: PSUR)* shall mean the report on safety of a medicinal product which provides a comprehensive and critical analysis of the risk-benefit balance of the medicinal product taking into consideration all available information. The marketing authorisation holder submits the report at predefined points in time after having obtained the marketing authorisation,

65. *Abuse of medicinal products* shall mean any persistent or sporadic, intentional excessive use of medicinal products which is accompanied by harmful physical or psychological effects,

66. *Risk management system* shall mean a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to a medicinal product, including the assessment of the effectiveness of those activities and interventions,

67. *Risk management plan (hereinafter: RMP)* shall mean a detailed description of the risk management system,

68. *Pharmacovigilance system* shall mean a system used by the marketing authorisation holder and by the Agency for Medicinal Products and Medical Devices to fulfil the tasks and responsibilities laid down by provisions of the Pharmacovigilance Act and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance,

69. *Pharmacovigilance system master file (hereinafter: PSMF)* shall mean a detailed description of the pharamacovigilance system used by the marketing authorisation holder with respect to one or more authorised medicinal products,

70. *Post-authorisation study (hereinafter PAS)* shall mean any study conducted in accordance with the terms of the summary of product characteristics or other terms laid down in the frames of marketing authorisation, or conducted during normal use of a medicinal product. It may be a clinical study, a non-interventional study or a post-authorisation safety study,

71. *Post-authorisation safety study (hereinafter: PASS*) shall mean any study relating to an authorised medicinal product conducted with the view to identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures,

72. *Compassionate use of medicinal products* shall mean a procedure for making an unauthorised medicinal product available to patients suffering from chronic, serious, or a life-threatening disease who cannot be treated satisfactorily by an authorised medicinal product, and are not eligible for clinical trials,

73. *Spontaneous report* shall mean any unsolicited communication to a competent authority, marketing authorisation holder or other establishment that describes an adverse reaction/event in a patient to whom one or more medicinal products have been administered and which does not derive from a study or any other organised data collection scheme,

74. *Pharmacovigilance Risk Assessment Committee (Hereinafter:PRAC)* shall mean a committee whose members include representatives of EU Member States and other appointed experts and which is responsible for making binding decisions, giving recommendations and advice regarding all aspects of risk management in line with Regulation (EU) No. 1235/2010 and Directive 2010/84/EZ,

75. *EudraVigilance* shall mean a central computer database of adverse reactions to medicinal products in the European Union,

76. *European Union reference dates list (hereinafter: EURD list)* shall mean the list of active substances and combinations of active substances for which Periodic Safety Update Reports (PSURs) shall be submitted in accordance with the EU reference dates and frequencies determined by the Committee for Medicinal Products for Human Use (CHMP) and the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh) following consultation with the Pharmacovigilance and Risk Assessment Committee (PRAC),

77. *Wholesale distribution of medicinal products* shall mean activities consisting of purchasing, receiving, storing, selling, supplying (apart from supplying medicinal products to end users), and entry and exit and/or import and export of medicinal products,

78. *Wholesaler* shall mean a natural or legal person established in the European Union holding the authorisation for wholesale distribution of medicinal products,

79. *Importer* shall mean a natural or legal person, established in the European Union engaging in import of medicinal products and holding the manufacturing authorisation for parts of production he/she engages in,

80. *Retail sale* shall mean ordering, holding and dispensing medicinal products on prescription or over-the-counter, as well as preparing and dispensing magistral and galenical preparations,

81. *Dispensing of medicinal products* shall mean the sale of a medicinal product to end users through retail outlets,

82. *Prescription of medicinal products* shall mean any medicinal prescription issued by a professional person qualified to do so,

83. *Brokering of medicinal products* shall mean all activities in relation to the sale or purchase of medicinal products, except for wholesale distribution, that do not include physical handling and that consist of negotiating independently and on behalf of another legal or natural person.

84. *Broker* shall mean a natural or legal person established in the European Union who holds an authorisation for the brokering of medicinal products,

85. *Public service obligation* shall mean obligation placed on wholesalers and marketing authorisation holders to guarantee timely, continued and appropriate delivery of medicinal products to meet the requirements of a specific geographical area,

86. *Good distribution practice* in *wholesale* shall mean the part of the quality assurance system which covers the storage and transport of medicinal products and ensures the compliance of the organisation, implementation and storage supervision with prescribed conditions, as well as transportation of medicinal products to the wholesale users,

87. *Responsible person for wholesale distribution of a medicinal product* shall mean a graduate pharmacist or a person, who meets the requirements laid down in Article 49 of Directive 2001/83/EC, and has at least two years of relevant work experience,

88. *Entry of medicinal products* shall mean wholesale distribution of medicinal products from an EU Member State into the Republic of Croatia,

89. *Exit of medicinal products* shall mean wholesale distribution of medicinal products from the Republic of Croatia into EU Member States,

90. *Third countries* shall mean the states other than the Member States of the European Union and the European Economic Area,

91. *Import of medicinal products* shall mean the wholesale distribution of medicinal products imported from the third countries to the Republic of Croatia,

92. *Export of medicinal products* shall mean wholesale distribution of medicinal products exported from the Republic of Croatia into the third countries,

93. *Parallel import* shall mean the entry into the Republic of Croatia of a medicinal product which was authorised for marketing in the exporting country and is substantially similar to the medicinal product with the marketing authorisation in the Republic of Croatia obtained according to the national procedure, the mutual recognition procedure or decentralised procedure, and which was entered from one EU Member State to another based on an authorisation for parallel importation issued by a body competent for medicinal products, provided that the parallel import was carried out by a wholesaler who has no business relations with the marketing authorisation holder,

94. *Parallel wholesale distribution of a medicinal product* shall mean entry of a medicinal product for which marketing authorisation was obtained according to the centralised procedure, from one EU Member State to another, if carried out by a wholesaler who has no business relations with the marketing authorisation holder,

95. *Specialised retail sale outlet for medicinal products* shall mean an outlet selling over-the-counter medicinal products pursuant to this Act and the ordinances issued pursuant to this Act,

96. *Croatian pharamcopoeia* shall mean a compilation of specialised texts and methods covering quality assessment, requirements for preparation, and procedures for quality control of medicinal products and medical devices. The Croatian pharmacopoeia is appropriately referenced to and harmonised with the European Pharmacopoeia,

97. *Agency for Medicinal Products and Medical Devices* shall mean a legal person with public authorities established pursuant to the Act on Medicinal Products and Medical Devices (Official Gazette 121/03), hereinafter referred to as the Agency, the scope of which in the area of medicinal products and medical devices is defined by this Act,

98. *Centralised procedure for marketing authorisation (hereinafter: CP)* shall mean the procedure for granting authorisations for marketing of medicinal products in the European Union, as provided for in Regulation (EC) No 726/2004/EC,

99. Dec*entralised procedure for marketing authorisations* (hereinafter: DCP) shall mean the marketing authorisations procedure initiated simultaneously in the reference EU Member State and in other EU Member States concerned. It is mandatory for medicinal products which are not subject to the CP pursuant to Regulation (EC) 726/2004 or MRP which have not yet obtained the authorisation for marketing in the European Union, and which will be marketed in more than one EU Member State, as stipulated in Directive 2001/83/EC,

100. *Mutual recognition procedure (hereinafter MRP)* shall mean the procedure simultaneously commenced by the reference EU Member State and the EU Member States concerned after the marketing authorisation for the relevant medicinal product was obtained in the reference EU Member State. The procedure shall be mandatory for those medicinal products which are not subject to the centralised procedure pursuant to Regulation (EC) No 726/2004 or to the DCP, but which will be marketed in more than one EU Member state, as stipulated by Directive 2001/83/EC,

101. *Reference Member State* shall mean the state which in the frames of the MRP or DCP compiles reports on the medicinal product dossiers, based on which the EU Member States concerned decide on acceptability of risk-benefit balance, i.e. about the assessment of the medicinal product quality, safety and efficacy, pursuant to the provisions of Directive 2001/83/EC,

102. *Concerned Member State in the mutual recognition procedure and decentralised procedure* shall mean the EU Member State which decides, in the course of the mutual recognition procedure or decentralised procedure, about the acceptability of the risk-benefit balance, i.e. assesses the quality, safety and efficacy of a medicinal product based on the product dossier report compiled by the reference EU Member State, in accordance with provisions of Directive 2001/83/EC,

103. *Coordination Group for Mutual Recognition and Decentralised Procedure, Human Medicinal Products (hereinafter CMD(h)* shall mean the group for the examination of any question relating to marketing authorisation of a medicinal product in two or more EU Member States in accordance with the mutual recognition procedure or the decentralised procedure. The Group acts on behalf of the bodies of the EU Member States responsible for medicinal products and it is seated at the European Agency for Medicinal Products,

104. *Committee for Medicinal Products for Human Use*, (hereinafter CHMP) shall mean the committee at the European Medicines Agency that is responsible for preparing opinions on

questions concerning medicines for human use in accordance with Regulation (EC) No. 726/2004**.** The members of the Committee are representatives of the EU Member States and nominated qualified experts,

105. *National procedure for granting marketing authorisations in the Republic of Croatia* shall mean the procedure for granting marketing authorisations to medicinal products which will be marketed only in the Republic of Croatia and for which the centralised procedure is not mandatory,

106. *European Medicines Agency* (hereinafter: EMA) shall mean the agency established pursuant to Regulation (EC) No. 726/2004,

107. *Quality control of medicinal products* shall mean the procedure to ensure the compliance of quality of a medicinal product with the quality requirements. The procedure involves laboratory tests, packaging and labelling checks, and examination of documents of medicinal products' samples,

108. *Official Control Authority Batch Release Certificate (hereinafter OCABR)* shall mean a certificate verifying that a batch of an immunological medicinal product or product from human blood or plasma has been tested in an official laboratory in accordance with OCABR guidelines,

109. *Repeat use procedure (hereinafter RUP)* shall mean a marketing authorisation procedure conducted for the same medicinal product for which the initial mutual recognition procedure or decentralised procedure has been completed, and which the marketing authorisation holder can subsequently use to enable recognition of the initial authorisation by the EU Member States that were not included in or that withdrew from the initial procedure,

110. *Simplified repeat use procedure* shall mean that for medicinal products authorised for marketing in the Republic of Croatia, the procedure referred to in item 109 of this Article has been simplified in accordance with *nCadreac agreement*.

II MEDICINAL PRODUCTS

Article 4

(1) Provisions of this Act shall apply to medicinal products for human use intended to be placed on the market and either prepared industrially or manufactured by a method involving an industrial process.

(2) In cases of doubt, where, taking into account all its characteristics, a product may fall within the definition of a 'medicinal product' as well as within the definition of a product covered by other legislation, the provisions of this Act shall apply.

Article 5

The provisions of this Act shall not apply to the following:

- magistral preparations,

- galenic products, with the exclusion of the quality control provisions,

- medicinal products intended for research and development, with the exclusion of medicinal products in clinical trials,

- intermediate products intended for further processing by an authorised manufacturer,

- whole blood, plasma or blood cells of human origin, except for plasma which is prepared by a method involving an industrial process,

- radionuclides in a sealed radiation source;

- advanced-therapy medicinal products which are prepared exclusively according to specific requirements and used in hospitals under professional responsibility of a physician, based on medical prescription for an individual patient in the Republic of Croatia.

Article 6

(1) Interchangeable medicinal products shall be the products which the Agency decides to be suitable for interchanging and places on the list of interchangeable medicinal products published on its website.

(2) When entering the products referred to in paragraph 1 of this Article on the list of interchangeable medicinal products, the Agency shall take into account the fact that the probability of clinically significant differences in the efficiency and safety of such medicinal products is either negligible or acceptably low.

(3) The decision on interchangeability of medicinal products shall be based on:

- identification of common or comparable characteristics of medicinal products or groups of medicinal products pursuant to this Act or ordinances issued pursuant to this Act,

- product characteristics approved in the marketing authorisation procedure,

- latest knowledge and discoveries in the field of biochemical science and profession,

- data on pharmacovigilance.

(4) The criteria for establishing interchangeability of medicinal products shall be prescribed in an ordinance laid down by the Minister.

Article 7

(1) The testing, manufacture, distribution, brokering and quality control of medicinal products shall be carried out by natural and legal persons who meet conditions for engaging in those activities.

(2) The Minister shall issue an ordinance laying down conditions for engaging in activities referred to in paragraph 1 of this Article.

1. TESTING OF MEDICINAL PRODUCTS

Article 8

(1) The quality, safety and efficacy of each medicinal product shall be tested before its placing on the market.

(2) The testing of medicinal products shall include pharmaceutical and pre-clinical tests and clinical trials.

(3) Tests and trials referred to in paragraph 2 of this Article shall be carried out in accordance with ordinances issued by the Minister.

Article 9

(1) Medicinal products shall be tested on the premises of legal persons who fulfil the conditions laid down in the ordinance referred to in Article 7 of this Act.

(2) Clinical trials shall be conducted only by natural or legal persons correspondingly authorised by the Minister.

(3) Medicinal products shall be tested on the premises of the legal persons referred to in paragraph 1 of this Article at the expense and upon request by a natural or a legal person requiring such tests or on request by the Minister or the Agency.

2. CLINICAL TRAILS OF MEDICINAL PRODUCTS

Article 10

Clinical trials of a medicinal product shall be conducted only in cases where the Central Ethics Committee and the ministry responsible for health (hereinafter the Ministry) assess that the expected benefits for an individual patient or other present or future patients outweigh the anticipated risks and burdens.

Article 11

(1) The clinical trial sponsor referred to in Article 3, item (30) of this Act (hereinafter: the clinical trial sponsor) or representative of the sponsor referred to in Article 3, item (31) shall submit the application for conducting a clinical trial.

(2) Clinical trial sponsors that are not established in the European Union shall designate authorised representatives seated in an EU Member State.

(3) A clinical trial sponsor may assign by a contract all or a part of her/his responsibilities to another natural or legal person, however this shall not relieve him from the responsibility for the relevant clinical trial.

(4) Applications for non-interventional trials shall be submitted by the marketing authorisation holders in the Republic of Croatia or the holders of the authorisations granted through the centralised procedure or the representatives of the marketing authorisation holders.

Article 12

(1) The Central Ethics Committee shall give opinions on the procedure for approval of the clinical, the non-interventional and the non-commercial trails in the Republic of Croatia.

(2) The Ministry shall grant approvals for conducting the clinical trials of medicinal products, including the non-commercial trials.

(3) The Agency shall grant approvals for conducting non-interventional trials, with the exception of the non-interventional trials referred to in Article 163 paragraph 1 of this Act.

Article 13

The Minister shall issue an ordinance laying down the method according to which the Central Ethics Committee shall submit its opinions and give approvals for the clinical, the non-interventional and the non-commercial trials of medicinal products as well as the required documents.

Article 14

(1) The Central Ethics Committee shall give written opinions on acceptability of the proposed clinical, non-interventional and non-commercial trials within the period of maximum 30 days from the receipt of a duly filed application and shall submit the same to the clinical- non-interventional- and non-commercial-trial applicant, to the Ministry and to the Agency.

(2) Within the period of 90 days of the receipt of a duly filed application, the Central Ethics Committee shall give the written opinion on acceptability of the proposed clinical trials of medicinal products intended for gene therapy, somatic-cell therapy, including also medicinal products containing genetically modified organisms.

(3) The time-limit referred to in paragraph 2 of this Article may be extended for a further period of 90 days in case of need to consult experts or commissions.

(4) The time for giving opinions on acceptability of clinical trials of xenogenic medicinal products shall not be limited.

Article 15

(1) After receiving a positive opinion of the Central Ethics Committee, an applicant for a clinical trial, including for the non-commercial clinical trial, shall submit a request to the Ministry for the authorisation of clinical trials in the Republic of Croatia.

(2) The Ministry shall grant or refuse the authorisation for clinical trial within 30 days from the receipt of a duly filed request.

(3) The time-limit referred to in paragraph 2 of this Article, may be extended by additional 30 days for clinical studies of medicinal products intended for gene therapy, somatic-cell therapy, including also medicinal products containing genetically modified organisms, and xenogenic medicinal products.

(4) Should the Ministry fail to either grant or refuse an authorisation within the time-limits referred to in paragraphs 2 and 3 of this Article, the authorisation shall be deemed granted, except when a written authorisation of the Ministry has to be obtained before commencing the clinical trials of a medicinal product intended for gene therapy, somatic-cell therapy, including also medicinal products containing genetically modified organisms, and clinical trials of xenogenic medicinal products.

(5) The Ministry shall refuse the authorisation for clinical trials of medicinal products for gene therapy if there is a risk of genome alteration in reproductive cells of trial subjects.

(6) The Ministry shall grant or refuse the authorisation for clinical trials, including non-commercial clinical trials, by passing a decision against which appeal shall not be allowed but an administrative procedure may be instituted.

(7) By way of derogation from paragraph 1 of this Article, an applicant may simultaneously submit a clinical trial request to the Central Ethics Committee and the Ministry.

(8) Applicants for a non-interventional trial shall submit their applications to the Agency.

(9) The Agency shall be obliged to either approve or refuse the authorisation, within 30 days from the day of the receipt of a duly filed application for conducting the non-interventional trial.

(10) The Agency shall grant or refuse the authorisation for conducting of non-interventional trial by passing a decision, against which appeal shall not be allowed but an administrative procedure may be instituted.

Article 16

(1) Clinical trial sponsors shall be required to inform the Central Ethics Committee and the Ministry about any significant amendments to a clinical trial.

(2) The Central Ethics Committee and the Ministry shall give their opinions about significant amendments to the clinical trials within the period of 35 days from the receipt of a duly filed request.

(3) After receiving a positive opinion of the Central Ethics Committee, a clinical trial sponsor may introduce significant amendments to a clinical trial in case the Ministry has failed to inform him about reasons for refusing the authorisation within the term referred to in paragraph 2 of this Article.

Article 17

(1) Clinical trials of medicinal products shall not be conducted without informed consent of the trial subjects.

(2) In exceptional cases, i.e. where a trial subject is unconscious, or suffering from severe mental impairment, or has no capacity to exercise her/his rights, or is a minor, the informed consent shall be given by his legal representative or the guardian, after he had been made aware of the risks and the objectives of the trial.

(3) Persons referred to in paragraphs 1 and 2 of this Article may, at any time, withdraw their informed consent for the participation in the clinical trial.

(4) Clinical trials shall not be conducted if potential risks of use of a medicinal product outweigh medical justification of the trial.

(5) Prisoners or persons who might be coerced into giving consent to participate in a clinical trial shall not be trial subjects.

Article 18

(1) The principles of medical ethics and compulsory protection of privacy and information about subjects shall be observed in conducting clinical trials, as provided for in the ordinance on clinical trials of medicinal products and the ordinance on good clinical practice issued by the Minister.

(2) Clinical trials of medicinal products shall be conducted only on the premises of the legal person referred to in Article 9 of this Act, with whom the sponsor or his authorised representative established in the European Union has signed the clinical trial agreement.

(3) Total costs of the clinical trial and expenses of the applicant, including expenses of medical and other services incurred by the legal person referred to in Article 9 of this Act, as well as compensations to investigators and subjects, shall be defined by the agreement referred to in paragraph 2 of this Article.

(4) The clinical trial applicant shall pay compensations to investigators and trial subjects referred to in paragraph 3 of this Article to the legal person with whom he has signed the clinical trial agreement.

(5) Before the beginning of a clinical trial, clinical trial sponsors or their authorised representatives established in the European Union must be insured against liability for injury, death, or treating of trial subjects related to the clinical trial.

Article 19

(1) The Ministry is under obligation to enter the following clinical trial data into the European database:

- on submitted applications for clinical trial authorisations,

- on amendments to applications referred to in subparagraph 1 of this paragraph,

- on amendments to trial protocols,

- on positive opinions given by the Central Ethics Committee,

- on completion of clinical trials, and

- on completed supervisions relating to observing of the good clinical practice.

(2) In addition to data referred to in paragraph 1 of this Article, the Ministry shall also submit other information on clinical trials in response to a reasoned request of an EU Member State, the EMA or the European Commission.

Article 20

(1) The Ministry may suspend a clinical trial or withdraw a clinical trial authorisation where on the grounds of verified facts it determines that the conditions based on which the authorisation was granted do not exist anymore, or in case of doubts regarding safety of subjects or scientific value of the clinical trial, about which the Ministry shall inform the

clinical trial sponsor or her/his representative, the Central Ethics Committee, the EMA or the European Commission.

(2) Before making the decision referred to in paragraph 1 of this Article, the Ministry shall require a written declaration/explanation of the sponsor, or his representative and/or the investigator.

(3) The declaration/explanation referred to in paragraph 2 of this Article shall be provided within seven days from the date of receipt of the Ministry's request, except in case of an immediate and significant risk.

Article 21

In the process of development and manufacture of an investigational medicinal product, while drafting the documentation relating to clinical trials, and in the course of clinical trials, the clinical trial sponsors and investigators shall comply with the provisions of this Act and observe the ordinances issued pursuant to this Act as well as the principles and standards laid down in relevant guidelines of the European Commission or the EMA.

3. PLACING MEDICINAL PRODUCTS ON THE MARKET

Article 22

(1) The Agency or the European Commission shall grant marketing authorisations for medicinal products in the Republic of Croatia.

(2) For the purpose of placing a medicinal product on the market, its quality, safety and efficacy shall be determined.

(3) The Agency shall grant marketing authorisations for medicinal products through the national procedure, the mutual recognition procedure and the decentralised procedure by means of the decision which shall mark the completion of the authorisation procedure carried out in accordance with this Act and ordinances issued persuant to this Act.

(4) The Republic of Croatia can be either the reference state or the concerned state in the mutual recognition procedure and decentralised procedure.

(5) The European Commission shall grant marketing authorisations based on the centralised procedure in accordance with the provisions of the Regulation (EC) No 726/2004.

(6) The marketing authorisation shall also be granted for radionuclide generators, radionuclide kits, radiopharmaceuticals, radionuclide precursors and industrially produced radiopharmaceuticals.

(7) When a medicinal product has been granted an initial authorisation for marketing in the European Union, any additional strengths, pharmaceutical forms, administration routes, types and sizes of packaging, as well as any variations and extensions shall also be granted an authorisation or shall be included in the initial marketing authorisation.

(8) All authorisations referred to in paragraph 7 of this Article shall be considered as belonging to the same global marketing authorisation.

Article 23

A marketing authorisation shall not be required for a radiopharmaceutical prepared at the time of use from authorised radionuclide generators, kits or radionuclide precursors by a person or by an establishment authorised to use such medicinal products in accordance with the manufacturer's instructions, and used exclusively in an approved health care establishment in accordance with special regulations.

Article 24

(1) The Agency may use professional services of institutions engaging in science and of certain experts in the field of medicinal products for some of the tasks involved in the marketing authorisation procedure.

(2) The persons referred to in paragraph 1 of this Article shall keep confidential all data that come to their knowledge while performing the entrusted tasks.

(3) , Employees of the Agency and experts referred to in paragraph 1 of this Article, responsible for reviewing the medicinal product dossiers within the marketing authorisation procedure, pharmaceutical inspectors and Agency inspectors performing their supervisory tasks in accordance with the provisions of this Act, shall act impartially and shall not be in a conflict of interest.

(4) It shall be deemed that the persons referred to in paragraph 3 of this Article are in a conflict of interest if:

- their personal interests affect their impartiality while performing their tasks within the marketing authorisation procedure, or

- it can be deemed with good reason that their personal interests affect their impartiality while performing their tasks within the marketing authorisation procedure, or

- their personal interests may affect their impartiality while performing their tasks within the marketing authorisation procedure.

(5) Once a year, the persons referred to in paragraph 3 of this Article shall submit their declarations on absence of the conflict of interest to the Committee for determining the existence of the conflict of interest.

(6) The Committee referred to in paragraph 5 of this Article shall consist of a president and four Committee members determining whether conflict-of-interest exists, who are appointed by the Minister for a four-year period.

(7) The Committee referred to in paragraph 5 of this Article shall adopt its rules of procedure.

Article 25

(1) Before initiating the marketing authorisation procedure, on the applicant’s request, the Agency may offer its advice on drawing up the application and the medicinal product dossier as well as expert advice as regards the quality, safety and efficacy of the medicinal product concerned.

(2) The Agency shall define the costs of the advice referred to in paragraph 1 herein in agreement with the Minister and shall be covered by the applicant.

Article 26

(1) An application for the marketing authorisation may be submitted by a natural or a legal person established in the European Union (hereinafter: the applicant).

(2) In order to obtain an authorisation to place a medicinal product on the market of the Republic of Croatia, the applicant shall submit an application to the Agency.

(3) ,The application referred to in paragraph 2 of this Article shall be accompanied by the medicinal product dossier in accordance with the ordinance referred to in paragraph 7 of this Article including the following particulars and documents:

a) name and permanent address of the applicant and, where applicable, of the manufacturer,

b) name of the medicinal product,

c) qualitative and quantitative particulars of all the constituents of the medicinal product, including the reference to its international non-proprietary name or, if one does not exist, the usual common name,

d) evaluation of the potential environmental risks posed by the medicinal product. The impact shall be assessed, and on a case-by-case basis, specific arrangements to limit the risks shall be envisaged,

e) description of the manufacturing method,

f) therapeutic indications, contra-indications and adverse reactions,

g) posology, pharmaceutical form, method and route of administration, and expected shelf life,

h) reasons for any precautionary and safety measures to be taken for the storage of the medicinal product, its administration to patients and for waste management, together with an indication of all potential risks presented by the medicinal product for the environment,

i) description of the control methods employed by the manufacturer,

j) where applicable, a written confirmation that the manufacturer of the medicinal product has verified compliance of the manufacturer of the active substance with principles and guidelines of good manufacturing practice by conducting audits. The written confirmation shall contain a reference to the date of the audit and a declaration that the outcome of the audit confirms that the manufacture complies with the principles and guidelines of good manufacturing practice,

k) results of:

– pharmaceutical (physico-chemical, biological and/or microbiological) tests;

– pre-clinical (toxicological and pharmacological) tests,

– clinical trials,

l) a summary of the applicant's pharmacovigilance system which shall include the following elements:

- proof that the applicant has at his disposal a qualified person responsible for pharmacovigilance in the EU,

- the EU Member State in which the qualified person responsible for pharmacovigilance in the EU resides and carries out her/his tasks,

- the contact details of the person qualified for pharmacovigilance in the EU;

- a statement signed by the applicant to the effect that the applicant has the necessary means to fulfil the tasks and responsibilities stipulated in the provisions of this Act relating to pharmacovigilance,

- a reference to the location where the pharmacovigilance system master file for the medicinal product (PSMF) is kept,

m) The risk management plan (RMP) describing the risk management system which the applicant will introduce for the medicinal product concerned, together with the summary thereof,

n) a statement to the effect that clinical trials carried out outside the European Union comply with the ethical requirements laid down in Directive 2001/20/EC,

o) a summary of product characteristics, a mock-up of the outer and of the immediate packaging of the medicinal product, together with a package leaflet,

p) a document showing that the manufacturer is authorised in his own country to produce medicinal products (manufacturing authorisation),

r) copies of the following

- any authorisation, obtained in another EU Member State or in a third country to place the medicinal product on the market, a summary of the safety data including the safety data contained in the periodic safety update reports, and, where available, suspected adverse reactions reports, together with the list of those EU Member States in which an application for authorisation is being examined;

- the summary of product characteristics proposed by the applicant in the authorisation procedure currently underway in the EU Member States or the one(s) last approved by competent authorities of other EU Member States; the package leaflet proposed in the authorisation procedure currently underway in the EU Member States, or the mock-ups of last approved one(s) by competent authorities of other EU Member States,

- details of any decision to refuse authorisation, whether in any EU Member State or a third country, and the reasons for such a decision,

s) a copy of any designation of the medicinal product as an orphan medicinal product, accompanied by a copy of the EMA's opinion.

(4) The documents and particulars concerning the results of the pharmaceutical and pre-clinical tests and the clinical trials referred in paragraph 3, item (k) of this Article shall be accompanied by detailed summaries provided by qualified persons.

(5) Besides information and documents referred to in paragraph 3 of this Article, the applicant shall also submit to the Agency the evidence that the applicant has at his disposal a qualified person responsible for pharmacovigilance with permanent residence in the Republic of Croatia and contact details of such person.

(6) The application referred to in paragraph 2 of this Article and the documents received by the Agency shall be classified according to data confidentiality in accordance with the data secrecy regulation and the corresponding by-law of the Agency.

(7) The Minister shall issue an ordinance laying down the method of granting marketing authorisations for medicinal products as well as the contents of the documents referred to in paragraphs 3, 4 and 5 of this Article.

Article 27

At the Agency's request, the applicant shall submit samples of the medicinal product and the reference standards required for quality control testing.

Article 28

In addition to the data and the documents referred to in Articles 26 and 29 of this Act, an application for authorisation to market a radionuclide generator, shall also contain the following information:

- a general description of the system together with a detailed description of the components of the system which may affect the composition or quality of the daughter radionuclide preparation,

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

Article 29

(1) Without prejudice to the regulations relating to the protection of industrial and intellectual property, the applicant referred to in Article 26, paragraph 1 of this Act shall not be required to provide the results of pre-clinical tests and of clinical trials, referred to in Article 26, paragraph 3, item (k) of this Act, if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised in an EU Member State or based on the centralised marketing authorisation procedure before not less than eight years.

(2) The marketing authorisation applicant shall not place on the market the generic medicinal product referred to in paragraph 1 of this Article until 10 years have elapsed from the initial authorisation of the reference product.

(3) The 10-year period referred to in paragraph 2 of this Article may be extended to a maximum of 11 years if, during the first eight years of the ten-year period the marketing authorisation holder of the reference medicinal product obtains an authorisation for one or more new therapeutic indications which, during the scientific evaluation prior to their

authorisation, are held by a scientific evaluation to bring a significant clinical benefit in comparison with existing therapies.

(4) The reference medicinal product referred to in paragraph 1 of this Article shall mean the one which is or has been authorised in an EU Member State in accordance with Directive 2001/83/EC or provisions of Regulation (EC) No 726/2004, based on fully documented quality, efficacy and safety of the medicinal product.

(5) The generic medicinal product referred to in paragraph 1 of this Article shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

(6) The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy. In such cases, additional information providing proof of the safety and/or efficacy of various salts, esters or derivatives of an authorised active substance must be supplied by the applicant.

(7) The various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form.

(8) Bioavailability studies need not be submitted by the applicant if he can demonstrate that the generic medicinal product meets the relevant criteria for bioequivalence testing as defined in the guidelines of the European Commission and of the EMA.

(9) For the purpose of submitting applications and placing generic medicinal products on the market, the protection periods referred to in paragraphs 1, 2 and 3 of this Article shall be calculated as of the date of the initial authorisation within the global authorisation referred to in Article 22, paragraphs 7 and 8 of this Act.

(10) The protection periods referred to in paragraphs 1, 2 and 3 of this Article shall also appropriately apply to the reference medicinal products used with a view to the submission of applications in accordance with Articles 32, 33, 34 and 35 of this Act.

Article 30

(1) In cases where an application is made for a new indication for a well-established active substance, a period of one year protection (data exclusivity) shall be granted to the applicant only for that new indication, provided that significant pre-clinical and clinical studies were carried out to demonstrate the efficacy of the relevant active substance in relation to the new indication.

(2) The application referred to in paragraph 1 of this Article shall be submitted in the frames of the authorisation procedure referred to in Article 26 of this Act or in the frames of the procedure of authorisation of variations.

Article 31

(1) In cases where the reference medicinal product referred to in Article 29, paragraph 4 of this Act is not authorised for marketing in the Republic of Croatia, the applicant for marketing

authorisation of a generic product shall indicate the EU Member State in which the reference medicinal product is or has been authorised, as well as the date of the initial authorisation.

(2) In cases where the reference medicinal product is or has been authorised for marketing in the Republic of Croatia, on request of the competent authority of the EU Member State, the Agency shall, within a month, submit a certificate showing that the reference medicinal product either is or has been authorised for marketing in the Republic of Croatia, accompanied by the data on the general composition of the reference medicinal product and also, if required, by any other information from the medicinal product dossier.

Article 32

In cases where the medicinal product does not fall within the definition of a generic medicinal product as provided in Article 29, paragraphs 5, 6, 7 and 8 of this Act or where the bioequivalence cannot be demonstrated through bioavailability studies or in case of variations in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration with respect to the reference medicinal product, the marketing authorisation applicant referred to in Article 26, paragraph 1 of this Act shall be required to attach to the application the results of the appropriate pre-clinical tests and clinical trials in accordance with Article 26, paragraph 3, item (k) of this Act.

Article 33

(1) Where a biological medicinal product which is similar to a reference biological product does not meet the conditions in the definition of generic medicinal products, owing to differences relating to raw materials or differences in manufacturing processes of the biological medicinal product and the reference biological medicinal product, the applicant referred to in Article 26, paragraph 1 of this Act shall be required to attach the results of appropriate pre-clinical tests or clinical trials to the application for marketing authorisation.

(2) For the biological medicinal products similar to the reference medicinal products, the content of supplementary data and the scope of studies referred to in paragraph 1 of this Article are laid down in Article 26, paragraph 7 of this Act and in the guidelines of the European Commission and the EMA.

(3) The applicant referred to in paragraph 1 of this Article shall not be required to submit results of other tests from the reference medicinal product’s dossier.

Article 34

(1) Without prejudice to the regulations relating to the protection of industrial and intellectual property, the applicant referred to in Article 26, paragraph 1 of this Act shall not be required to provide the results of pre-clinical tests or clinical trials referred to in Article 26, paragraph 3,item (k) of this Act if he can demonstrate that the active substance(s) of the medicinal product(s) have been in well-established medicinal use in the European Union for at least ten years, with recognised efficacy and an acceptable level of safety in terms of the conditions set out in the ordinance referred to in Article 26, paragraph 7 of this Act.

(2) In the event referred to in paragraph 1 of this Article, the applicant shall be required to replace the test and trial results referred to in Article 26, paragraph 3, item (k) of this Act by detailed information from appropriate scientific literature.

Article 35

In the case of medicinal products containing a new combination of active substances not hitherto used for therapeutic purposes but only as individual substances in the composition of medicinal products authorised in the EU, the applicant referred to in Article 26, paragraph 1 of this Act shall be required to provide the results of new pre-clinical tests or new clinical trials relating to that combination in accordance with Article 26, paragraph 3, item (k) of this Act and requirements laid down in the ordinance referred to in Article 26, paragraph 7 of this Act, but shall not have to provide scientific references or results of pre-clinical tests or of clinical trials relating to each individual active substance.

Article 36

The marketing authorisation holder may allow another applicant to use the pharmaceutical, pre-clinical and clinical documentation of a medicinal product, based on which the authorisation was granted, with the view to examining subsequent applications relating to other medicinal products possessing the same qualitative and quantitative composition in terms of active substances and the same pharmaceutical form.

Article 37

(1) The Agency shall grant or refuse a marketing authorisation for medicinal products within a maximum of 210 days after the application has been found duly filed.

(2) Whether the application referred to in paragraph 1 of this Article has been duly filed shall be determined within a maximum of 30 days of its receipt about which the Agency shall notify the applicant. An application shall be considered duly filed if the Agency determines that all provided data, documents and files comply with the requirements laid down in this Act and the ordinances issued pursuant to this Act.

(3) Should the Agency find that the application has been filed improperly, the applicant shall be required to amend it within the time period set by the Agency by way of a decision.

(4) In the course of the authorisation procedure, the Agency may by way of a decision require supplementary data and/or documents and/or files or appropriate explanation of the applicant to be provided within certain time limit.

(5) Should in the course of the authorisation procedure the Agency pass a decision referred to in paragraphs 3 or 4 of this Article, requiring from the applicant to submit supplementary data and/or documents and/or files or an appropriate explanation, the time limit laid down in paragraph 1 of this Article shall be suspended from the date the applicant received the decision until the date of submission of the amended application. The Agency may require the applicant’s explanation in the course of the authorisation procedure.

(6) The authorisation shall be either granted or refused by way of passing a decision against which no complaint is allowed, but an administrative dispute may be initiated.

(7) Provisions of paragraphs 2, 3, 4, 5 and 6 of this Article shall appropriately apply also to the procedures for variations approval, authorisation renewal, as well as for the repeal and transfer of a marketing authorisation.

(8) The expenses incurred in the process of granting, refusing, renewing, amending, transferring and repealing of an authorisation shall be determined by the Agency, with the consent of the Minister, and shall be covered by the applicant.

(9) The expenses incurred due to the applicant's withdrawal from the procedures for granting, renewing or amending of the marketing authorisation shall be determined by the Agency, with the consent of the Minister, and shall be settled by the applicant.

Article 38

(1) The Agency shall assign authorisation numbers to medicinal products included in the marketing authorisation procedure.

(2) The authorisation numbers referred to in paragraph (1) of this Article shall remain the same, i.e. shall not be changed, throughout the procedures involving variations approval, renewal and transfer of a marketing authorisation of a medicinal product.

Article 39

During the authorisation procedure, the Agency may submit the medicinal product, its starting materials and, if need be, its intermediate products or other constituent materials, for testing by its own laboratory or in a laboratory authorised for the purpose, in order to ensure that the control methods employed by the manufacturer and described in the product dossier accompanying the application in accordance with Article 26, paragraph (3), item (i) of this Act are satisfactory.

Article 40

(1) In the course of authorisation, the Agency shall determine whether the manufacturers and the importers of medicinal products from third countries carry out the manufacture in compliance with particulars supplied pursuant to Article 26, paragraph 3, item (e) of this Act, and/or carry out quality control according to methods described in the particulars supplied in accordance with Article 26, paragraph 3, item (i) of this Act.

(2) Where manufacturers or importers referred to in paragraph 1 of this Act have certain stages of a product manufacture and/or of the quality control carried out by other legal or natural persons, the Agency shall determine whether those legal or natural persons comply with manufacturing conditions laid down in Article 26, paragraph 3, item (e) of this Act, and/or carry out quality control in accordance with the methods referred to in Article 26, paragraph 3, item (i) of this Act.

(3) If based on the submitted dossier the Agency is not able to verify that the manufacturers and importers of medicinal products comply with the conditions referred to in paragraphs 1 and 2 of this Article, it shall notify the Agency's pharmaceutical inspectors who are in charge of supervision.

(4) The inspection costs referred to in paragraph 3 of this Act shall be settled by the manufacturer or the authorisation applicant.

Article 41

(1) The Agency shall approve the summary of product characteristics, the package leaflet and the labelling of the medicinal product during the authorisation procedure and shall send the approval to the marketing authorisation holder.

(2) The Agency shall ensure that the data provided in the approved summary of product characteristics are harmonised with the data accepted during the authorisation procedure or those subsequently approved.

(3) On its website, the Agency shall regularly make publicly available the information relating to the authorised marketing authorisations, summaries of product characteristics, package leaflets, and all conditions for obtaining marketing authorisations, with pertaining time lines set in accordance with Articles 46, 47 and 48 of this Act.

Article 42

(1) During the authorisation procedure, the Agency shall draw up assessment reports on the medicinal product dossiers accompanied by comments and opinions about the results of the pharmaceutical and pre-clinical tests, the clinical trials, the risk management plan and the pharmacovigilance system.

(2) The Agency shall update the assessment report whenever new information becomes available which is important for the evaluation of the quality, safety and/or efficacy of the medicinal product concerned.

(3) The Agency shall make publicly available its assessment report on a medicinal product dossier together with the explanation of opinions provided for each indication, but shall not reveal any confidential information.

(4) The published assessment report on a medicinal product dossier shall include a summary written in terms easily comprehensible to the general public, which shall include the conditions of use of the medicinal products.

Article 43

(1) The granting of a marketing authorisation for the same medicinal product in two or more EU Member States shall be subject to the mutual recognition procedure or the decentralised procedure.

(2) Upon learning that the applied authorisation procedure for the same medicinal product is already underway in another EU Member State, the Agency shall issue a decision to suspend the procedure applied for and shall instruct the applicant to initiate the mutual recognition procedure or decentralised procedure for the authorisation of the relevant medicinal product.

(3) Where based on data referred to in Article 26, paragraph 3, item (r) of this Act the Agency learns that at the time of application in the Republic of Croatia the medicinal product has already received a marketing authorisation in another EU Member State, the Agency shall by means of a decision suspend the procedure, except if the application was submitted in accordance with the mutual recognition procedure.

(4) The applicant shall be required to submit an application for the marketing authorisation based on an identical medicinal product dossier in all concerned EU Member States in accordance with the mutual recognition procedure or the decentralised procedure.

(5) The applicant shall request one of the concerned EU Member States involved in the mutual recognition procedure or the decentralised authorisation procedure to act as a reference state and to prepare an assessment report on the medicinal product dossier and to provide the summary of product characteristics, the package leaflet and the labelling.

(6) Following the completion of the mutual recognition procedure and the decentralised procedure, the Agency shall accept the assessment report on the medicinal product dossier prepared by the reference state as well as the summary of product characteristics, the package leaflet and the labelling, except in cases laid down in Article 44 of this Act.

(7) Within the period of five days after the completion of the mutual recognition procedure or the decentralised procedure, the authorisation applicant shall submit to the Agency the corresponding translation into Croatian language of the summary of product characteristics, the package leaflet and the labelling.

(8) The Agency shall grant the marketing authorisation for the relevant medicinal product within the period of 30 days following the completion of the mutual recognition procedure or the decentralised procedure.

(9) The minister shall issue an ordinance laying down the method of granting the marketing authorisation referred to in this Article as well as the contents of the relevant dossier.

Article 44

(1) If during the mutual recognition procedure or the decentralised procedure the Agency, in the role of the competent authority of a concerned state, refuses to accept the assessment report on the medicinal product dossier, as well as the summary of product characteristics, the package leaflet and the labelling, in line with Article 43, paragraph 6 of this Act on the grounds of potential serious risk to public health, it shall give a detailed exposition of reasons for such refusal and shall accordingly notify the reference country, other concerned states and the applicant.

(2) Should, on the grounds of potential serious risk to public health, the concerned state/s in the mutual recognition procedure or the decentralised procedure for granting a marketing authorisation refuse to accept a medicinal product dossier assessment report with the summary of product characteristics, the package leaflet and the labelling, submitted by the Agency as the competent authority of the reference state, the Agency shall refer the matter to the consideration of the CMD(h).

(3) In cases referred to in paragraphs 1 and 2 of this Article, at the meeting of the CMD(h) the Agency shall use its best endeavours to reach agreement on the action to be taken.

(4) In case the agreement referred to in paragraph 3 of this Article is not reached within the period of 60 days of notifying the CMD (h), the reference state shall immediately inform the EMA thereby starting the arbitration proceedings referred to in paragraph 10 of this Article.

(5) In case the EU Member States have already adopted divergent decisions concerning the authorisation of the medicinal product or its revocation or suspension, the Agency, the competent authorities of other EU Member States, the European Commission and the marketing authorisation holder may suggest to the CHMP to initiate the arbitration proceedings referred to in Article 10.

(6) In order to promote the harmonisation of the marketing authorisations for medicinal products authorised in the European Union, the Agency shall once a year forward to the CMD(h) a list of medicinal products for which a harmonised summary of product characteristics should be drawn up.

(7) The European Commission and the Agency in cooperation with the EMA, may ask the CHMP to act in accordance with paragraph 5 of this Act as regards the list of medicinal products referred to in paragraph 6 of this Article.

(8) The Agency, the competent authorities of other EU Member States, the European Commission, the applicant or the marketing authorisation holder shall, in cases where the interests of the European Union are involved, refer the matter to the CHMP for application of arbitration proceedings referred to in paragraph 10 of this Act before any decision is reached on an application for a marketing authorisation or on the suspension or revocation or any other variations of a marketing authorisation which appear to be necessary.

(9) If arbitration proceedings are initiated relating to pharmacovigilance of an authorised medicinal product, the matter shall be referred to the Pharmacovigilance Risk Assessment Committee (PRAC).

(10) The CHMP shall conduct the arbitration proceedings and the European Commission shall issue opinions in accordance with Articles 32, 33 and 34 of Directive 2001/83/EC.

Article 45

(1) The marketing authorisation holder shall be responsible for placing the medicinal product on the market and for its marketing in accordance with this Act and the ordinances issued pursuant to this Act.

(2) If the marketing authorisation holder is not the manufacturer of the relevant medicinal product, he shall be required to have a written agreement with the manufacturer(s) of the medicinal product.

(3) For medicinal products authorised for marketing by the Agency, the marketing authorisation holder who is not established in the Republic of Croatia shall be required to designate a representative established in the Republic of Croatia.

(4) The designation of the representative referred to in paragraph 3 of this Act shall not relieve the marketing authorisation holder of his legal responsibility**.**

Article 46

(1) In the frames of the marketing authorisation, the Agency may impose the following conditions on the marketing authorisation holder:

- to take certain measures for ensuring the safe use of the medicinal product to be included in the risk management system, and/or

- to conduct post-authorisation safety studies, and/or

- to comply with obligations on the recording or reporting of suspected adverse reactions which are stricter than those referred to in pharmacovigilance provisions of this Act, and/or

- to comply with any other conditions or restrictions with regard to the safe and effective use of the medicinal product, and/or

- to ensure the existence of an adequate pharmacovigilance system, and/or

- to conduct post-authorisation efficacy studies where concerns relating to some aspects of the efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed.

(2) In the marketing authorisation referred to in paragraph 1 of this Article, the Agency shall lay down deadlines for the fulfilment of conditions listed in paragraph 1 of this Article.

(3) If the marketing authorisation holder fails to comply with a condition/the conditions from paragraph 1 of this Article, the Agency shall revoke the marketing authorisation by issuing a decision which cannot be appealed, however administrative proceedings can be instituted against it.

Article 47

(1) In exceptional circumstances and based on a written request of the applicant, the Agency may grant a conditional marketing authorisation under which the marketing authorisation holder shall assume certain obligations, in particular relating to the safety of the medicinal product, notification to the Agency of any incident relating to its use, and action to be taken.

(2) The marketing authorisation referred to in paragraph 1 of this Article may be granted only when the applicant is unable to provide comprehensive data on the efficacy and safety of the medicinal product under normal conditions of use, for objective and substantiated reasons in accordance with the ordinance referred to in Article 26, paragraph 7 of this Act.

(3) Continuation of the validity of the marketing authorisation referred to in paragraph 1 of this Article shall be linked to the annual reassessment of the conditions laid down in the marketing authorisation.

(4) If the marketing authorisation holder fails to meet the conditions laid down in this Article, the Agency shall revoke the relevant authorisation by passing a decision which cannot be appealed, however administrative proceedings can be instituted against it.

Article 48

(1) After granting a marketing authorisation for a medicinal product, in justified cases the Agency may impose the following obligations on the marketing authorisation holder:

- to conduct a post-authorisation safety study if there are concerns about risks of use of an authorised medicinal product,

- to conduct a post-authorisation efficacy testing when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly,

(2) In case where the same risks as those referred to in the first subparagraph of paragraph 1 of this Article apply to more than one medicinal product, after consulting the PRAC, the

Agency shall instruct the marketing authorisation holders to conduct mutual post-authorisation safety studies.

(3) The Agency shall duly justify and notify the marketing authorisation holder in writing about the imposition of obligations referred to in the first and the second subparagraphs of paragraph,1 of this Article, and shall include the objectives and timeframes for the submission of application and conduct of the studies.

(4) Should, within 30 days of receipt of the notification referred to in paragraph 3 of this Article, the marketing authorisation holder request the opportunity to present written observations in response to the imposition of the obligation referred to in this Article, the Agency shall require the submission of such observations within a maximum of 60 days.

(5) On the basis of the written observations submitted by the marketing authorisation holder, the Agency shall either confirm or withdraw the obligation referred to in paragraph 1, subparagraph (1) and/ or (2) of this Article.

(6) Where the Agency confirms the obligation referred to in paragraph 1, subparagraph (1) and/or (2) of this Article, it shall pass a decision based on which the marketing authorisation shall be varied to include the obligation from paragraph 1, subparagraph (1) and/or (2) of this Article as a condition of the marketing authorisation and the marketing authorisation holder shall accordingly update the risk management system.

Article 49

(1) The marketing authorisation holder shall incorporate the conditions and obligations referred to in Articles 46, 47 and 48 of this Act in his risk management system.

(2) The Agency shall notify the EMA about the marketing authorisations for medicinal products granted in accordance with Articles 46, 47 and 48 of this Act.

Article 50

(1) After obtaining a marketing authorisation for a medicinal product, the marketing authorisation holder shall be required to:

a) take account of scientific and technical progress and introduce any variations that may be required to enable the medicinal product to be manufactured and checked by means of generally accepted scientific methods,

b) forthwith provide the Agency with any new information which might entail amendments to the data, documents and files of the medicinal product provided in the frames of the marketing authorisation procedure or the arbitration proceedings in the European Union and/or the ordinance referred to in Article 26, paragraph 7 of this Act,

c) forthwith inform the Agency of any restriction or prohibition imposed by the competent authorities of other states in which the medicinal product is marketed and of any other new information which might influence the benefits and risks of the medicinal product concerned. The marketing authorisation holder shall supply the Agency with both positive and negative results of clinical and other studies in all indications and populations of subjects, whether or not included in the marketing authorisation, as well as data on the use of the medicinal product where such use is not covered by the marketing authorisation,

d) ensure that the product information is kept up to date with the current scientific knowledge, including the conclusions of public reports relating to assessment of the medicinal product dossier and recommendations of the EMA made public by means of the European medicines web-portal.

(2) In the case referred to in paragraph 1 of this Article the Agency may require that the marketing authorisation holder initiates the procedure for variation(s) approval or to amend, *ex officio*, the authorisation for placing the medicinal product on the market.

(3) In order to enable continuous assessment of the risk-benefit balance, the Agency may at any time ask the marketing authorisation holder to forward data demonstrating that the risk-benefit balance of the medicinal product remains favourable.

(4) The Agency may at any time ask the marketing authorisation holder to submit a copy of the pharmacovigilance system master file. The marketing authorisation holder shall submit the copy at the latest seven days after receipt of the request.

Article 51

(1) In cases referred to in Article 50, paragraph 1, items (a) and (b) of this Act, the marketing authorisation holder shall submit the application for the variation approval to the Agency.

(2) In cases referred to in Article 50, paragraph 1, items c) and d) of this Act, the marketing authorisation holder shall submit an application for the variation approval to the Agency where the variation entails amendments to data in the approved medicinal product dossier.

(3) To the application for the variations approval referred to in paragraphs 1 and 2 of this Act, the marketing authorisation holder shall attach the data and/or documents and/or medicinal product files, as required by the type of variation.

Article 52

(1) Amendments to the marketing authorisation referred to in Articles 50 and 51 of this Act shall be granted for the period before the expiry of the marketing authorisation whose amendment is required.

(2) Where an approved variation entails amendments to data in the decision to grant authorisation, in addition to approval of the variation the Agency shall pass the decision on amendment of the authorisation decision. Such decision which cannot be appealed, but administrative proceedings can be instituted against it.

(3) When an approved variation entails amendments to the summary of product characteristics, and/or the package leaflet and/or the labelling, alongside with the approved variation the Agency shall authorise a new amended summary of product characteristics, and/or the package leaflet and/or the labelling.

(4) The Agency shall grant or refuse a variation approval and the decision on the marketing authorisation amendment, as required by the type of variation, within a maximum 180 days from the receipt of a duly filed application.

(5) The Minister shall issue an ordinance specifying the methods for approving amendments and the contents of the documentation to be submitted for the purpose of a variation approval.

Article 53

(1) The Agency shall grant marketing authorisations for medicinal products for the period of five years.

(2) Not later than nine months before the marketing authorisation ceases to be valid, an application for its renewal may be submitted to the Agency.

(3) The Agency may renew the marketing authorisation for a further period of next five years subject to reassessment of the product's risk-benefit balance.

(4) In addition to the application for renewal of the marketing authorisation, the marketing authorisation holder shall provide the Agency with a consolidated version of the file in respect of quality, safety and efficacy, including the evaluation of data contained in suspected adverse reactions reports and in the periodic safety update reports submitted in accordance with pharmacovigilance provisions of this Act, and information on all variations introduced since the marketing authorisation was granted until the date of application for its renewal.

(5) Once renewed, the marketing authorisation shall be valid for an unlimited period, unless the Agency decides, on justified grounds relating to pharmacovigilance, including exposure of an insufficient number of patients to the medicinal product concerned, to proceed with one additional renewal in accordance with paragraphs 3 and 4 of this Article.

(6) The Minister shall issue an ordinance laying down the contents of the file referred to in paragraph 4 of this Article, submitted for the purpose of the marketing authorisation renewal.

Article 54

(1) The Agency shall revoke any marketing authorisation for a medicinal product which within three years of its granting is not followed by the actual placing on the market of the Republic of Croatia.

(2) When an authorised product previously placed on the market of the Republic of Croatia is no longer actually present on the market for a period of three consecutive years, the Agency shall revoke the authorisation for that product.

(3) By way of derogation from paragraphs 1 and 2 of this Article, the Agency shall not revoke the marketing authorisation on public health grounds, if a valid authorisation in the Republic of Croatia represents the condition for granting and/or renewal of the medicinal product authorisation in other states, or in other exceptional circumstances, which shall be duly justified in writing by the marketing authorisation holder.

Article 55

(1) The marketing authorisation holder shall forthwith notify the Agency in writing about the date of first actual market placement of the medicinal product, but not later than within 15 days taking into account the various presentations and doses authorised.

(2) Should a marketing authorisation holder decide to discontinue marketing of a medicinal product or to withdraw it from the market, either temporarily or permanently, before the expiry of its marketing authorisation or should he decide to apply for the revocation of the marketing authorisation or not to apply for the authorisation renewal, he shall notify the

Agency accordingly at least two months before the interruption in the placing on the market of the product, except in case of an urgent withdrawal procedure or other exceptional circumstances.

(3) In the case referred to in paragraph 2 of this Article, the marketing authorisation holder is required to inform the Agency about the reasons for his decision to discontinue the market supply of the medicinal product concerned.

(4) The marketing authorisation holder must notify the Agency of the cases referred to in paragraph 2 of this Article which took place in a third country, when they were based on the reasons referred to in Article 58, paragraph 1, subparagraphs 1 to 9 of this Act or of the reasons referred to in Article 62, paragraphs 1 to 6 of this Act.

(5) The marketing authorisation holder must notify the EMA of the cases referred to in paragraph 2 of this Article which took place in an EU Member State or a third country, when they were based on the reasons referred to in Article 58, paragraph 1, subparagraphs 1 to 9 of this Act or on the reasons referred to in Article 62, paragraphs 1 to 6 of this Act.

(6) Upon request by the Agency, particularly in the context of pharmacovigilance, the marketing authorisation holder shall submit the data relating to the volume of sales of the medicinal product and data relating to the volume of prescriptions.

Article 56

(1) Upon request by the marketing authorisation holder, the Agency shall issue a decision on revoking the marketing authorisation.

(2) The decision referred to in paragraph 1 of this Article cannot be appealed, however administrative proceedings can be instituted against it.

(3) The contents of the documents to be submitted for the purpose of revoking a marketing authorisation shall be provided in an ordinance issued by the Minister.

Article 57

(1) The Agency shall pass a decision based on which the marketing authorisation shall be refused if, after verification of the particulars and documents listed in Articles 26, 29, 30, 32, 33, 34, 35 and 36 of this Act and the ordinance referred to in Article 26, paragraph 7 of this Act, it is clear that:

- the risk-benefit balance is not considered to be favourable, or

- the therapeutic efficacy of the medicinal product is not sufficiently substantiated, or

- the qualitative and quantitative composition of the medicinal product is not as declared, or

- the labelling and the package leaflet do not comply with the provisions of this Act or if the data provided on the label or the package leaflet do not comply with the data provided in the summary of product characteristics, or

- the data, documents and files attached to the application do not fulfil the requirements laid down in Articles 26, 29, 30, 31, 32, 33, 34, 35 and 36 of this Act.

(2) The applicant or the holder of the marketing authorisation shall be responsible for the accuracy of the data and documents as well as the files attached to the application for marketing authorisation of a medicinal product.

Article 58

(1) The Agency shall suspend the execution of, revoke or amend a marketing authorisation in one of the following cases:

- the medicinal product is unacceptably harmful, or

- the therapeutic efficacy of the medicinal is not satisfactory, or

- the risk-benefit balance is unfavourable, or

- the qualitative and/or quantitative composition of the medicinal product are not as declared, or

- the quality and composition of the medicinal product and of the intermediate product have not been subjected to control, or

- the data provided in the authorised medicinal product files are not accurate, or

- the data were not amended in accordance with Articles 50 and 51 of this Act, or

- the conditions and obligations referred to Articles 46, 47 and 48 of this Act have not been fulfilled, or

- the medicinal product is not manufactured in accordance with the methods referred to in Article 26, paragraph 3, item (e) of this Act and quality control is not carried out in accordance with the control methods referred to in Article 26, paragraph 3, item (i) of this Act, or

- the medicinal product has not been on the market of the Republic of Croatia for three consecutive years after it has been authorised for marketing in accordance with the provisions of Article 54 of this Act, or

- the medicinal product was placed on the market contrary to the provisions of this Act, or

- the data on the marketing authorisation holder are inaccurate, or

- the package leaflet and the labelling of the medicinal product do not comply with the provisions of this Act, or

- the manufacturing authorisation does not comply with the provisions of this Act, or

- the marketing authorisation holder no longer fulfils the conditions and obligations laid down in this Act and in the ordinances issued pursuant to this Act.

(2) The therapeutic efficacy of a medicinal product referred to in paragraph 1, subparagraph (2) of this Article shall be considered unsatisfactory where its use fails to produce therapeutic effects.

(3) The decision to revoke or suspend the execution of a marketing authorisation cannot be appealed, however administrative proceedings can be instituted against it.

(4) The Agency shall regularly update the list of the decisions on revoked marketing authorisations on its website.

Article 59

Authorisation of a medicinal product shall not affect the financial and criminal liability of the manufacturer and/or of the marketing authorisation holder.

Article 60

(1) The marketing authorisation holder can apply for transfer of the authorisation to another natural or legal person that complies with the conditions laid down in the provisions of this Act.

(2) The medicinal product placed on the market based on an earlier authorisation, may remain on the market for a maximum period of 18 months following the transfer, unless the authorisation ceases to be valid before that.

(3) The marketing authorisation holder shall be responsible for the medicinal product referred to in paragraph 2 of this Article after the transfer of the authorisation.

(4) By virtue of an ordinance, the Minister shall in more detail define the method, the time limits and the contents of files to be submitted for the purpose of the marketing authorisation transfer.

Article 61

(1) For the purpose of human health protection, the Ministry or the Agency may in justified cases decide that the Agency shall, *ex officio,* grant the marketing authorisation to a medicinal product which neither has an authorisation nor was the authorisation applied for in the Republic of Croatia, but which has been authorised in another EU Member State,

(2) In the case referred to in paragraph 1 of this Article, the Agency shall ask the competent authority of the EU Member State in which the medicinal product has been authorised, to provide the report on the medicinal product dossier as well as the valid marketing authorisation.

(3) Prior to the authorisation referred to in paragraph 1 of this Article, the Agency shall notify the authorisation holder of the EU Member State about its intention to, *ex officio,* grant the authorisation in the Republic of Croatia.

(4) The Agency shall either give the authorisation referred to in paragraph 1 of this Article to the marketing authorisation holder from the EU Member State where the product is authorised or to the wholesaler that places the product on the market of the Republic of Croatia.

(5) The marketing authorisation holder referred to in paragraph 4 of this Article shall ensure that the summary of product characteristics, the package leaflet, the labelling, the advertising as well as the pharmacovigilance of the medicinal product comply with provisions of this Act.

(6) Upon request by the competent authority of the EU Member State conducting the procedure in accordance with paragraph 1 of this Article for a medicinal product authorised in the Republic of Croatia, the Agency shall provide the report on the product dossier and the valid marketing authorisation within the period of 30 days of the request.

Article 62

(1) The Agency shall suspend the market placement of the medicinal product and request its withdrawal from the market in one of the following cases:

- the medicinal product is unacceptably harmful, or

- the therapeutic effect of medicinal product is insufficient, or

- the risk-benefit balance is unfavourable, or

- the qualitative and/or quantitative composition of the medicinal product is not as declared, or

- the quality and composition of the medicinal product and intermediate product have not been subjected to control, or

- the medicinal product is not manufactured in accordance with the manufacturing authorisation, or

- the medicinal product is falsified.

(2) The Agency may suspend the marketing of a medicinal product and/or request the withdrawal of a medicinal product from the market in the cases referred to in Article 58, paragraph 1, subparagraphs 5 to 14 of this Act.

(3) The Agency may limit the suspension or withdrawal referred to in paragraph 1 of this Article to a specific batch of the medicinal product.

(4) In exceptional circumstances, during a transitional period and based on the assessment of risk-benefit balance, the Agency may allow the supply of a withdrawn medicinal product only to patients who are already being treated with the medicinal product.

(5) Where a medicinal product withdrawn from the market poses a serious direct threat to human health, the Agency shall forthwith notify the EU Member States.

(6) The suspension of marketing of medicinal products or the withdrawal of medicinal products from the market shall be initiated by the marketing authorisation holder or the holder of an authorisation for parallel imports, by the Agency *ex officio*, or on request by the pharmaceutical inspector. The marketing authorisation holder shall notify the Agency about the suspension or withdrawal of the medicinal product from the market not later than 24 hours after becoming aware of reasons for initiation of measures referred to in paragraph 1 of this Article.

(7) For a medicinal product which is on the market of the Republic of Croatia on the basis of an entry or import approval in line with Article 129 of this Act, the procedure referred to in paragraph 6 of this Article shall be initiated by the wholesaler responsible for the placement of the medicinal product on the Croatian market.

(8) By virtue of an ordinance, the Minister shall lay down in more detail the suspension of the placement and the withdrawal of medicinal products from the market as well as time limits and notification methods relating to the suspension and the withdrawal.

4. TRADITIONAL HERBAL MEDICINAL PRODUCTS

Article 63

(1) The procedure for marketing authorisation of traditional herbal medicinal products is a simplified registration procedure, i.e. the traditional-use registration.

(2) The traditional-use registration shall apply to medicinal products which fulfil the following criteria:

- they have indications exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are designed for use without the supervision of a medical practitioner,

- they are exclusively intended for administration in accordance with a specified strength and posology,

- they are intended for external or oral use or for inhalation,

- the period of traditional use of the herbal medicinal product, or a corresponding medicinal product is at least 30 years preceding the date of application, including at least 15 years within the European Union,

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

(3) A corresponding product, as referred to in paragraph 2, subparagraph (4) of this Article, is characterised by having the same active ingredients, irrespective of the excipients used, the same or similar intended purpose, equivalent strength and posology and the same or similar route of administration as the traditional herbal medicinal product applied for.

(4) Traditional herbal medicinal products can also contain vitamins and minerals for the safety of which there is well-documented evidence. The action of the vitamins or minerals is ancillary to that of the herbal active ingredients regarding the specified claimed indication(s).

(5) If in the course of registration of a traditional medicinal product the Agency determines that the product satisfies the criteria for placing on the market or for the registration of a homeopathic medicinal product, the provisions of this Act referring to the traditional herbal medicinal products shall not apply.

(6) The Minister shall by way of an ordinance lay down the registration, the form and the contents of documents to be submitted for obtaining the marketing authorisation, the evidence of traditional medicinal use, and the labelling and advertising rules applicable to the traditional herbal medicinal products.

(7) With the consent of the Minister, the Agency shall lay down and the applicant shall cover the costs of issue, refusal, renewal, amendment, transfer and revoking of the decision on the registration of a traditional herbal medicinal product.

Article 64

(1) The registration of a traditional herbal medicinal product shall be refused if the data and documents accompanying the application differ from those required and if one of the following reasons is established:

– the quantitative and/or qualitative composition is not as declared, or

– the indications do not comply with the conditions laid down in Article 63, paragraph 2, subparagraph (1) of this Act, or

– the traditional herbal medicinal product could be harmful under usual conditions of use, or

– the data on traditional use are insufficient, especially if pharmacological effects or efficacy are not plausible on the basis of long-standing use and experience, or

– pharmaceutical quality is not satisfactorily demonstrated.

(2) The Agency shall inform the European Commission, and any other competent authority that may so require, about the decision to refuse the registration of a traditional herbal medicinal product as well as about the reasons behind such decision.

Article 65

The provisions of this Act relating to the placement of a medicinal product on the market, production, classification, advertising, distribution, importation, quality control, pharmacovigilance, suspension of marketing and withdrawal from the market and supervision shall appropriately apply also to the traditional herbal medicinal products, except if otherwise provided for by this Act or an ensuing regulation.

5. HOMEOPATHIC MEDICINAL PRODUCTS

Article 66

(1) Placing on the market of homeopathic medicinal products shall be subject to the possession of a marketing authorisation granted by the Agency or a decision on enrolment in the register issued by the Agency pursuant to the provisions of this Act and ordinances issued pursuant to this Act.

(2) The provisions of this Act relating to homeopathic medicinal products shall apply to anthroposophic medicinal products prepared by a homeopathic method, described in the current version of pharmacopoeias being in effect in EU Member States.

Article 67

Applications for obtaining marketing authorisations for homeopathic medicinal products shall be submitted to the Agency, accompanied by the file laid down in Articles 26, 29, 30, 31, 32, 33, 34, 35 and 36 of this Act.

Article 68

(1) A simplified procedure for obtaining marketing authorisation for homeopathic medicinal products, or a register enrolment procedure for homeopathic medicinal products, shall be conducted for homeopathic medicinal products placed on the market without therapeutic indications.

(2) The enrolment in the register of homeopathic medicinal products shall be conducted for homeopathic medicinal products complying with the following requirements:

– that they are intended for oral or topical administration,

– that there is no reference to their therapeutic indications or data referring to the indication in the package leaflet or on the product label of the homeopathic medicinal product,

– that they are sufficiently diluted to guarantee safe use of the medicinal product; in particular, homeopathic medicinal products shall not contain more than one part per 10000 mother tincture, or more than 1/100th of the smallest therapeutic dose of the active substance which would be required for the medicinal product referred to in Article 3, item 1 of this Act to be dispensed on medical prescription.

(3) In the register enrolment procedure for a homeopathic medicinal product the Agency shall specify dispensing classification of the homeopathic medicinal product.

Article 69

(1) The application for enrolment in the register of a homeopathic medicinal product referred to in Article 68 of this Act may comprise batches of homeopathic medicinal products derived from the same homeopathic source or sources.

(2) The application for enrolment in the register of a homeopathic medicinal product shall be supported by the following:

– the scientific name or another pharmacopoeial name stated in a pharmacopoeia of the homeopathic source or sources, and a description of diverse administration methods, pharmaceutical forms and dilutions for which enrolment in the register is applied for,

– the file showing how homeopathic source or sources are obtained and tested and providing evidence on its/their homeopathic nature on the basis of the relevant bibliography,

– the manufacture and quality control file for every pharmaceutical form and the description of the dilution and potentisation method,

– the stability data for the homeopathic medicinal product,

– the manufacturing authorisation,

– a copy of the decision on the enrolment in the register or of the marketing authorisation of the homeopathic medicinal product in other EU Member States,

– a mock-up of outer and immediate packaging of the medicinal product for which enrolment in the register is applied for.

(3) The application for enrolment in the register of a homeopathic medicinal product need not be accompanied by evidence of its therapeutic efficacy.

(4) The Minister shall issue an ordinance laying down in greater detail the register enrolment procedure and the contents of the file for enrolment in the register of a homeopathic medicinal product.

(5) The costs for the granting, refusing, renewing, amending, transferring and revoking of the marketing authorisation or the decision on the enrolment in the register of a homeopathic medicinal product shall by determined by the Agency, subject to the approval by the Minister, and incurred by the applicant.

Article 70

In addition to a clear indication „homeopathic medicinal product“, only the following particulars shall appear on the outer and immediate packaging and, as required, the package leaflet for homeopathic medicinal products referred to in Article 68 of this Act:

- the scientific name of a homeopathic source or sources and the indication of dilution using pharmacopoeial symbols; where the homeopathic medicinal product contains two or more homeopathic sources, in addition to the scientific names of the sources, an invented name of the medicinal product may appear on the label,

- the name and address of the holder of the decision of enrolment in the register of a homeopathic medicinal product and, in necessary, the manufacturer’s name and address,

- the pharmaceutical form,

- the indication „homeopathic medicinal product without proven therapeutic indications“,

- the method of administration and, if necessary, the route of administration,

- the content of the packaging expressed in weight, volume or units of dosage of the homeopathic medicinal product,

- special storage precautions, if applicable,

- expiry date of the homeopathic medicinal product (month and year),

- a warning instructing patients to consult a physician if symptoms fail to disappear during use of the homeopathic medicinal product,

- a special warning, if necessary,

- dispensing of the homeopathic medicinal product,

- batch number,

- number of the decision on the enrolment in the register of the homeopathic medicinal product.

Article 71

(1) The provisions of this Act concerning the product label and the package leaflet shall also appropriately apply to homeopathic medicinal products.

(2) Homeopathic nature of the medicinal product shall be clearly and legibly indicated on the outer and immediate packaging of the homeopathic medicinal product.

(3) The provisions of this Act concerning advertising of medicinal products shall also appropriately apply to homeopathic medicinal products.

(4) By way of exception, when advertising homeopathic medicinal products referred to in Article 68 of this Act only the data specified in Article 70 of this Act may be used.

(5) The provisions of this Act concerning marketing, manufacture, distribution, import, quality control, suspension of marketing and withdrawal from the market and supervision of medicinal products shall also appropriately apply to homeopathic medicinal products, if not otherwise laid down by this Act.

(6) Provisions of Article 44, paragraphs 4 to 10 of this Act shall not apply to homeopathic medicinal products referred to in Article 68 of this Act.

(7) The provisions of this Act concerning pharmacovigilance shall also appropriately apply to homeopathic medicinal products with marketing authorisation.

6. MANUFACTURE

Article 72

(1) Natural and legal persons seated in the Republic of Croatia may manufacture intermediate products, medicinal products and/or investigational medicinal products only on the basis of and in accordance with a manufacturing authorisation.

(2) The manufacturing authorisation is compulsory for:

- a plant or plants where a pharmaceutical form and/or a group of medicinal products will be manufactured,

- the entire manufacturing process or certain parts of the manufacturing process,

- manufacture of medicinal products intended only for exports and/or exit.

(3) Importers of medicinal products from third countries shall have obtained a manufacturing authorisation.

Article 73

(1) Natural and legal persons referred to in Article 72, paragraph 1 of this Act shall comply at least with the following requirements:

- given the scope and complexity of manufacture of a medicinal product or a group of medicinal products, they must have the adequate number of qualified persons in the field of in pharmacy, chemistry, biology, biochemistry, biotechnology, chemical technology, medicine, dental medicine, veterinary medicine or other corresponding professions,

- they must have employed a qualified person for the release of a medicinal product batch who should be permanently available,

- they must have employed key personnel for the manufacture, quality checks and distribution of medicinal products,

- they must have at their disposal suitable premises and equipment requisite for the manufacture, quality control, storage and delivery of medicinal products,

- they must observe the principles and guidelines of Good Manufacturing Practice.

(2) Specific conditions set out in paragraph 1 of this Article to be satisfied by natural and legal presons referred to in Article 72, paragraph 1 of this Act, shall be laid down in an ordinance issued by the Minister.

Article 74

(1) A manufacturing authorisation holder, in addition to complying with the requirements referred to in Article 73 of this Act, shall also:

- enable the person responsible for the release of a medicinal product batch to conduct his activities independently, and ensure all requisite resources,

- ensure that all manufacturing procedures for a specific medicinal product are conducted in accordance with the medicinal product file approved in the procedure of granting authorisation, or, for an investigational medicinal product, in accordance with the medicinal product data approved in the procedure of granting authorisation for conducting a clinical trial,

- in the manufacture, use only active substances manufactured in accordance with the Good Manufacturing Practice, for active substances in distribution, in accordance with good practice in wholesale distribution of active substances; and ensure use of excipients of appropriate quality for the manufacture of medicinal products,

- inform the Agency and the marketing authorisation holder in a written form and without delay, if he should come to knowledge or if a suspicion arises that medicinal products authorised by the manufacturing authorisation have been counterfeited,

- ensure that manufacturers, importers and wholesalers from which he purchases active substances possess the authorisation for conducting these activities granted by a competent authority of an EU Member State where they are seated,

- establish the authenticity and quality of active substances and excipients,

- at any time, enable access to the manufacturing site to representatives of the competent authority.

(2) The Minister shall issue an ordinance laying down the requirements of Good Manufacturing Practice for medicinal products, active substances and excipients and the method for setting these requirements and for the entry into the register of manufacturers and importers of active substances.

(3) The requirements of good practice in the wholesale distribution of active substances and entry into the register of active substances wholesalers shall be laid down by an ordinance issued by the Minister.

Article 75

(1) For the purpose of obtaining a manufacturing authorisation, a natural or a legal person seated in the Republic of Croatia shall submit an application to the Agency.

(2) Along with the application referred to in paragraph 1 of this Article and the evidence about the compliance with the requirements of the Good Manufacturing Practice referred to in Article 73 of this Act, the applicant shall enclose the file containing the following data and documents:

a) full name and head office of the legal or natural person,

b) evidence of entry in the court register, or in the register of crafts and trades,

c) evidence of entry of the activity in the court register, or in the register of crafts and trades,

d) evidence of professional competencies and employment contract with a person responsible for the release of a medicinal product batch,

e) evidence of professional competencies and employment contract with the key personnel corresponding to the scope of manufacture,

f) personal data of the person responsible for the release of a medicinal product batch and for the key personnel,

g) data on the premises and equipment for manufacture, quality control and storage of medicinal products,

h) description of the manufacturing process or a part of the manufacturing process of a medicinal product for which the authorisation is applied for, or for other parts of the manufacturing process, such as sterilisation of active substances or excipients,

i) a list of medicinal products and pharmaceutical forms for which the authorisation is applied for,

j) master file of the manufacturing site.

Article 76

In the procedure of granting the manufacturing authorisation, an Agency inspector shall deliver an opinion on the compliance with the requirements of Good Manufacturing Practice.

Article 77

(1) The Agency shall grant or refuse the manufacturing authorisation for a medicinal product within 90 days from the date of receipt of a duly filed application.

(2) An application referred to in paragraph 1 of this Article shall be deemed duly filed if within 30 days of its receipt the Agency has established that the application is duly completed and that all the data and documents, or the file, referred to in Article 75 of this Act have been submitted.

(3) Should the Agency establish that the application is not duly filed, it shall invite the applicant by a conclusion to correct or supplement the application or to submit a written explanation within a maximum of 30 days.

(4) The Agency may, during the procedure of granting a manufacturing authorisation, request by a conclusion from the applicant to submit an additional file, or data or documents, or an appropriate explanation, for the submission of which a time limit shall be set.

(5) Should the Agency request the applicant to correct or supplement the application, the time limit referred to in paragraph 1 of this Article shall be suspended until the day of submission of the corrected or supplemented application or during the period approved to the applicant for the submission of a written explanation.

(6) The manufacturing authorisation referred to in paragraph 1 of this Article shall be granted or refused by a decision that cannot be appealed, but against which administrative proceedings can be instituted.

Article 78

(1) If the applicant complies with all the requirements laid down by provisions of this Act and the ensuing ordinances, the Agency shall grant the manufacturing authorisation for an indefinite period of time.

(2) If it is established that the applicant has failed to comply with all the requirements set, the Agency may issue a conditional manufacturing authorisation setting time limits for rectifying the established deficiencies.

(3) The authorisation referred to in paragraph 2 of this Article shall cease to be valid if, after the expiry of the time limit for rectifying the deficiencies, these deficiencies have not been rectified.

(4) The costs of issuing, withholding, amending and revoking a manufacturing authorisation shall be determined by the Agency, subject to the approval by the Minister, and incurred by the applicant or the manufacturing authorisation holder.

Article 79

(1) For any amendment to the file, or data and documents on the basis of which the manufacturing authorisation was granted, a manufacturing authorisation holder shall submit an application with the Agency for approval of any such amendment.

(2) , The manufacturing authorisation holder shall be accompany the application referred to in paragraph 1 of this Article by data and documents, or the file, depending on the type of amendment.

(3) Should the Agency establish that the application is not duly filed, it shall invite the applicant by a conclusion to correct or supplement the application or to submit a written explanation within a maximum of 15 days.

(4) The Agency may, during the procedure of the authorisation of an amendment to the manufacturing authorisation by a conclusion request the applicant to submit an additional file, or data or documents, or an appropriate explanation, for the submission of which a time limit shall be set.

(5) Should the Agency request the applicant to correct or supplement the application, the time limit referred to in paragraph 6 of this Article shall be suspended until the day of submission of the corrected or supplemented application or during the period approved to the applicant for the submission of a written explanation.

(6) If the amendments relate to data and documents referred to in Articles 73 and 75 of this Act, the Agency shall grant or refuse the approval of the amendment, depending on the type of amendment, within a time limit of maximum 30 days from the day of receipt of a duly filed application. By way of exception, this time limit may be extended to 90 days from the day of receipt of a duly filed application.

(7) If the approved amendment requires an amendment to the manufacturing authorisation, the Agency shall issue a decision that cannot be appealed, but against which administrative proceedings can be instituted.

Article 80

(1) The Agency shall, *ex officio*, issue a decision on revoking of the manufacturing authorisation if it is established that the manufacturer does not comply with the requirements laid down by this Act and the ordinances issued pursuant to this Act.

(2) On the basis of a written application of the authorisation holder the Agency shall by a decision revoke the manufacturing authorisation if the authorisation holder ceases its activity.

(3) The decision on revoking or withdrawing of the manufacturing authorisation cannot be appealed, but administrative proceedings can be instituted against it.

Article 81

(1) Import of medicinal products shall be conducted by importers of medicinal products complying with the requirements of Good Manufacturing Practice in the extent that applies to them.

(2) For conducting the activity referred to in 1 of this Article, a manufacturing authorisation shall be required.

(3) Importers importing medicinal products from third countries, and who do not have at their disposal premises and equipment for quality control of every batch of imported medicinal products, may for that purpose conclude a contract with a legal or natural person possessing a manufacturing authorisation that covers quality control of medicinal products.

(4) Batches of medicinal products on which quality control was conducted in another EU Member State of the European Union shall not be subject to additional quality control, but

shall be released in the Republic of Croatia on the basis of a certificate of quality control of a medicinal product batch in an EU Member State of the European Union signed by a responsible person for release of a medicinal product batch.

(5) When a medicinal product is imported from a state which has concluded an agreement on mutual recognition in the field of medicinal products with the European Union, a medicinal product shall be placed on the market in the Republic of Croatia on the basis of a certificate of quality control from the exporting country.

Article 82

(1) The manufacture of an active substance used as a starting material covers also the entire manufacturing process and parts of the manufacturing process, importation and procedures such as weighing, re-packaging or packaging of the active substance before its incorporation in the medicinal product.

(2) The procedures referred to in paragraph 1 of this Article shall be conducted in accordance with the Good Manufacturing Practice for active substances.

(3) The wholesaler and/or the importer who conducts the procedures of weighing, re-packaging and packaging of the active substance shall comply with the requirements of Good Manufacturing Practice for active substances.

Article 83

(1) Natural or legal persons referred to in Articles 72 and 84 of this Act may import active substances under the following conditions:

- that the active substance is manufactured in accordance with requirements of Good Manufacturing Practice aligned with those laid down by the European Union,

- that the delivery of the active substance is accompanied by a written certificate of a competent authority of an exporting third country certifying that:

a) the active substance is manufactured at a manufacturing site where requirements of Good Manufacturing Practice aligned with those laid down by the European Union are applied,

b) the Good Manufacturing Practice is under regular, stringent and transparent supervision at the manufacturing site and

c) the exporting country, in the case of established incompliance in supervision, is obliged to inform the European Union without delay.

(2) The requirements referred in subparagraph 2, paragraph 1 of this Article shall not apply it the exporting country is on the list of countries approved by the European Commission.

(3) By way of derogation from the provision of subparagraph 2, paragraph 1 of this Article, with a view of ensuring the availability of medicinal products, the imported active substance need not have a written certificate during the validity of the certificate of Good Manufacturing Practice if at the manufacturing site of the active substance intended for export supervision was conducted by an EU Member State of the European Union, and if the requirements of

Good Manufacturing Practice for the active substance laid down in the European Union have been complied with.

(4) In the case when the derogation of paragraph 3 of this Article is used, the Agency shall inform the European Union thereof.

(5) The Minister shall issue an ordinance laying down the requirements for import of active substances.

Article 84

Natural or legal persons seated in the Republic of Croatia conducting the activities of manufacture, import and supply of active substances shall enrol in the register of manufacturers, importers, or wholesalers of active substances.

Article 85

(1) A natural or legal persons shall submit the application for enrolment in the register referred to in Article 84 of this Act not later than 60 days before the day of the planned beginning of conducting that activity.

(2) The application referred to in paragraph 1 of this Article shall be accompanied by the file containing the following data and documents:

a) full name and head office of the legal or natural person,

b) evidence of entry in the court register, or in the register of crafts and trades,

c) evidence of entry of the activity in the court register, or in the register of crafts and trades,

d) data on active substances that will be manufactured, imported or sold in wholesale trade,

e) data on the premises and equipment in accordance with operations/activities that will be conducted,

f) data and documents on the person responsible for release of a batch of intermediate product and/or active substance.

Article 86

(1) In the procedure of the enrolment in the register of manufacturers, importers or wholesalers of active substances, the Agency shall, on the basis of a risk assessment, decide on conducting supervision, of which it shall notify the applicant in writing within 60 days from the day of the receipt of a duly filed application for enrolment in the register.

(2) If the Agency notifies in writing the applicant of the conducting of supervision in accordance with paragraph 1 of this Article, prior to the supervision, the applicant must not begin conducting the activities referred to in Article 84 of this Act.

(3) After the conducted supervision or if, on the basis of a risk assessment, supervision has not been conducted, the Agency shall, within 60 days from the day of the receipt of a duly

filed application, or the supervision conducted, grant or refuse enrolment in the register by a decision.

(4) The decision granting or refusing enrolment in the register cannot be appealed, but administrative proceedings can be instituted against it.

(5) A duly filed application referred to in paragraph 1 of this Article means that the Agency has established that the application is duly completed and that all data and documents or the file referred to in Article 85 of this Act have been submitted.

(6) Should the Agency establish that the application is not duly filed it shall invite the applicant by a conclusion to correct or supplement the application or to submit a written explanation within a maximum of 15 days.

(7) The Agency may, during the procedure of enrolment in the register, request by a conclusion from the applicant to submit an additional file, or data or documents, or an appropriate explanation and set the time limit for their submission.

(8) Should the Agency request the applicant to correct or supplement the application, the time limit referred to in paragraph 3 of this Article shall be suspended until the day of the submission of the corrected or supplemented application. Likewise, the time limit referred to in paragraph 1 of this Article shall be suspended for the time allowed to the applicant to provide written explanation.

Article 87

In the procedure of enrolment in a register referred to in Article 86, paragraph 1 of this Act, an Agency inspector shall deliver an opinion on complying with the requirements of Good Manufacturing Practice for active substances.

Article 88

(1) The holder of the enrolment in the register shall once a year report to the Agency all amendments to the file, or in data and documents, on the basis of which the decision on the enrolment in the register was issued and shall submit an application for the approval of the amendment(s) of the enrolment in the register.

(2) For amendment(s) that may affect the quality or the safety of the active substance, the holder of the enrolment in the register shall submit an application for the approval of the amendment(s) to the enrolment in the register.

(3) The holder of the enrolment in the register shall supplement the application referred to in paragraphs 1 and 2 of this Article with the data and documents, or the file, depending on the type of amendment(s).

(4) Should the Agency establish that the application is not duly filed, it shall invite the applicant by a conclusion to correct or supplement the application or to submit a written explanation within a maximum of eight days.

(5) The Agency may, during the procedure of approval of the amendment to enrolment in the register by a conclusion, request from the applicant to submit an additional file, or data or documents, or an appropriate explanation, and set the time limit for the submission thereof.

(6) Should the Agency request the applicant to correct or supplement the application, the time limit referred to in paragraph 7 of this Article shall be suspended until the day of submission of the corrected or supplemented application. The time limit from paragraph 7 of this Article shall be suspended also during the period approved to the applicant for the submission of a written explanation.

(7) The Agency shall grant or refuse the approval of amendment(s) to the enrolment in the register within 30 days from the day of the receipt of a duly filed application.

(8) If the approved amendment requires a modification of the decision on the enrolment in the register, the Agency shall issue a decision, which cannot be appealed, but against which administrative proceedings can be instituted.

Article 89

(1) The certificate of the compliance with the Good Manufacturing Practice shall be issued by the Agency's inspection, within 90 days from conducting supervision of the Good Manufacturing Practice at the request of the manufacturer or the importer.

(2) The Minister shall lay down in an ordinance the method of the issuing the certificate of compliance with the Good Manufacturing Practice.

Article 90

(1) The Agency, at the request of the European Commission or a Member State of the European Union, shall provide data on granted authorisations referred to in Article 72 of this Act.

(2) Data on the granted manufacturing authorisations, on revoking manufacturing authorisations and on certificates of compliance with the Good Manufacturing Practice shall be entered into the EMA (EudraGMP) database.

Article 91

The provisions of this Act relating to the manufacture of medicinal products shall apply appropriately to the manufacture of investigational medicinal products, if not otherwise laid down by this Act.

7. LABELLING, PACKAGE LEAFLET AND THE SUMMARY OF PRODUCT CHARACTERISTICS

Article 92

(1) The following particulars shall appear on the outer and immediate packaging of a medicinal product in the Croatian language or, where there is no outer packaging, only on the immediate packaging:

a) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for infants, children or adults; where the product contains up to three active substances, the international non-proprietary name (INN) shall be included, or, if one does not exist, other common name

b) the qualitative and the quantitative composition in active substances, using common names, for each dosage unit of the medicinal product, or depending on the pharmaceutical form, per volume or weight

c) the pharmaceutical form and content in weight, volume or units of dosage

d) list of excipients of known action or efficacy and, in the event of medicinal products intended for parenteral or topical use and for ophthalmologic medicinal products, all excipients shall be indicated

e) the method of administration and, if necessary, the route of administration; space shall be provided for the prescribed dose to be indicated

f) a special warning that the medicinal product must be stored out of the reach and sight of children

g) specific precautions, if necessary

h) clearly indicated expiry date (month and year)

i) special storage precautions, if applicable

j) special waste management measures for unused medicinal products or waste materials derived from such medicinal products, if appropriate, along with instructions for the appropriate system for their collection

k) name and address of the marketing authorisation holder, or, where applicable, name of the authorised representative of the marketing authorisation holder

l) number of the marketing authorisation

m) batch number

n) in case of over-the-counter medicinal products, the instructions for use of such medicinal products, including the indications

o) dispensing of the medicinal product.

(2) Medicinal products, with the exception of radiopharmaceuticals, must have a safety indication on the packaging. The Minister shall lay down in an ordinance the types of medicinal products that must have a safety indication and the manner of labelling of medicinal products with a safety indication.

(3) Excipients referred to in paragraph 1, item d) of this Article shall be listed in accordance with a European Commission guideline.

Article 93

(1) Where the immediate packaging takes the form of a blister or in case of a small packaging, not all the data referred to in Article 92, paragraph 1 of this Act shall be required.

(2) Where the immediate packaging takes the form of a blister and it is placed in the outer packaging which complies with requirements referred to in Article 92, paragraph 1 of this Act, it shall contain at least the following information:

- name of the medicinal product in line with Article 92, paragraph 1, item a) of this Act

- name of the marketing authorisation holder, or the name of the manufacturer

- expiry date

- batch number.

(3) In the event of a small immediate packaging that cannot contain all data referred to in Article 92, paragraph 1 of this Act, it shall contain at least the following:

- name of the medicinal product in line with Article 92, paragraph 1, item a) of this Act and, if necessary, administration route

- method of administration

- expiry date

- batch number

- content in weight, volume or units of dosage.

Article 94

(1) The data given on the outer and immediate packaging medicinal product shall be easily legible, comprehensible and indelible.

(2) The data given on the outer and immediate packaging medicinal product shall be written in the Croatian language and Latin script.

(3) In addition to data in the Croatian language and Latin script, data in other languages may appear, provided that the content of the data appearing on the outer and immediate packaging of the medicinal product is identical to the content of the data in the Croatian language.

(4) The name of the medicinal product referred to in Article 92, paragraph 1, item a) of this Act, shall be also be provided in the Braille on the packaging. Upon the request of the patients' association, the marketing authorisation holder shall provide and deliver the format of the package leaflet acceptable to the blind and visually impaired people to the association concerned.

(5) The Minister shall issue an ordinance laying down in greater detail the labelling of medicinal products.

Article 95

Outer packaging and the package leaflet may contain symbols or pictograms approved by the Agency, to clarify certain information in accordance with the text of the summary of product characteristics that are useful for the user, but excluding any elements of promotional nature.

Article 96

(1) A package leaflet shall be inserted into each medicinal product packaging.

(2) By way of exception from paragraph 1 of this Article, the package leaflet shall not be obligatory where all the required information referred to in Articles 92 and 95 of this Act is directly conveyed on the outer packaging or on the immediate packaging of a medicinal product.

Article 97

(1) The package leaflet must be written in a clear and comprehensible manner for the user, if necessary in consultation with an expert healthcare professional, and should be written in the Croatian language and Latin script.

(2) In addition to data in the Croatian language and Latin script, other languages may also be used, provided that the content of the data appearing in the leaflet is identical to the content of the data in the Croatian language.

Article 98

(1) The package leaflet shall be drawn up in accordance with the summary of product characteristics; it shall include, in the following order:

a) for the identification of the medicinal product:

- the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for infants, children or adults. The common name shall be included where the product contains only one active substance and if its name is a protected name,

- the pharmaco-therapeutic group (ATC classification) or type of activity in terms easily comprehensible for the patient,

b) the therapeutic indications,

c) a list of information which is necessary before the medicinal product is taken:

- contra-indications,

- appropriate precautions for use medicinal product,

- interaction with other medicinal products and other forms of interaction (e.g. alcohol, tobacco, foodstuffs) which may affect the action of the medicinal product,

- special warnings,

d) the necessary and usual instructions for proper use, and in particular:

- the dosage,

- the method and, if necessary, route of administration,

- the frequency of administration, specifying the appropriate time at which the medicinal product may or must be administered; and, as appropriate, depending on the nature of the product:

- the duration of treatment, where it should be limited,

- the action to be taken in case of an overdose (such as symptoms, emergency procedures),

- what to do when one or more doses have not been taken,

- indication, if necessary, of the risk of withdrawal effects,

- a specific recommendation to consult the doctor or the pharmacist, as appropriate, for any clarification on the use of the product,

e) description of adverse reactions which may occur under normal use of the medicinal product and, if necessary, action to be taken in such a case; patients should be expressly asked to notify their healthcare professional or the Agency of any adverse reaction in accordance with the provisions of this Act,

f) a reference to the expiry date indicated on the label, with:

- a warning against using the product after expiry date,

- where appropriate, special storage precautions,

- if necessary, a warning concerning certain visible signs of quality derogation,

- the full qualitative composition (in active substances and excipients) and the quantitative composition in active substances, using common names,

- the pharmaceutical form and content in weight, volume or units of dosage,

- the name and address of the marketing authorisation holder, and where applicable, the name of the authorised representative of the marketing authorisation holder,

- the name and address of the manufacturer,

g) for medicinal products authorised by the mutual recognition procedure or by decentralised authorisation procedure which have been approved under different name, names of medicinal product in other European Union Member States,

h) date of the latest revision of the leaflet.

(2) When indicating data referred to in paragraph 1, subparagraph c) of this Article, warnings related to special conditions of certain categories of users of medicinal products should be especially given, for example children, pregnant or breastfeeding women, the elderly, persons with specific pathological conditions, and indicate, possible effects on the ability to drive vehicles or to operate machinery and warnings related to excipients that might affect the efficacy and safe use of the medicinal product.

(3) Excipients that might affect the efficacy and safe use of the medicinal product shall be stated in accordance with the European Commission guidelines.

(4) The package leaflet shall reflect the results of consultations with target patient groups to ensure that it is legible, clear and easy to use.

(5) The Minister shall issue an ordinance laying down the contents and manner of inserting the package leaflet.

Article 99

(1) In the procedure of granting authorisation, in accordance with Article 26, paragraph 3, item o) of this Act, the application shall be accompanied with one or more mock-ups of the outer and immediate packaging of the medicinal product, along with the proposed leaflet of the medicinal product.

(2) In the context of the approval procedure, the applicant shall submit to the Agency also the results of the assessment of the comprehensibility of the package leaflet conducted in consultation with target patient groups.

Article 100

(1) The summary of product characteristics shall contain, in the order indicated below, the following information:

1. name of the medicinal product followed by the strength and the pharmaceutical form,

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

3. pharmaceutical form,

4. clinical particulars:

4.1. therapeutic indications

4.2. posology and method of administration for adults and, where necessary, for children

4.3. contra-indications

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

4.5. interaction with other medicinal products and other forms of interactions

4.6. use during pregnancy and lactation

4.7. effects on ability to drive and to use machines

4.8. undesirable effects

4.9. overdose (symptoms, emergency procedures, antidotes)

5. pharmacological properties:

5.1. pharmacodynamic properties

5.2. pharmacokinetic properties

5.3. preclinical safety data

6. pharmaceutical particulars:

6.1. list of excipients

6.2. major incompatibilities

6.3. shelf life, when necessary after reconstitution of the medicinal product or when the immediate packaging is opened for the first time

6.4. special precautions for storage

6.5. nature and contents of container

6.6. special waste management measures for unused medicinal product or for waste residue deriving from medicinal products, where applicable

7. name and address of the marketing authorisation holder

8. marketing authorisation number

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

10. date of the latest summary text revision

11. for radiopharmaceuticals, full details of internal radiation dosimetry

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

(2) For authorisations granted in accordance with Articles 29, 30, 31, 32, 33, 34, 35 and 36 of this Act, parts of the summary of product characteristics of the reference medicinal product that relate to indications or dosage forms that are still under patent protection at the time of marketing of the medicinal product shall not be included in the text of the summary of product characteristics.

(3) Standard text clearly indicating to healthcare professionals to report any suspicion of an adverse reaction in accordance with the provisions of this Act and ensuing ordinances shall be included in the summary of product characteristics.

(4) The Minister shall lay down in an ordinance the content and the manner of inclusion of the summary of product characteristics.

Article 101

Orphan medicinal products may, on the basis of a written reasoned application submitted by the applicant, be marketed with a label in only one of the languages of one of the European Union Member States.

Article 102

(1) For medicinal products that are not intended to be directly used by the user or the patient, or in case of problems in the market supply of the medicinal product, and in accordance with the measures necessary for preserving human health, the Agency may approve exemption from the requirement that specific data must appear on the label and on the leaflet.

(2) In the cases referred to in paragraph 1 of this Article, the Agency may approve full or partial exemption from the requirement that the label and the leaflet must be in the Croatian language, provided that the text is in Latin script, pursuant to a written reasoned application submitted by the applicant.

Article 103

(1) The outer packaging and the container of radiopharmaceuticals shall be labelled in accordance with the regulations governing safe transport of radioactive materials.

(2) The label on the protective container of radiopharmaceuticals must contain data referred to in Article 92 of this Act.

(3) Along with data referred to in Article 92 of this Act, the following data shall appear on the protective container of radiopharmaceuticals:

- full explanations of the symbols indicated on the bottle

- quantity of radioactivity per dose or per bottle in a specific period of time, if necessary

- number of capsules or, for liquids, number of millilitres in the container.

(4) The label on the bottles of radiopharmaceuticals shall contain the following data:

- name or the indication of the medicinal product, including the name or the chemical symbol for radionuclides,

- batch number and the expiry date,

- international symbol for radioactivity,

- name and address of the manufacturer,

- quantity of radioactivity per dose or per bottle in a specific period of time.

Article 104

(1) The marketing authorisation holder shall ensure that the exhaustive instructions for use are inserted in the packaging of radiopharmaceuticals, radionuclide generators, radionuclide kits and radionuclide precursors.

(2) The instructions for use referred to in paragraph 1 of this Article shall contain data referred to in Article 98 of this Act, along with the precaution measures to be taken by the user and the patient when preparing and using the medicinal product as well as special precaution measures to be taken when disposing of the packaging of the medicinal product and of its unused content.

Article 105

Therapeutic indications shall not be stated on the outer and immediate packaging of the product and in the package leaflet, if the product does not have a marketing authorisation as a medicinal product or a homeopathic medicinal product.

8. CLASSIFICATION OF MEDICINAL PRODUCTS

Article 106

(1) The dispensing of a medicinal product shall be regulated by a decision to grant a marketing authorisation.

(2) In respect of the method for dispensing, medicinal products shall be classified into two categories:

- medicinal products subject to medical prescription,

- medicinal products not subject to medical prescription.

Article 107

In respect of the place of dispensing, medicinal products shall be classified into the following categories:

1. medicinal products subject to medical prescription dispensed in pharmacies,

2. medicinal products not subject to medical prescription dispensed in pharmacies, and

3. medicinal products not subject to medical prescription dispensed in pharmacies and specialised retail sale outlets.

Article 108

(1) In the procedure for granting, renewing or amending marketing authorisations, the Agency may define the following methods for prescribing of medicinal products:

1. medicinal products on medical prescription for renewable delivery

2. medicinal products on medical prescription for non-renewable delivery

3. medicinal products subject to special medical prescription

4. medicinal products on restricted medical prescription.

(2) In the Republic of Croatia, a medicinal product that has been granted a marketing authorisation in line with the provisions of this Act may be dispensed upon prescription prescribed by an authorised person from another EU Member State.

(3) Detailed criteria for the classification, prescription and dispensing of medicinal products shall be laid down by the Minister in an ordinance.

Article 109

(1) Medicinal products shall be subject to medical prescription where they:

— are likely to present a danger either directly or indirectly, even when used correctly, if utilised without medical supervision, or

— are frequently and to a very wide extent used incorrectly, and as a result are likely to present a direct or indirect danger to human health, or

— contain substances or preparations thereof, the activity and/or adverse reactions of which require further investigation, or

— are normally prescribed by a doctor to be administered parenterally.

(2) Medicinal products not covered by the criteria from paragraph 1 of this Article may be dispensed without medical prescription.

Article 110

When new facts are brought to its attention, the Agency shall examine the current classification of a medicinal product by applying the criteria listed in Article 109 of this Act and in the ordinance referred to in Article 108, paragraph 3, of this Act.

Article 111

(1) The Agency shall post a list of medicinal products subject to medical prescription in the Republic of Croatia on its Internet pages.

(2) The list of medicinal products from paragraph 1 of this Article shall be updated at least once a year.

(3) Each year, the Agency shall submit the list of medicinal products from paragraph 1 of this Article and its amendments to the European Commission and Member States of the European Union.

Article 112

Where a change of classification of a medicinal product from a medicinal product subject to medical prescription to a medicinal product not subject to medical prescription has been first authorised on the basis of significant pre-clinical tests or clinical trials, the Agency shall not refer to the results of those tests or trials when examining an application by another holder of marketing authorisation for a change of classification of the same substance for one year after the initial change was authorised.

9. DISTRIBUTION OF MEDICINAL PRODUCTS

Article 113

(1) Only medicinal products in respect of which a marketing authorisation has been granted in accordance with Article 22, paragraph 1, of this Act and medicinal products in respect of which an authorisation for parallel imports or parallel distribution has been granted may be distributed in the Republic of Croatia.

(2) By way of derogation from the provision of paragraph 1 of this Article, a batch of the medicinal product may be distributed for no longer than 18 months following the expiry or revocation of the marketing authorisation, unless its shelf life expires first.

Article 114

(1) All legal and natural persons and government bodies who come in possession of medicinal products in any way whatsoever shall ensure that they are transported, handled and stored in accordance with prescribed conditions in order to prevent both any changes in their quality or their abuse.

(2) The Minister shall issue an ordinance on good distribution practice in wholesale of medicinal products.

Article 115

Wholesale distribution of medicinal products in the Republic of Croatia may be carried out by:

- natural and legal persons who are established in the Republic of Croatia and who hold the Agency's authorisation for wholesale distribution of medicinal products (wholesale distributors of medicinal products);

- natural and legal persons who are authorised for the wholesale distribution of medicinal products established outside of the Republic of Croatia, i.e. in any EU Member State of the European Union, and who satisfy the conditions for the wholesale distribution of medicinal products in the country where they are established, and who have notified the Agency about the beginning of their operations on the territory of the Republic of Croatia,

- manufacturers of medicinal products who are established in the Republic of Croatia or any EU Member State of the European Union if they manufacture these medicinal products and if these medicinal products are authorised in the Republic of Croatia.

Article 116

Brokering of medicinal product may be carried out by natural and legal persons who are established in the Republic of Croatia or in any Member State of the European Union and who have permanent address and contact details in the Republic of Croatia or in any Member State of the European in order to ensure identification, location, communication and supervision of their activities.

Article 117

(1) Wholesale distributors shall be allowed to procure medicinal products directly from manufacturers, importers, brokers or from other wholesale distributors who hold the relevant authorisation granted by the competent authority.

(2) Wholesale distributors from paragraph 1 of this Article shall verify whether the medicinal product manufacturer, importer, broker or any other wholesale distributor holds the relevant authorisation for wholesale distribution.

(3) The provisions of paragraphs 1 and 2 of this Article shall also apply to brokers.

Article 118

(1) Wholesale distributors and manufacturers may supply medicinal products to:

– pharmacies and pharmacy depots,

– specialised retail sale outlets for medicinal products,

– other wholesale distributors,

– healthcare institutions and other legal persons holding the relevant healthcare license,

- private surgeries in quantities required for treatment of acute conditions.

(2) The Minister shall issue a list and the required quantities of medicinal products allowed to the surgeries referred to in paragraph 1, subparagraph 5 of this Article.

(3) Wholesale distributors shall ensure the supply of medicinal products within the shortest possible time.

(4) The conditions for exports of medicinal products to third countries and transit of medicinal products, which are not imported, from third countries, shall be laid down by the Minister in an ordinance.

Article 119

(1) The wholesale distributor shall procure a wholesale distribution authorisation for each location intended for wholesale distribution in the Republic of Croatia.

(2) In addition to general requirements for wholesale distribution, the applicants shall meet the following minimum requirements to be granted an authorisation for wholesale distribution:

- have at their disposal suitable premises, appliances and equipment, in order to ensure proper storage and wholesale distribution of medicinal products,

- have adequate staff, and in particular qualified persons responsible for wholesale distribution of medicinal products as well as for documentation review,

- observe the principles of good distribution practice in wholesale of medicinal products.

Article 120

(1) A holder of the authorisation for wholesale distribution shall satisfy the following conditions:

- have a plan for emergency recall of the medicinal product in line with the Agency's decision or in agreement with the manufacturer or the marketing authorisation holder and keep documents enabling such recall,

- keep records of orders, deliveries and brokering in a written, electronic or any other form;

- operate a quality assurance system which defines processes, responsibilities and risk management,

- make systematic checks to make sure that the medicinal products he receives are not falsified by using safety features on packs in line with Article 92, paragraph 2 hereof,

- immediately notify the Agency of any falsified medicinal product received or offered or any medicinal products suspected of being falsified,

- ensure timely, permanent and appropriate supply of the territory of the Republic of Croatia with medicinal products.

(2) The conditions laid down in subparagraphs 1, 2, 3 and 5 of paragraph 1 of this Article shall also accordingly apply to natural and legal persons engaged in brokering of medicinal products.

(3) The Minister shall issue an ordinance establishing detailed conditions, documents and data for the granting of the authorisation for wholesale distribution and brokering of medicinal products and the procedure for application referred to in Article 121 of this Act.

Article 121

Natural and legal persons who are established outside of the Republic of Croatia, but in a Member State of the European Union, and who satisfy the conditions for the wholesale distribution or brokering of medicinal products in the country where they are established, shall notify the Agency about the beginning of their operations on the territory of the Republic of Croatia.

Article 122

(1) On the request of the European Commission or any Member State of the European Union, the Agency shall provide data on the granted authorisations referred to in Article 115 of this Act.

(2) The data about granted authorisations for wholesale distribution and the data about their revocation shall be entered into the EMA's database.

Article 123

(1) The Agency shall grant the authorisation for wholesale distribution or brokering within 90 days of receipt of a duly filed application.

(2) Should the Agency establish that the application is not duly filed, i.e. that it is not supported by required data and documents, it shall issue a conclusion requiring from the applicant to correct or amend the application within a time limit it shall specify.

(3) During the procedure for granting authorisations referred to in paragraph 1 of this Article, the Agency may issue a conclusion requiring from the applicant to submit additional data or documents or to provide the relevant explanation within a time limit it shall specify.

(4) Should the Agency require from the applicant correction or amendment of the application, the time limit referred to in paragraph 1 of this Article shall be suspended until such time as the required corrected or amended application has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant to give an oral or written explanation.

(5) The authorisation for wholesale distribution or brokering of medicinal products shall be granted or refused by a decision that cannot be appealed, but against which administrative proceedings can be instituted.

(6) The provisions of paragraphs 2, 3 and 4 of this Article shall also accordingly apply to the procedure for varying the authorisation for wholesale distribution and brokering licenses of medicinal products and the procedure for their revocation.

(7) The Agency, subject to the approval by the Minister, shall determine the costs of the grant, refusal, variation or revocation of authorisations for wholesale distribution or brokering. The costs shall be borne by applicants or holders of authorisations.

Article 124

(1) The Agency shall revoke the authorisation for wholesale distribution or brokering granted to wholesale distributors or brokers established in the Republic of Croatia if they no longer satisfy the conditions on the basis of which the authorisation has been granted or the stipulated conditions for the performance of their activity.

(2) On the basis of the written application submitted by the authorisation holder, the Agency shall issue a decision to revoke authorisations from paragraph 1 of this Article if the authorisation holder has ceased to perform his activity.

(3) The Agency shall forthwith notify the Member States of the European Union and the European Commission about the revocation of authorisations from paragraph 1 of this Article.

(4) The authorisation for wholesale distribution or brokering shall be revoked by a decision that cannot be appealed, but against which administrative proceedings can be instituted.

Article 125

Where the Agency establishes that the wholesale distributor or the broker performing activity pursuant to Article 121 of this Act no longer satisfies the conditions for the performance of this activity, it shall notify the European Commission and the competent Member State of the European Union accordingly.

Article 126

(1) The wholesale distributor and the broker shall notify the Agency in writing about any changes related to conditions, documents and data on the basis of which the authorisation has been granted.

(2) Wholesaler distributors and brokers performing activity in accordance with Article 121 of this Act shall report any changes to data and documents that occurred after they had notified the beginning of performance of their activity in the Republic of Croatia.

(3) If the approved variation of the authorisations from paragraph 1 of this Article requires variations of authorisation for wholesale distribution and brokering, the Agency shall issue a decision that cannot be appealed, but against which administrative proceedings can be instituted.

(4) The Agency shall issue the decision referred to in paragraph 3 of this Article within 90 days of the receipt of a duly filed application.

Article 127

(1) The pharmaceutical inspection of the Ministry shall issue a certificate of good medicinal products wholesale distribution practice within 90 days of inspection of the good distribution practice in wholesale conducted and on the request of the wholesale distributor or the broker.

(2) Issuing of certificates of good medicinal product wholesale distribution practice shall be laid down by the ordinance to be issued by the Minister.

Article 128

(1) The Agency's approval for entry or import shall not be required for:

- medicinal products authorised for wholesale distribution by the Agency or the European Commission,

- medicinal products authorised for parallel importation or parallel distribution,

- active substances and excipients,

- intermediate products or medicinal products, where some production processes are carried out in the Republic of Croatia.

(2) The provision of paragraph 1 of this Article shall not apply to the approval for entry or importation of:

- medicinal products made of human blood or plasma,

- immunological medicinal products,

- radiopharmaceuticals.

(3) The Minister shall issue an ordinance establishing detailed conditions for granting the approval for entry or importation of medicinal products from paragraph 2 of this Article.

Article 129

(1) The Agency may exceptionally allow the entry or importation of medicinal products which are not authorised in the Republic of Croatia:

– if there is a medically justified need to protect human health,

– for research purposes,

– for pharmaceutical testing,

– for pre-clinical tests,

–in case of natural disasters or other emergencies,

– for emergency treatments of individual patients with a medicinal product prescribed by a medical doctor or dental medicine doctor in charge.

(2) The Minister shall issue an ordinance establishing detailed conditions for entry or importation of medicinal products from paragraph 1 of this Article.

(3) Provisions of a special act on combating narcotics abuse shall apply to import, export, transportation and transit of narcotics, substances for their manufacture and medicinal products containing narcotics.

Article 130

(1) Parallel imports of a medicinal product may be carried out by wholesale distributors who are authorised for wholesale distribution of medicinal products and who are not in any business relationship with the holder of the marketing authorisation for the concerned medicinal product.

(2) The Minister shall issue an ordinance establishing detailed conditions, documents and data for granting an authorisation for parallel imports of medicinal products.

Article 131

(1) Wholesale distributors who are not marketing authorisation holders, and who on the basis of the authorisation for parallel import of medicinal products from another Member State of the European Union to the Republic of Croatia, shall forthwith notify the Agency and the marketing authorisation holder and not later than 15 days prior to the importation.

(2) Wholesale distributors from paragraph 1 of this Article shall submit a notification to the marketing authorisation holder and the EMA for any medicinal product which is authorised in accordance with Regulation (EC) No. 726/2004.

Article 132

(1) The Agency shall grant an authorisation for parallel imports of a medicinal product within 90 days of receipt of a duly filed application.

(2) Should the Agency establish that the application is not duly filed i.e. that it is not supported by required data and documents, it shall issue a conclusion requiring from the applicant to correct or amend the application within a time limit it shall specify.

(3) During the procedure for granting authorisations referred to in paragraph 1 of this Article, the Agency may issue a conclusion requiring from the applicant to submit additional data or documents or to provide the relevant explanation, within a time limit it shall specify.

(4) Should the Agency require from the applicant to correct or amend the application, the time limit referred to in paragraph 1 of this Article shall be suspended until such time as the required corrected or amended application has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant to give a written explanation.

(5) The authorisation for parallel imports of medicinal products shall be granted or refused by a decision that cannot be appealed, but against which administrative proceedings can be instituted.

(6) The provisions of paragraphs 2, 3 and 4 of this Article shall also appropriately apply to the procedure for varying the authorisation for parallel imports of medicinal products.

(7) The Agency, subject to approval by the Minister, shall determine the costs of the grant, refusal or variation of authorisations for parallel imports of medicinal products. The costs shall be borne by applicants or holders of authorisations.

Article 133

(1) The Agency shall revoke the authorisation for parallel imports of the medicinal product if the authorisation holder or the medicinal product no longer satisfies the conditions on the basis of which the authorisation has been granted.

(2) The authorisation for parallel imports shall be revoked by a decision that cannot be appealed, but against which administrative proceedings can be instituted.

Article 134

(1) The holder of the authorisation for parallel imports of the medicinal product shall notify the Agency in writing about all changes related to the dossier and to the documents and data on the basis of which the authorisation has been granted.

(2) If the approved variation of the authorisation from paragraph 1 of this Article requires a variation of the authorisation for parallel imports of medicinal products, the Agency shall issue a decision to vary the authorisation that cannot be appealed, but against which administrative proceedings can be instituted.

(3) The Agency shall issue a decision to vary the authorisation for parallel imports within 90 days of receipt of a duly filed application.

Article 135

(1) Retail sale of medicinal products shall be carried out by legal and natural persons authorised to engage in pharmacist activity in accordance with a special act as well as by

specialised retail stores authorised by the Agency to engage in retail sale of medicinal products.

(2) In accordance with Article 106, paragraph 2, of this Act, medicinal products subject to medical prescription shall be dispensed exclusively in pharmacies, while medicinal products not subject to medical prescription shall be also dispensed in specialised retail sale outlets for medicinal products in line with the marketing authorisation granted by the Agency.

(3) If the medicinal product can be dispensed in specialised retail sale outlets for medicinal products, the Agency may determine restrictions in respect of its strengths and pack sizes.

(4) The ordinance on the conditions for the granting of the authorisation to specialised retail sale outlets for medicinal products shall be issued by the Minister.

Article 136

(1) Natural and legal persons engaged in pharmacist activity in the Republic of Croatia may over the Internet offer for distance selling, in line with a special regulaton, medicinal products which are not subject to medical prescription.

(2) Natural or legal persons from paragraph 1 of this Article, who over the Internet offer medicinal products for distance selling, shall provide the Agency with the following data:

- name or corporate name and permanent address of the place of activity from where those medicinal products are supplied,

- the starting date of the activity of offering medicinal products for sale at a distance,

- the address of the website used for that purpose and all relevant information necessary to identify that website.

(3) The web page from paragraph 2 of this Article, which offers distance selling of medicinal products, shall contain at least the following:

- the contact details of the Agency,

- a hyperlink to the website of the Agency with data about legal and natural persons offering distance selling of medicinal products,

- the common logo of a defined form for the European Union, clearly displayed on every page of the website that relates to the offer for sale at a distance to the public of medicinal products. The common logo shall contain a hyperlink to the list of legal and natural persons offering distance selling of medicinal products.

(4) The ordinance on the conditions for the offering of medicinal products for distance selling over the Internet shall be issued by the Minister.

Article 137

The web page of the Agency shall contain:

- information on the national legislation applicable to the offering of medicinal products for distance selling over the Internet, including information on the fact that there may be differences between EU Member States regarding classification of medicinal products and the conditions for their supply,

- information on the purpose of the common logo,

- the list of persons offering the medicinal products for distance selling over the Internet in accordance with Article 136 of this Act as well as their website addresses,

- background information on the risks related to medicinal products supplied illegally to the public by means of unauthorised information society services;

- a hyperlink to the website of the EMA with data about the distance selling of medicinal products.

Article 138

(1) The Agency shall grant the authorisation for retail sale of medicinal products in specialised retail sale outlets within 90 days of receipt of a duly filed application.

(2) If the Agency finds out that the application is not duly filed, i.e. that the stipulated data and documents have not been submitted, it shall issue a conclusion requiring from the applicant to correct or supplement the application within a time limit it shall specify.

(3) During the procedure for granting the authorisation from paragraph 1 of this Article, the Agency may issue a conclusion requiring from the applicant to supply additional data or documents or the relevant explanation and may set the time limit for the submission.

(4) If the Agency requires from the applicant to correct or supplement the application, the time limit from paragraph 1 of this Article shall not run until the corrected or supplemented application has been submitted. Likewise, the time limit from paragraph 1 of this Article shall be suspended for the time allowed to the applicant to give an oral or written explanation.

(5) The authorisation for retail sale of medicinal products in specialised retail sale outlets shall be granted by a decision that cannot be appealed, but against which administrative proceedings can be instituted.

(6) The provisions of paragraphs 2, 3 and 4 of this Article shall accordingly apply to procedures for variation of the authorisation for retail sale of medicinal products in specialised retail sale outlets and for revocation of this authorisation.

(7) The costs in the procedure for granting, refusing, varying and revoking the authorisation for retail sale of medicinal products shall be defined by the Agency, subject to approval by the Minister, and borne by the applicant or the holder of the authorisation.

Article 139

(1) The Agency shall revoke the authorisation granted to the specialised retail sale outlet for medicinal products if it has established that the holder of the authorisation no longer satisfies the conditions on the basis of which the authorisation has been granted or that he no longer

satisfies the conditions for the activity of retail sale of medicinal products in a specialised retail sale outlet.

(2) On the basis of the written application submitted by the authorisation holder, the Agency shall issue a decision revoking the authorisation from paragraph 1 of this Article if the authorisation holder has ceased to perform his activity.

(3) The authorisation for retail sale of medicinal products shall be revoked by a decision that cannot be appealed, but against which administrative proceedings can be instituted.

Article 140

(1) The holder of the authorisation for retail sale of medicinal products shall notify the Agency in writing about any changes related to the conditions, documents and data on the basis of which the authorisation has been granted.

(2) Natural or legal persons engaging in distance selling of medicinal products over the Internet in accordance with Article 136 of this Act shall notify the Agency in writing about any changes to documents and data on the basis of which they filed the application for the performance of their activities.

(3) The Agency shall issue a decision on variation of the authorisation for retail sale of medicinal products in specialised retail sale outlets within 90 days of receipt of a duly filed application.

(4) If the approved variation of the authorisation from paragraph 1 of this Article requires a variation of the decision granting authorisation for retail sale of medicinal products in specialised retail sale outlets, the Agency shall adopt a decision that cannot be appealed, but against which administrative proceedings can be instituted.

Article 141

(1) All natural and legal persons engaged in wholesale distribution of medicinal products and legal and natural persons engaged in retail sale of medicinal products shall submit annual reports on the sale of medicinal products to the Agency.

(2) A type of data and the method for drafting of reports from paragraph 1 of this Article shall be laid down by the Minister in an ordinance.

Article 142

The ordinance on the wholesale distribution and retail sale of narcotic drugs, substances that may be used for the preparation of narcotic drugs and medicinal products containing narcotic substances shall be issued by the Minister.

Article 143

(1) Medicinal products of inappropriate quality, efficacy and safety as well as expired medicinal products shall not be marketed and shall be considered as waste.

(2) Rules and regulations governing the area of waste management shall also apply to the waste management referred to in paragraph 1 of this Article.

10. PHARMACOVIGILANCE

Article 144

(1) The Agency may lay down that medicinal products approved placing on the market of the Republic of Croatia be additionally monitored for their safety profile.

(2) Medicinal products from paragraph 1 of this Article must bear a special label.

Article 145

(1) Any healthcare professional who comes in contact with patients/users of a medicinal product, any manufacturer of a medicinal product and a marketing authorisation holder, holder of an authorisation for parallel import, importer and wholesaler shall notify the Agency in writing about any suspected adverse reactions, in particular about serious and unexpected adverse reactions, while in the case of vaccines they shall also notify the Croatian National Institute of Public Health.

(2) A healthcare professional shall report serious adverse reactions to the Agency within 30 days after their knowledge and later as necessary by filing subsequent reports. Serious adverse reactions with a fatal outcome shall be forthwith reported to the Agency in writing or by phone, subject to the subsequent written notification.

(3) A healthcare professional who participates in a clinical trial as investigator shall forthwith report all serious adverse events to a clinical trial sponsor, except if he is not required to do this by the trial protocol and the investigator's brochure.

(4) The ordinance on pharmacovigilance shall be issued by the Minister.

Article 146

(1) A patient/user of the medicinal product may directly notify the Agency or the marketing authorisation holder of any suspected adverse reactions of medicinal products and vaccines.

(2) Suspected adverse reactions may be reported by the patient/the user of the medicinal product, while for persons with incapacity to contract, persons with serious mental disorders or minors, the suspected adverse reactions may be reported by a parent, legal guardian or caregiver.

Article 147

(1) The marketing authorisation holder shall operate a pharmacovigilance system for the fulfilment of his pharmacovigilance tasks provided for by the provisions of this Act and the ensuing ordinance.

(2) The marketing authorisation holder shall, by means of the pharmacovigilance system, evaluate all safety information scientifically, consider options for risk minimisation and prevention and take regulatory action as necessary.

(3) The marketing authorisation holder shall perform a regular audit of the pharmacovigilance system.

(4) The marketing authorisation holder shall place a note concerning the main findings of the audit on the pharmacovigilance system master file (PSMF) and, based on the audit findings, ensure that an appropriate corrective action plan is prepared and implemented.

(5) Once the corrective actions have been fully implemented, the authorisation holder may remove the note referred to in paragraph 4 of this Article.

Article 148

(1) As part of the pharmacovigilance system, the marketing authorisation holder shall:

a) have permanently and continuously at his disposal:

- an appropriately qualified person responsible for pharmacovigilance in the European Union and

- an appropriately qualified person responsible for pharmacovigilance in the Republic of Croatia;

b) maintain and make available on Agency's request a pharmacovigilance system master file,

c) operate a risk management system for each authorised medicinal product,

d) monitor the outcome of risk minimisation measures which are contained in the risk management plan or which are laid down as conditions pursuant to Articles 46, 47 and 48 of this Act,

e) update the risk management system and monitor pharmacovigilance data to determine whether there are new risks or whether risks have changed or whether there are changes to the benefit-risk balance of medicinal products.

(2) Tasks of the person responsible for pharmacovigilance in the European Union and in the Republic of Croatia, referred to in subparagraph a) of paragraph 1 of this Article may be performed by a single person.

Article 149

(1) Holders of marketing authorisations granted before 21 July 2012 shall not be required to operate a risk management system for each authorised medicinal product pursuant to Article 148, paragraph 1, item c) of this Act.

(2) The Agency may, by way of derogation from paragraph 1 of this Article, stipulate that the authorisation holder is to operate the risk management system if there are concerns about the risks affecting the risk-benefit balance of an authorised medicinal product.

(3) Pursuant to paragraph 2 of this Article, the Agency shall also oblige the marketing authorisation holder to submit a detailed description of the risk-management system which he intends to introduce for the medicinal product concerned.

(4) The Agency may stipulate the fulfilling of the obligation from paragraphs 2 and 3 of this Article in duly justified cases, with a written announcement including the timeframe for submission of the detailed description of the risk-management system.

(5) If the marketing authorisation holder so requests, the Agency shall provide the marketing authorisation holder with an opportunity to present written observations in response to the imposition of the obligation from paragraphs 2 and 3 of this Article, within 30 days of receipt of the written notification of the obligation.

(6) On the basis of the written observations submitted by the marketing authorisation holder, the Agency shall make a decision on the obligation from paragraphs 2 and 3 of this Article.

(7) Where the Agency confirms the decision from paragraph 6 of this Article, the Agency shall issue a decision on varying of the marketing authorisation to include the obligation to conduct measures in accordance with Article 46, paragraph 1, subparagraph 1 of this Act.

Article 150

The marketing authorisation holder shall:

- keep records of all suspected adverse reactions in the Republic of Croatia, other Member States of the European Union or third countries reported to him, either spontaneously by patients/users of the medicinal product or a healthcare professional or reported during the post-authorisation study,

- make available the data from subparagraph 1 of this paragraph at one location in the European Union.

Article 151

(1) Marketing authorisation holders shall submit electronically to the Eudravigilance database:

- information on all non-serious suspected adverse reactions that occur in the Republic of Croatia within 90 days following the day on which the marketing authorisation holder concerned gained knowledge of the event,

- information on all serious suspected adverse reactions that occur in the Republic of Croatia within 15 days following the day on which the marketing authorisation holder concerned gained knowledge of the event,

- information on all non-serious suspected adverse reactions that occur in the Member States of the European Union, within 90 days following the day on which the marketing authorisation holder concerned gained knowledge of the event,

- any information on all serious suspected adverse reactions that occur in the Member States of the European Union within 15 days following the day on which the marketing authorisation holder concerned gained knowledge of the event,

- information on all serious suspected adverse reactions that occur in the third countries within 15 days following the day on which the marketing authorisation holder concerned gained knowledge of the event,

(2) Marketing authorisation holders shall establish procedures in order to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports. They shall also collect follow-up information on these reports and submit the updates to the Eudravigilance database.

(3) Marketing authorisation holders shall collaborate with the Agency and the EMA in the detection of duplicates of suspected adverse reaction reports.

(4) Marketing authorisation holders shall submit electronically all suspected adverse reactions from paragraph 1, subparagraphs 1 and 2 of this Article to the Agency until the functional system for their submission to the Eudravigilance database has been established.

(5) The Agency shall submit electronically all suspected adverse reactions reports received pursuant to paragraph 4 of this Article to the Eudravigilance database in accordance with timeframes referred to in paragraph 1, subparagraphs 1 and 2 of this Article.

Article 152

(1) The sponsor shall:

- keep detailed records of all adverse events which are reported to him by the investigator and submit these records to the Agency and/or the Central Ethics Committee and/or the Ministry, if they so request

- forthwith, and in any case no later than seven days after knowledge, ensure that all relevant information about suspected serious unexpected adverse reactions that are fatal or life-threatening is communicated electronically to Eudravigilance

- submit the relevant follow-up information about the knowledge from the second subparagraph of this paragraph within eight days as from the expiry of deadline from the second subparagraph of this paragraph

- forthwith, but within a maximum of fifteen days of first knowledge, report all other suspected serious unexpected adverse reactions electronically to Eudravigilance

- inform investigators about all suspected serious unexpected adverse reactions

- submit the report on the medicinal product undergoing a clinical trial for a period of not more than one year to the Agency and the Central Ethics Committee, and exceptionally on the request by the Agency and/or the Central Ethics Committee.

(2) The sponsor of the clinical trial shall electronically report adverse reactions from paragraph 1, subparagraphs 2, 3 and 4 of this Article which occurred in the Republic of Croatia to the Agency.

Article 153

(1) The Agency shall operate a pharmacovigilance system for the fulfilment of its pharmacovigilance tasks and its participation in the European Union pharmacovigilance activities.

(2) The pharmacovigilance system shall be used to collect information on the risks of medicinal products as regards patients' or or the purpose of public health protection.

(3) The information from paragraph 2 of this Article shall in particular refer to adverse reactions arising from use of the medicinal product within the terms of the marketing authorisation as well as from use outside the terms of the marketing authorisation, and to adverse reactions associated with occupational exposure.

(4) The Agency shall, by means of the pharmacovigilance system referred to in paragraph 1 of this Article, evaluate all safety information scientifically, consider options for risk minimisation and prevention and take regulatory action concerning the marketing authorisation as necessary.

(5) The Agency shall perform a regular audit of its pharmacovigilance system and report the results to the European Commission on 21 September 2013 at the latest and then every two years thereafter.

(6) The Agency shall, on the request of the European Commission and under the coordination of the EMA, participate in international harmonisation and standardisation of technical measures in relation to pharmacovigilance.

Article 154

(1) Within the framework of the system of pharmacovigilance, the Agency shall:

- keep records of all reported suspected adverse reactions which have occurred on the territory of the Republic of Croatia

- involve patients/ users of medicinal products and healthcare professionals, as appropriate, in the follow-up of any reports they receive

- take all appropriate measures to obtain accurate and verifiable data for the scientific evaluation of suspected adverse reaction reports

- ensure, through the methods for collecting information and where necessary through the follow-up of suspected adverse reaction reports, that all appropriate measures are taken to identify clearly any biological medicinal product prescribed, dispensed, or sold on the territory of the Republic of Croatia which is the subject of a suspected adverse reaction report, with due regard to the name of the medicinal product and the batch number

- facilitate patient reporting through the provision of web-based formats in addition to current reporting formats

- collaborate with the EMA and marketing authorisation holders in the detection of duplicates of suspected adverse reaction reports

- within 15 days following the receipt of the reports of serious suspected adverse reactions or suspected transmission of infectious agents via the medicinal product, submit the reports electronically to the Eudravigilance database

- within 90 days after knowledge on non-serious suspected adverse reactions which occurred on the territory of the Republic of Croatia, submit the reports electronically to the Eudravigilance database

- ensure that reports of suspected adverse reactions arising from an error associated with the use of a medicinal product that are brought to its attention are made available to the Eudravigilance database.

(2) The Agency may involve the marketing authorisation holder in the follow-up of any reports on adverse reactions that occurred on the territory of the Republic of Croatia.

Article 155

(1) The Agency may delegate any task entrusted to it under the provisions of this Act which relates to pharmacovigilance to a competent authority of another EU Member State subject to a written agreement of the latter.

(2) The Agency may represent no more than one other EU Member State.

(3) If the Agency delegates any of the tasks from paragraph 1 of this Article, it shall inform in writing the Commission, the EMA and all competent authorities of other EU Member States and it shall make that information public.

(4) If the Agency performs the tasks from paragraph 1 of this Article for another EU Member State of the European Union, the costs shall be determined by the Agency.

Article 156

The costs of pharmacovigilance tasks carried out by the Agency shall be determined by the Agency and borne by the authorisation holder.

Article 157

(1) The Agency shall set up and maintain a national medicines web-portal which shall be linked to the European medicines web-portal of the EMA.

(2) By means of the national medicines web-portal from paragraph 1 of this Article, the Agency shall make publicly available the following data and documents:

- public assessment reports, together with a summary thereof,

- summaries of product characteristics and package leaflets,

- summaries of risk management plans,

- list of medicinal products subject to an additional post-authorisation follow-up,

- information on the different ways of reporting suspected adverse reactions to medicinal products to the Agency by healthcare professionals and patients/users of medicinal products, and forms, including the web-based structured forms,

- any other safety information important for use of medicinal products (news, letters to healthcare providers, etc.).

Article 158

(1) If the marketing authorisation holder intends to make a public announcement of information on pharmacovigilance that affects the use of a medicinal product, he shall be required to inform the Agency, the EMA and the European Commission in writing before the public announcement is made.

(2) If the marketing authorisation holder makes a public announcement relating to information from paragraph 1 of this Article, he shall ensure that information to the public is presented objectively and is not misleading.

Article 159

(1) The Agency may restrict the conditions and the measures for the prescription and supply for the medicinal products that are under the risk minimisation programme if it considers that the introduction of such restrictions is in the interest of patients and the safe use of these medicinal products.

(2) In the event from paragraph 1 of this Article, the Agency may lay down the conditions to be satisfied by healthcare providers in order to prescribe and supply these medicinal products.

Article 160

(1) Unless urgent public announcements are required for the protection of public health, the Agency shall inform the Ministry, other EU Member States and the European Commission not less than 24 hours prior to a public announcement relating to information on pharmacovigilance concerns.

(2) In cooperation with the EMA, the Agency shall release a common announcement on the safety of active substances contained in medicinal products that are authorised in more than one Member State of the European Union.

(3) Any information of a personal or commercially confidential nature from paragraphs 1 and 2 of this Article shall be omitted unless its public disclosure is necessary for the protection of public health.

Article 161

(1) Regarding authorised medicinal products, the Agency shall:

- monitor the outcome of risk minimisation measures contained in risk management plans and of the conditions referred to in Articles 46, 47 and 48 of this Act,

- assess updates to the risk management systems,

- monitor the data in the Eudravigilance database to determine whether there are new risks or whether risks have changed and whether those risks impact on the risk-benefit balance.

(2) In the event of new risks or risks that have changed or changes to the risk-benefit balance being detected, the Agency shall notify the EMA and the marketing authorisation holder.

(3) If the authorisation holder detects new risks or risks that have changed or changes to the risk-benefit balance, he shall notify the Agency and the EMA thereof.

Article 162

(1) The authorisation holder may conduct a non-interventional post-authorisation safety study, either voluntarily or pursuant to obligations imposed in accordance with Article 46 or Article 48 of this Act, and which involves the collection of safety data from patients or healthcare professionals.

(2) The costs of the study from paragraph 1 of this Article shall be borne by the authorisation holder.

(3) The study from paragraph 1 of this Article shall not be performed where the act of conducting the study promotes the use of a medicinal product.

(4) Payments to healthcare professionals for participating in studies from paragraph 1 of this Article shall be restricted to the compensation for time and expenses incurred.

(5) While a study from paragraph 1 of this Article is being conducted, the authorisation holder shall monitor the data generated and consider their implications for the risk-benefit balance of the medicinal product concerned.

(6) If the marketing authorisation holder has any new information which might influence the evaluation of the risk-benefit balance of the medicinal product, he shall file the application with the Agency for authorisation of variation in accordance with Articles 50, 51 and 52 of this Act.

(7) The authorisation holder shall file the application for authorisation of the variation from paragraph 6 of this Article without prejudice to obligation to enter the information on the results of the study from paragraph 1 of this Article in the periodic safety update reports.

Article 163

(1) The authorisation holder shall submit to the Pharmacovigilance Risk Assessment Committee a draft protocol of the safety study from Article 162, paragraph 1 of this Act, which is to be conducted pursuant to the obligations stipulated by Article 46 or Article 48 of this Act, except in the case referred to in paragraph 2 of this Article.

(2) The authorisation holder shall submit to the Agency a draft protocol of the safety study from Article 162, paragraph 1 of this Act, which is to be conducted only in the Republic of Croatia, subject to the request by the Agency in line with Article 48 of this Act.

(3) Within 30 days of the submission of the draft protocol referred to in paragraph 2 of this Article, the Agency shall:

a) provide a written notification of approval for the draft protocol or

b) provide a written notification about the shortfalls when:

- it considers that the conduct of the study promotes the use of a medicinal product,

- it considers that the design of the study does not fulfil the study objectives, or

c) provide a letter notifying the marketing authorisation holder that the study is a clinical trial falling under the scope of Directive 2001/20/EC.

(4) The study from paragraph 1 of this Article may commence in the Republic of Croatia subject to a written endorsement by the PRAC, and following the submission of the approved draft study protocol to the Agency by the authorisation holder.

(5) The study from paragraph 2 of this Article may commence following the written approval by the Agency.

Article 164

(1) After a study from Article 163, paragraph 1 of this Act has commenced, the marketing authorisation holder shall submit to the PRAC and obtain their written endorsement for any substantial amendments to the protocol, before their implementation.

(2) The marketing authorisation holder shall notify the Agency of any approved substantial amendments to the study protocol referred to in paragraph 1 of this Article prior to their implementation.

(3) Following the commencement of the study from paragraph 2 of Article 163 of this Act, the marketing authorisation holder shall submit to the Agency any substantial amendments to the draft study protocol and obtain their written approval prior to their implementation.

Article 165

(1) Upon the completion of the study from Article 163, paragraph 1 of this Act, the marketing authorisation holder shall submit, within 12 months from the end of data collection, a final study report and a summary of the study results to the PRAC, unless a written postponement or a written waiver has been granted by the PRAC.

(2) Upon the completion of the study from Article 163, paragraph 2, of this Act, the marketing authorisation holder shall submit, within 12 months from the end of data collection, a final study report and a summary of the study results to the Agency, unless a written postponement or a written waiver has been granted by the Agency.

(3) If the results of the studies referred to in paragraphs 1 and 2 of this Article have any impact on the marketing authorisation, the marketing authorisation holder shall submit an application to vary the marketing authorisation in accordance with Articles 50, 51 and 52 of this Act.

Article 166

If the results of the study from Article 163, paragraph 1 of this Act have an impact on the marketing authorisation in the Republic of Croatia, the Agency shall take necessary measures in respect of the marketing authorisation pursuant to the conclusions of the coordination group for MRP and CRP or in line with the decision of the European Commission.

Article 167

Urgent European Union procedure on the basis of data related to pharmacovigilance shall be conducted in accordance with the provisions of Articles 107.i, 107.j and 107.k of Directive 2001/83/EC.

Article 168

The marketing authorisation holder shall submit periodic safety update reports to the Agency immediately upon request or in accordance with the following time frames:

- where a medicinal product has not yet been placed on the market, at least every six months following authorisation and until the placing on the market,

- where a medicinal product has been placed on the market, at least every six months during the first two years following the initial placing on the market, once a year for the following two years and at three-yearly intervals thereafter.

Article 169

(1) For authorisations granted pursuant to Articles 29, 34, 63 and 68 of this Act, the marketing authorisation holder shall make available the periodic safety update reports to the Agency in the following cases:

- where such obligation has been laid down in accordance with Article 46 or 48 of this Act or

- based on the request by the Agency regarding the concerns relating to pharmacovigilance data or due to the lack of periodic safety update reports relating to an active substance after the marketing authorisation has been granted.

(2) The Agency shall submit the assessment reports of the requested periodic safety update reports from paragraph 1 of this Article to the PRAC.

Article 170

(1) The Agency shall specify the frequency with which the periodic safety update reports are to be submitted in the marketing authorisation, unless it is specified by the EURD list.

(2) The dates of submission of PSUR according to the specified frequency shall be calculated from the date of the authorisation.

(3) For authorisations which were granted before 21 July 2012, and for which the frequency and dates of submission of the periodic safety update reports are not laid down in the decision on granting of the marketing authorisation, marketing authorisation holders shall submit the periodic safety update reports in accordance with Article 168 of this Act.

(4) The obligation to submit PSUR in accordance with paragraphs 1 and 3 of this Article shall exist until a different frequency or different dates for the submission thereof are laid down in the decision on granting of the marketing authorisation or in line with the EURD list.

Article 171

(1) The Agency shall assess the PSUR in order to determine any new safety risks or changes to the risks or changes to the risk-benefit balance.

(2) Following the assessment from paragraph 1 of this Article, the Agency may request the marketing authorisation holder to initiate the authorisation variation procedure or it may, *ex officio* amend the marketing authorisation, suspend it or revoke it.

Article 172

(1) The Agency may participate in the work of the CMD(h) for the purpose of the common assessment of PSUR related to more than one marketing authorisation.

(2) If the assessment from paragraph 1 of this Article has an impact on the marketing authorisation in the Republic of Croatia, the Agency shall take necessary measures in respect of the authorisation in consultations with the CMD(h) or in line with the decision of the European Commission.

(3) If the assessment of the PSUR requires a variation of the authorisation, the marketing authorisation holder shall submit to the Agency an application for a variation, including an updated summary of product characteristics and package leaflet.

11. QUALITY CONTROL OF MEDICINAL PRODUCTS

Article 173

(1) Within the meaning of this Act, quality control shall apply to the procedure for establishing conformity of the medicinal product quality with its predefined quality specifications in accordance with this Act and regulations issued pursuant to this Act.

(2) The Agency is authorised for official quality control of medicinal products on the territory of the Republic of Croatia and is a member of the European Network of Official Medicines Control Laboratories.

(3) Quality control can be:

- regular

- special quality control

- quality control of medicinal products in distribution

- out-of-schedule quality control and

- quality control performed in the procedure for the granting and renewal of the marketing authorisation or in the procedure for authorisation of variations to the dossier of the medicinal product that are related to its quality specifications.

(4) The Minister shall issue an ordinance on the quality control method referred to in paragraph 1 of this Article.

(5) The costs of quality control from paragraph 3 of this Article shall be determined by the Agency subject to approval by the Minister.

Article 174

(1) The medicinal product manufacturer shall perform regular quality control of each batch of the medicinal product.

(2) For each batch of the medicinal product authorised in the Republic of Croatia the authorisation holder shall ensure that the batch is released on the market of the European Union.

(3) The authorisation holder shall ensure that each batch of the medicinal product authorised in the Republic of Croatia undergoes quality control in the European Union, except in the case referred to in Article 81, paragraph 5 of this Act.

Article 175

(1) The marketing authorisation holder must ensure that each batch of medicinal products derived from human blood or human plasma and of vaccines is subject to a special quality control.

(2) The Agency shall conduct a special quality control of each batch of the medicinal product derived from human blood or human plasma and of vaccines, unless any such batch is manufactured in other Member States of the European Union or in the states that are signatories to the mutual recognition procedure and in respect of which the competent authority conducted quality control and issued a certificate of quality control for the territory of the European Union (Official Control Authority Batch Release Certificate or hereinafter: OCABR Certificate).

(3) The Agency shall carry out quality control from paragraph 1 of this Article within 60 days of receipt of a duly filed application and prescribed documents.

(4) The costs of quality control from paragraph 1 of this Article shall be borne by the applicant for special quality control.

Article 176

(1) The Agency shall conduct quality control of medicinal products taken from distribution by the pharmaceutical inspection according to the schedule at least once in five years for each pharmaceutical form and each strength of the medicinal product.

(2) The Agency may conduct quality control of galenic preparations taken from distribution by the pharmaceutical inspection.

(3) The Agency shall conduct quality control within 60 days of receipt of the sample of the medicinal product or the galenic preparation from distribution.

(4) The costs of quality control and sampling of medicinal products or galenic preparations shall be borne by:

- the marketing authorisation holder or holder of the authorisation for parallel imports of the medicinal product, and by the wholesale distributor or the importer if the medicinal product is not authorised,

- the healthcare institution or the pharmacy which prepared the galenic preparation.

Article 177

(1) Out-of-schedule quality control shall be conducted on the request of the Ministry or the Agency in the event of any unusual signs or suspected quality defects or suspected falsified medicinal products or galenic preparations, and it shall be carried out by the Agency.

(2) The Agency shall conduct out-of-schedule quality control of the medicinal product or the galenic preparation within 60 days of receipt of samples and of the report on suspected quality defects.

(3) The costs of quality control of the medicinal product or the galenic preparation from paragraph 1 of this Article shall be borne by:

- the applicant for out-of-schedule quality control, i.e. the Ministry or the Agency, if the medicinal product or the galenic preparation is not defective

- the marketing authorisation holder or holder of the authorisation for parallel imports, and the wholesale distributor or the importer if the medicinal product is not authorised, in case of defective medicinal products

- the legal or natural person if he has caused quality defects of the medicinal product by its incorrect handling in production, preparation, distribution or warehousing

- the healthcare institution or the pharmacy which prepared the galenic preparation if the galenic preparation is defective.

(4) The costs of samples of the medicinal product or the galenic preparation shall be borne by the marketing authorisation holder and by the healthcare institution or the pharmacy which prepared the galenic preparation, respectively.

Article 178

(1) Quality control of the medicinal product conducted as part of the procedure for granting and renewing marketing authorisation, the procedure for granting authorisation for parallel imports and the procedure for authorisation of variations of the medicinal product dossier shall be conducted on the Agency's request if, according to Agency's opinion, it is necessary for making a decision.

(2) The costs of quality control from paragraph 1 of this Article shall be borne by the applicant.

Article 179

(1) The quality control methods given in the accepted medicinal product dossier, which is submitted with the application for marketing authorisation or the application for parallel imports, shall be used in the quality control of medicinal products. If such methods are not available, the methods adopted by the Agency shall be used.

(2) The scope of quality control of individual medicinal products shall be determined by the Agency.

(3) The quality of a medicinal product or raw materials for its manufacture, including raw materials for its immediate packaging, shall comply with the Croatian Pharmacopoeia, while the medicinal product shall be manufactured and subjected to quality control in accordance with procedures and requirements of the valid European Pharmacopoeia. Where a medicinal product is not included in either Croatian Pharmacopoeia or European Pharmacopoeia, its quality shall comply with a pharmacopoeia recognised in the European Union or with other internationally recognised standards.

Article 180

(1) The register of the performed quality control shall be kept by:

- marketing authorisation holders

- holders of authorisations for parallel imports

- wholesalers.

(2) The register of the performed quality control of the galenic preparation shall be kept by the healthcare institution or the pharmacy which prepared the galenic preparation.

(3) The Agency shall keep the register of all performed quality controls.

(4) The registers from paragraphs 1, 2 and 3 of this Article shall be kept for a year after the expiry of the shelf life of the pertaining medicinal product or galenic preparation.

(5) The contents and the method for keeping of registers from paragraphs 1, 2 and 3 of this Article shall be laid down by the Minister in an ordinance.

Article 181

(1) Healthcare professionals who come in contact with a medicinal product or with a user of the medicinal product, as well as legal and natural persons who manufacture or distribute medicinal products, shall inform the Agency in writing of any incompliance in the quality of the medicinal product brought to their attention.

(2) In the event of suspected falsified medicinal products, the persons from paragraph 1 of this Article shall notify the Agency of their suspicion within 24 hours.

(3) The ordinance on the method for monitoring incompliances in the quality of medicinal products shall be issued by the Minister.

12. ADVERTISING OF MEDICINAL PRODUCTS

Article 182

For the purposes of this Act, advertising of medicinal products shall include any form of information which is designed to promote its prescription, supply, sale or consumption and which is provided in a written, oral, pictorial, audio, electronic, digital or any other form.

Article 183

(1) Medicinal products referred to in Article 106, paragraph 2, subparagraphs 1 and 2 of this Act may be advertised in scientific literature, at symposia and conferences and to healthcare professionals.

(2) Medicinal products referred to in Article 106, paragraph 2, subparagraph 2 of this Act may be advertised to the public.

(3) The advertising of medicinal products referred to in Article 106, paragraph 2, subparagraph 1 of this Act to the public shall be prohibited.

(4) The prohibition contained in paragraph 3 of this Article shall not apply to public health campaigns for the promotion of vaccination, seroprophylaxis and chemoprophylaxis programmes drawn by the Minister in accordance with the Act on the Protection of the Population against Communicable Diseases.

(5) The advertising of any medicinal product unauthorised in the Republic of Croatia, except at symposia and conferences and in scientific literature and provided that the procedure for granting of the marketing authorisation pursuant to this Act has been instituted and that only common name of the medicinal product is used, without any mentioning of the manufacturer, shall be prohibited.

(6) Restrictions from paragraph 5 of this Article shall not apply to international conferences and symposia held in the Republic of Croatia.

Article 184

(1) The advertising of a medicinal product shall encourage the rational use of the medicinal product, by presenting it objectively, and it shall not been misleading.

(2) The method for advertising of a medicinal product shall be laid down by the Minister in an ordinance.

Article 185

The advertising of a product shall not contain any claim on its medicinal properties unless the product is authorised as a medicinal product or registered as a traditional herbal medicinal product.

13. SUPPLY OF THE CROATIAN MARKET WITH MEDICINAL PRODUCTS

Article 186

(1) The marketing authorisation holder, as well as any natural or legal person engaged in distribution of the concerned medicinal product on the territory of the Republic of Croatia, shall ensure, within the limits of their responsibilities, a suitable and continuous supply of medicinal products.

(2) The Agency shall be competent for monitoring the supply of medicinal products on the territory of the Republic of Croatia.

(3) In case of circumstances which could result in a disturbed supply of a medicinal product or its shortage on the Croatian market, the marketing authorisation holder shall forthwith

notify the Agency and the Ministry in writing. He shall also notify the Croatian Institute for Health Insurance (hereinafter: the Institute) if the medicinal product is included in its reimbursement list.

(4) The Ministry and the Agency shall take appropriate measures to ensure the regular supply of medicinal products in the Republic of Croatia.

Article 187

(1) The Agency shall monitor the consumption of medicinal products in the Republic of Croatia.

(2) The Agency shall submit a report on the consumption of medicinal products from paragraph 1 of this Article to the Minister and it shall propose measures to supervise their consumption to the Minister.

(3) The ordinance on the method for drafting reports and on types of data from paragraph 2 of this Article shall be issued by the Minister.

Article 188

(1) The marketing authorisation holder shall submit to the Institute the price proposal for a medicinal product included in the basic or the supplementary reimbursement list of the Institute, i.e. he shall submit the price proposal for a new medicinal product that is in the process of inclusion into the basic or the supplementary Institute's reimbursement list of medicinal products.

(2) The Institute is under obligation, based on the decision taken by the Institute's Administration Board, to adopt a decision on the proposed price of a medicinal product that is included in the basic or in the supplementary reimbursement list of the Institute or of a new medicinal product that is in the process of inclusion into the basic or the supplementary reimbursement list of the Institute within 90 days from the day of the receipt of a duly filed proposal.

(3) The decision adopted by the Institute, referred in paragraph 2 of this Article cannot be appealed, but administrative proceedings can be instituted against it.

(4) The Institute shall notify, on annual basis, the European Commission of the adoption of the basic and the supplementary reimbursement list of the Institute.

(5) The criteria and the method for the wholesale pricing of medicinal products as well as the reporting shall be laid down by the Minister in an ordinance.

Article 189

(1) The marketing authorisation holder for a medicinal product included in the basic or in the supplementary reimbursement list of the Institute may submit to the Institute a proposal for the increase of the price of the medicinal product concerned.

(2) Based on the proposal referred to in paragraph 1 of this Article and taking into account the need to ensure optimum supply of population with medicinal products that are necessary for

the provision of health care, the Institute shall request the Minister's consent for the price increase referred to in paragraph 1 of this Article.

(3) The Institute shall issue decisions about proposals referred to in paragraph 1 of this Article within 90 day from the day of the receipt of the proposal.

(4) The time-limit from paragraph 3 of this Article may be extended up to 60 days.

(5) The decision referred to in paragraph 3 of this Article cannot be appealed, but administrative proceedings can be instituted against it.

(6) Once a year the Institute shall provide to the European Commission the list of medicinal products approved for a price increase.

Article 190

(1) The marketing authorisation holder may submit a proposal to the Institute for the inclusion of a medicinal product into the basic, or into the supplementary reimbursement list of the Institute.

(2) In addition to the person referred to in paragraph 1 of this Article, the Institute's Committee for Medicinal Products, committees for medicinal products of various healthcare institutions and hospitals, expert groups of Croatian Medical Association and other professional bodies and referral centres of the Ministry may also submit proposals for a change of status or amendment of a therapeutic indication or a change of prescription guidelines for a medicinal product that is already included into the basic or the supplementary reimbursement list of the Institute.

(3) Where there is a justified need to administer a certain medicinal product, the Institute's Committee for Medicinal Products and the committees for medicinal products of various healthcare institutions / hospitals may propose the medicinal product to be added to the Institute's basic or the supplementary reimbursement list of medicinal products under its non-proprietary name.

(4) Subject to the decision taken by the Administration Board of the Institute, the Institute is obliged to adopt decisions about proposals referred to in paragraphs 1 and 2 of this Act within 90 days from the day of the receipt of the duly filed proposals.

(5) The time-limit for the adoption of the decision referred to in paragraph 4 of this Article, and the time-limit for the adoption of the decision referred to in Article 188 of this Act may not exceed cumulatively 180 days.

(6) The decision referred to in paragraph 4 of this Article cannot be appealed, but administrative proceedings can be instituted against it.

(7) The criteria for inclusion of medicinal products in the Institute's basic or supplementary reimbursement list of medicinal products shall be laid down by the Minister in an ordinance.

Article 191

(1) The decision on the removal of medicinal products from the Institute's basic or supplementary reimbursement list of medicinal products, on the basis of a previously obtained

opinion of the Institute's Committee for Medicinal Products, shall be taken by the Administration Board of the Institute.

(2) If a medicinal product is to be removed from the basic or the supplementary Institute's reimbursement list of medicinal products, and there is a justified need for its continued administering, the medicinal product may be added to the basic Institute's reimbursement list of medicinal products under its non-proprietary name.

(3) The decision on the removal of a medicinal product from the basic or the supplementary Institute's reimbursement list of medicinal products shall be adopted by the Institute.

(4) The decision referred to in paragraph 3 of this Article cannot be appealed, but administrative proceedings can be instituted against it.

Article 192

Natural and legal persons – holders of marketing authorisations for the wholesale distribution of medicinal products, shall sell the medicinal products included in the basic or the supplementary reimbursement list of the Institute at the prices set in accordance with the ordinance on the criteria and the method for pricing of medicinal products in wholesale distribution, and on the method for reporting thereon.

III. SUPERVISION

Article 193

(1) The supervision of the implementation of the provisions of this Act in respect of medicinal products, investigational medicinal products, active substances and excipients, and especially the supervision of testing, production and manufacture, distribution, brokering, quality control, quality control and advertising of medicinal products shall be carried out by the pharmaceutical inspectorate of the Ministry.

(2) The supervision of the implementation of the provisions of this Act in regard of supervision of the production of medicinal products, investigational medicinal products, active substances and excipients, and the supervision of pharmacovigilance shall be performed by the Agency.

(3) The activities of the pharmaceutical inspectorate referred to in paragraph 1 of this Article may be carried out by senior pharmaceutical inspectors and pharmaceutical inspectors.

(4) The costs of the supervision from paragraph 1 of this Article shall be laid down by the Minister.

Article 194

(1) The activities of a pharmaceutical inspector may be carried out by persons with undergraduate and graduate qualifications or integrated undergraduate and graduate qualifications in healthcare or other related field, a three-year experience in the relevant field and who have taken and passed the state qualifying exam.

(2) The activities of an Agency inspector may be carried out by persons with undergraduate and graduate qualifications or integrated undergraduate and graduate qualifications in healthcare or other related field, and with a three-year experience in the relevant field.

(3) The pharmaceutical inspectors shall be committed to continuing education in good laboratory practice, clinical trials and wholesale distribution of medicinal products.

(4) The Agency inspectors shall be committed to continuing education in good manufacturing practice and pharmacovigilance.

Article 195

The Minister may authorise experts in the field of medicinal products to perform certain professional activities while carrying out inspection if the inspection requires specific expertise.

Article 196

(1) Pharmaceutical inspectors and Agency inspectors shall have official identity cards and badges in evidence of their official capacity, identity and authority.

(2) The form and the contents of official identity cards and badges as well as the manner of issuance and maintenance of the register of issued official identity cards shall be laid down by the Minister in an ordinance.

Article 197

The pharmaceutical inspector and the Agency inspector shall be independent in conducting inspection and he shall conduct inspection, issue decisions and take measures within the limits of rights, obligations and authorities laid down by this Act and any other relevant regulation.

Article 198

Legal and natural persons shall enable the pharmaceutical inspector and the Agency inspector to carry out inspection and, at their request, make available the requisite quantity of samples of the medicinal product for the purpose of quality control and provide any necessary data and information.

Article 199

(1) When conducting an inspection, the pharmaceutical inspector and the Agency inspector shall have the right to:

- inspect business premises, facilities, installations, devices, equipment,

- inspect raw materials, active substances, excipients, intermediate products, medicinal products,

- inspect agreements, records and any other quality system documents or other business documents; if documents are supplied electronically, he may require to see them and have their printout,

- take copies of documents, subject to making the relevant note in the inspection report,

- take free samples of medicinal products and raw materials for quality control purposes,

- take and use free data from official records and other databases related to persons, if necessary for inspection,

- inspect personal documents for the purpose of identification,

- take photographs or record data on other visual media about persons, premises, facilities, installations, equipment and so on from subparagraph 1 of this paragraph for the purpose of presentation of evidence.

(2) In addition to the rights listed in paragraph 1 of this Article, the pharmaceutical inspector shall have the right to exclude from distribution medicinal products which do not comply with the provisions of this Act.

(3) The pharmaceutical inspector and the Agency inspector shall have the right to conduct unannounced inspections at any time.

Article 200

If the pharmaceutical inspector and the Agency inspector are physically prevented from carrying out the inspection, they may request help from the police.

Article 201

(1) In the performance of the inspection from paragraph 1 of Article 193 of this Act, the pharmaceutical inspector shall have both the right and duty to:

1. order the performance of activities in accordance with the conditions laid down by this Act and other regulations

2. order the removal of identified irregularities and deficiencies within a specified time limit

3. prohibit the performance of activities which are contrary to this Act and other regulations

4. temporarily prohibit the work to any legal or natural person who does not satisfy the conditions in respect of employees, equipment, instruments and pemises

5. prohibit the work to any natural or legal person engaged in testing, production and manufacture, distribution, brokering and quality control of medicinal products without the Agency's authorisation or licence

6. order the ban on placing of the medicinal product on the market:

- if the medicinal product is falsified,

- if the shelf life of the medicinal product has expired,

- if it has been established that the medicinal product is kept or handled contrary to regulations,

- in the cases where this Act stipulates product suspension and recall,

- prohibit the performance of a clinical trial of a medicinal product or the performance of a clinical trial at any individual investigation site if it is not performed in accordance with the provisions of this Act, regulations issued pursuant to this Act and principles of good clinical practice

7. file an application with the Agency for the suspension or recall of the batches which do not comply with the conditions laid down by this Act and other regulations

8. declare the product which is found defective as waste and order its handing over to the person authorised in accordance with the rules and regulations governing waste management

9. prohibit the work and submit a proposal to the Agency for the revocation of the authorisation for conducting the activity if noncompliance with the conditions laid down by this Act or any other regulation may jeopardise the life and health of people

10. prohibit the sale of the product if therapeutic indications are given on its immediate or outer packaging and the product is not authorised as the medicinal product or as the homeopathic medicinal product

11. prohibit the advertising of the product which is attributed medical indications and which is not a medicinal product within the meaning of this Act

12. prohibit the distribution of the product if it is established that it contains an active substance or a substance related to the active substance and it is not a medicinal product within the meaning of this Act

13. temporarily suspend the execution of the decision on the marketing authorisation for a medicinal product due to a violation of the provisions of this Act

14. order other measures to be taken as authorised by this Act and other regulations.

(2) In the performance of the inspection from paragraph 2 of Article 193 of this Act, the Agency inspector shall have both the right and duty to:

1. prohibit the work to any natural or legal person engaged in the production without the Agency's authorisation or licence

2. order the performance of activities in accordance with the conditions laid down by this Act and other regulations

3. order the removal of identified irregularities and deficiencies within a specified time limit

4. prohibit performance of activities that are contrary to this Act and other regulations

5. temporarily prohibit working to any legal or natural person who does not satisfy the conditions in respect of employees, equipment, instruments and premises

6. submit a proposal for revocation of the marketing authorisation if the marketing authorisation holder does not operate a pharmacovigilance system, have a person qualified for

pharmacovigilance or fulfil other pharmacovigilance tasks laid down by the provisions of this Act

7. order other measures to be taken as authorised by this Act and other regulations.

Article 202

If a sampled medicinal product is found to be defective during the inspection, the costs of quality control, recall or disposal of a defective medicinal product shall be borne by the natural or legal person who placed on the market or imported a defective medicinal product or by the natural or legal person who has caused defects by the inappropriate storage or handling of the medicinal product.

Article 203

When a pharmaceutical inspector and an Agency inspector discover during the inspection that a misdemeanour or a criminal act was committed by the infringement of regulations, they shall immediately, and within a maximum of 15 days after completion of the the inspection, file an information or a report to the competent authority.

Article 204

(1) The pharmaceutical inspector may also carry out inspections on the request of the Agency, the European Commission or the EMA in the Republic of Croatia, other Member States of the European Union or in third countries.

(2) The Agency inspector may also carry out inspections on the request of the Ministry, the European Commission or the EMA in the Republic of Croatia, in other Member States of the European Union or in third countries.

Article 205

(1) When conducting an inspection, the pharmaceutical inspector and the Agency inspector shall observe special confidentiality regulations.

(2) The legal or natural person shall explain the scope of confidentiality under the relevant bylaws to the pharmaceutical inspector and the Agency inspector.

Article 206

(1) The pharmaceutical inspector and the Agency inspector shall issue oral decisions in the following cases:

- where threat to human health or life requires immediate implementation of a certain measure

- where some evidence could be hidden, replaced or destroyed unless a measure is immediately taken.

(2) The pharmaceutical inspector and the Agency inspector may order immediate execution of their oral decision. The decision shall be entered in the inspection report.

(3) The pharmaceutical inspector and the Agency inspector shall draw up a written communication of the oral decision within eight days of passing the oral decision.

Article 207

No appeal can be filed against decisions of pharmaceutical inspectors and Agency inspectors, but an administrative action can be instituted.

Article 208

(1) The pharmaceutical inspector and the Agency inspector shall draw up reports on completed inspections, established status and taken or ordered measures, as well as on performed activities.

(2) A copy of the report referred to in paragraph 1 of this Article shall be sent to a natural person or a responsible person of the legal person whose premises were inspected.

Article 209

Activities of pharmaceutical inspectors and Agency inspectors shall be governed by the provisions of the Act on General Administrative Procedure.

Article 201

(1) Pharmaceutical inspectors and Agency inspectors shall keep registers of the performed inspections.

(2) The method for register keeping shall be laid down by the Minister in an ordinance.

Article 211

The pharmaceutical inspector and the Agency inspector shall be responsible for:

- any failure to take or order measures under their competence

- exceeding their authorities

- any failure to submit a claim or report to competent authorities about established irregularities or defects.

IV. THE AGENCY FOR MEDICINAL PRODUCTS AND MEDICAL DEVICES

Article 212

(1) The Agency shall engage in the following activities:

- grant marketing authorisations for medicinal products and homeopathic medicinal products

- carry out registration procedures for traditional herbal medicinal products and homeopathic medicinal products

- grant authorisations for parallel imports of medicinal products

- make expert assessments of quality, efficacy and safety of medicinal products

- perform laboratory analyses of medical devices

- perform tasks of the official laboratory for quality control for the Republic of Croatia

- perform quality control of medicinal products and homeopathic medicinal products, and issue certificates of quality control

- analyse and assess adverse reactions and safety of subjects in clinical trials

- prepare the Croatian Pharmacopoeia

- issue the Croatian Pharmacopoeia and other expert publications from its scope of work

- perform pharmacovigilance tasks

- grant manufacturing authorisations to manufacturers and importers of medicinal products and investigational medicinal products

- keep the register of manufacturers, importers and wholesale distributors of active substances and excipients

- grant authorisations for wholesale distribution of medicinal products

- grant authorisations for retail sale of medicinal products in specialised retail sale outlets

- grant authorisations for brokering of medicinal products

- give approval for entry and importation of medicinal products

- give approval for emergency entry and importation of medicinal products

- monitor adverse reactions and defects of medicinal products

- initiate procedures for the suspension of marketing of medicinal products and make product recalls

- monitor the supply of medicinal products

- monitor the consumption of medicinal products and promote their rational use

- propose measures to the Minister to supervise the consumption of medicinal products

- engage in waste management activities (for its own needs)

- ensure education and provide information on medicinal products

- provide expert advice from its scope of activities

- provide expert guidelines from its scope of activities

- propose harmonisation of regulations on medicinal products with those of the European Union as well as with the regulations and guidelines of international institutions

- establish international cooperation in the field of medicinal products

- carry out inspection of the manufacture of medicinal products, investigational medicinal products, active substances and excipients and the surveillance of pharmacovigilance

- keep the register of manufacturers of medical devices, the register of medical devices and the register of wholesale distributors of medical devices

- analyse and evaluate adverse events in clinical trials of medical devices

- grant authorisation for the retail sale of medical devices in specialised retail sale outlets

-keep the register of medical devices marketed in the Republic of Croatia

- operate a vigilance system for medical devices, and monitor safety of medical devices

- carry out the procedure for classification of medical devices

- issue certificates of free sale of medical devices

- ensure education and provide information about medical devices

- establish international cooperation in the field of medical devices

- propose harmonisation of regulations on medical devices with those of the European Union as well as with the regulations and guidelines of international institutions

- perform other tasks in the field of medicinal products in line with this Act and the ordinances issued pursuant to this Act and in the field of medical devices in accordance with the Medical Devices Act and ordinances issued pursuant to that Act.

(2) The representatives of the Agency shall participate in the work, i.e. the activities from paragraph 1 of this Article, of the European Union authorities active in the field of medicinal products and medical devices.

Article 213

(1) The Agency shall have its Statute, which shall define the organisational structure, authorities and decision making process of its individual bodies, as well as conditions and procedures for appointing the Head and regulating other issues of importance for the Agency's activities and operations.

(2) The Agency's Administration Board shall adopt the Statute subject to approval by the Government of the Republic of Croatia.

Article 214

(1) In addition to the Statute, the Agency shall have its by-laws in line with this Act and other regulations.

(2) The rights and obligations of the Agency's employees and other employment-related issues shall be laid down in the Labour Relations Bylaw.

(3) The Administration Board shall adopt the Labour Relations Bylaw and other bylaws of the Agency, unless this Act and the Statute require their adoption by the Agency's Head.

Article 215

The bodies of the Agency are the Administration Board, the Head, the Scientific Council and other bodies defined by the Statute.

Article 216

(1) The Agency shall be managed by its Administration Board.

(2) The Administration Board of the Agency shall consist of five members.

(3) The president and the members of the Administration Board shall be appointed by the Government of the Republic of Croatia on the proposal by the Minister.

(4) The members of the Administration Board shall be appointed for a four-year period.

Article 217

The Government of the Republic of Croatia may relieve a member of the Agency's Administration Board from his duty before the expiry of his term of office in the following cases:

- if the member himself demands to be relieved from duty

- if he seriously or repeatedly violates the law and other regulations related to the Agency's operations and activities

- if his work causes damage to the Agency

- in other cases laid down by law and the Statute.

Article 218

The Administration Board shall:

- adopt the Agency's Labour Relations Bylaw and other bylaws

- adopt the Agency's business and financial plans

- adopt the Agency's annual accounts and business reports

- appoint and relieve from duty the Agency's Head

- make decisions on the Agency's internal organisational structure

- make decisions on other issues defined in the Agency's Statute.

Article 219

(1) The Agency's Head shall manage the Agency's operations.

(2) The Agency's Head shall be appointed for a term of four years. After the expiry of his term of office, the Head may be re-appointed without restrictions on the number of his terms of office.

Article 220

The Agency's Head shall:

- run and manage the Agency's operations

- act as the Agency's agent and representative

- propose the adoption of regulations under his competence to the Administration Board

- make decisions on other matters defined by the Statute.

Article 221

The Administration Board shall relieve the Head from his duty before the expiry of his term of office if he:

- requests to be relieved

- fails to observe the Agency's regulations and bylaws

- unjustifiably refuses to implement decisions of the Agency's Administration Board issued within the limits of its competence

- causes substantial damage to the Agency by working in an unconscionable or inaccurate manner

- frequently neglects his duties or performs them an unconscionable manner thus causing difficulties in the Agency's operations.

Article 222

(1) The Agency's assets shall consist of operating funds which shall be provided by its founder, or acquired through the provision of services or acquired from other sources.

(2) The funds for the Agency's activities shall be provided from:

- the Agency's operating revenues (from the provision of services and from annual fees) and

- other sources in accordance with this Act and other regulations.

(3) The Agency shall charge annual fees for authorisations granted in accordance with the provisions of this Act and the Medical Devices Act.

(4) The amount of the annual fee from paragraphs 2 and 3 of this Article shall be defined by the Agency, subject to approval by the Minister, and shall be borne by legal or natural persons who have been granted authorisations pursuant to the provisions of this Act and the Medical Devices Act.

Article 223

Legal aspects of the Agency's operations shall be supervised by the Ministry.

Article 224

The Agency shall submit annual reports on its work to the Minister and to the Government of the Republic of Croatia.

Article 225

General labour regulations and the collective agreement shall govern the legal status of the Agency's employees, employment conditions, salaries and other issues that are not regulated by this Act.

V. PENAL PROVISIONS

Article 226

(1) Natural and legal persons shall be liable to a fine between HRK 100,000.00 and HRK 150,000.00 for the following misdemeanours:

1. for placing medicinal products on the market without performed trials or for conducting trials of medicinal products contrary to the provisions of this Act and regulations issued pursuant to this Act (Article 8, paragraph 1)

2. for failure to report to the Central Ethics Committee and the Ministry any substantial amendment to a clinical trial (Article 16, paragraph 1)

3. for conducting a clinical trial without informed consent of the trial subject (Article 17, paragraph 1)

4. for paying fees to investigators and trial subjects contrary to the provision of Article 18, paragraph 4 of this Act

5. for placing medicinal products on the market of the Republic of Croatia without the required marketing authorisation (Article 22, paragraphs 1, 3 and 5 and Article 113, paragraph 1)

6. for providing incorrect data in the dossier accompanying the marketing authorisation application (Article 26, paragraph 3 and Articles 28, 29, 32, 33, 34, 35 and 36)

7. for failing to satisfy the conditions and fulfil the obligations laid down by the provision of Article 46, paragraph 1, Article 47, paragraph 1 and Article 48, paragraph 1 of this Act

8. for failing to act in accordance with the provisions of Article 50 ,paragraph 1, and Articles 51 and 55 of this Act, after the granting of the marketing authorisation

9. for failing to suspend the placing of the medicinal product on the market or making a product recall (Article 62, paragraphs 6 and 7)

10. for placing traditional herbal or homeopathic medicinal products on the market without the Agency's authorisation or the Agency's decision on registration (Articles 63 and 66, and Article 68, paragraph 1)

11. for providing incorrect data in the dossier accompanying the application for entry in the register of homeopathic medicinal products (Article 69, paragraphs 2 and 3)

12. for manufacturing medicinal products, investigational medicinal products, active substances or excipients in the Republic of Croatia without the manufacturing authorisation (Article 72)

13. for providing incorrect data in the application for manufacturing authorisation and for failing to inform the Agency about any changes of data on the grounds of which the manufacturing authorisation has been granted (Article 75, paragraph 2 and Article 79, paragraph 1)

14. for engaging in import of medicinal products contrary to the provision of Article 81 of this Act

15. for failing to comply with the requirements of good manufacturing practice for active substances in the manufacture of active substances (Article 82 of this Act)

16. for importing active substances contrary to the provision of Article 83 of this Act

17. for failing to label a radiopharmaceutical in accordance with the provision of Article 103 of this Act

18. for providing therapeutic indications on immediate and outer packaging of the product and in its package leaflet if this product is not authorised as a medicinal product or a homeopathic medicinal product (Article 105)

19. for engaging in wholesale distribution or retail sale without the appropriate authorisation (Article 115, Article 119, paragraph 1 and Article 135)

20. for engaging in brokering of medicinal products without the appropriate authorisation (Article 116)

21. for not being authorised for parallel imports of medicinal products (Article 130, paragraph 1)

22. for dispensing medicinal products in outlets different than those given in the marketing authorisation (Article 135, paragraphs 2 and 3);

23. for offering medicinal products not subject to medical prescription for distance selling over the Internet contrary to the provisions of this Act and regulations issued pursuant to this Act (Article 136, paragraphs 1, 2 and 3)

24. for failing to carry out regular quality control of every batch of medicinal products (Article 174, paragraph 1)

25. for failing to ensure releasing of a batch of a medicinal product on the market of the European Union for each batch of the medicinal product authorised for marketing in the Republic of Croatia (Article 174, paragraph 2)

26. for failing to ensure conducting of quality control in the European Union for each batch of the medicinal product authorised for marketing in the Republic of Croatia (Article 174, paragraph 3)

27. for failing to subject a medicinal product to a special quality control (Article 175, paragraph 1)

28. for advertising medicinal products contrary to the provisions of this Act and regulations issued pursuant to this Act (Article 183)

29. for claiming that the product has medicinal properties in the advertisement if the concerned product is not authorised as a medicinal product or registered as a traditional herbal medicinal product (Article 185)

30. for acting contrary to the provision of Article 186, paragraphs 1 and 3 of this Act

31. for not selling medicinal products at the prices set in accordance with the ordinance on the criteria and the method for pricing of medicinal products in wholesale distribution, and on the method for reporting thereon (Article 192)

32. for failing to enable a pharmaceutical inspector and an Agency inspector to carry out inspection in accordance with the provisions of this Act and regulations issued pursuant to this Act (Articles 198 and 199)

33. for failing to act, within the time limit, in accordance with the final decision issued by the pharmaceutical inspector and the Agency inspector, ordering them to take certain measures and actions or prohibiting them to continue working (Article 201).

(2) For misdemeanours referred to in paragraph 1 of this Article the responsible persons of legal persons shall also be liable to a fine between HRK 10,000.00 and HRK 15,000.00.

Article 227

(1) Natural and legal persons shall be liable to a fine between HRK 70,000.00 and HRK 100,000.00 for the following misdemeanours:

1. for conducting unauthorised clinical trials of medicinal products or non-interventional trials of medicinal products (Article 9, paragraph 2 and Article 12, paragraphs 2 and 3)

2. for conducting or allowing clinical trials of medicinal products contrary to the provision of Article 18, paragraph 2 of this Act

3. for distributing medicinal products whose marketing authorisations are not valid (Article 53, paragraph 1)

4. for advertising homeopathic medicinal products from Article 71, paragraphs 3 and 4, of this Act

5. for manufacturing, importing or delivering active substances without registration in the register of manufacturers, importers or wholesale distributors of active substances (Article 84)

6. for providing incorrect data in dossier accompanying the application for registration in the register of manufacturers, importers or wholesale distributors of active substances (Article 85, paragraph 2)

7. for failing to file annual reports to the Agency about all changes in documents and data on the basis of which the manufacturer, importer or wholesale distributor of active substances was registered in the register or for failing to file an application for variation/s (Article 88, paragraphs 1 and 2)

8. for placing a medicinal product on the market of the Republic of Croatia which is not labelled or does not contain a package leaflet in accordance with the provisions of this Act and regulations issued pursuant to this Act (Articles 92, paragraphs 1 and 2, Article 93, paragraphs 2 and 3, Article 95, Article 96, paragraph 1 and Article 98, paragraphs 1 and 2)

9. for failing to check with target patient groups if the package leaflet is legible, clear and easy to use (Article 98, paragraph 4)

10. for failing to provide a detailed package leaflet with a radiopharmaceutical (Article 104)

11. for dispensing a medicinal product in a manner and at the place other than that given in the marketing authorisation (Articles 106 and 107)

12. for failing to ensure transportation, holding and storage of medicinal products in accordance with defined conditions (Article 114, paragraph 1)

13. for failing to notify the Agency about the beginning of performing operations on the territory of the Republic of Croatia (Article 121)

14. for failing to notify the Agency about any changes to the conditions, documents and data on the basis of which the authorisation for wholesale distribution or brokering has been granted (Article 126, paragraphs 1 and 2)

15. for entry or import a medicinal product without the required authorisation (Article 128, paragraphs 1 and 2 and Article 129, paragraph 1)

16. for failing to notify the Agency and the marketing authorisation holder 15 days prior to the entry of the medicinal product on the basis of the authorisation for parallel imports (Article 131)

17. for failing to notify the Agency about all changes to the dossier and to the documents and data on the basis of which the authorisation for parallel imports of the medicinal product has been granted (Article 134, paragraph 1)

18. for failing to notify the Agency about all changes related to the conditions, documents and data based on which the authorisation has been granted (Article 140, paragraph 1)

19. for failing to submit data about sale of medicinal products to the Agency (Article 141, paragraph 1)

20. for failing to act in accordance with Article 143 of this Act

21. for failing to establish the pharmacovigilance system for the performance of pharmacovigilance tasks in accordance with Article 147 and Article 148, paragraph 1 of this Act

22. for failing to fulfil the obligations from Article 150 of this Act

23. for failing to fulfil the obligation from Article 151, paragraphs 1, 2, 3 and 4 and Article 152 of this Act

24. for failing to notify the Agency in writing prior to the public announcement of information on pharmacovigilance relating to administering of a medicinal product (Article 158)

25. for failing to act in accordance with the provisions of Article 163, paragraphs 1 and 2, Article 164 and Article 165 of this Act

26. for failing to submit PSUR to the Agency in defined cases and within specified time limits (Articles 168 and Article 169, paragraph 1)

27. for placing a medicinal product on the Croatian market if its quality, including the quality of all raw materials for its production and materials for immediate packaging, does not comply with the Croatian Pharmacopoeia or other pharmacopoeias as referred to in Article 179, paragraph 3, of this Act

28. for failing to maintain the register of regular, special and out-of-schedule quality controls in accordance with the provisions of this Act and regulations issued pursuant to this Act (Article 180, paragraphs 1, 2 and 4).

(2) For misdemeanours referred to in paragraph 1 of this Article, responsible persons of legal persons shall also be liable to a fine between HRK 7,000.00 and HRK 10,000.00.

Article 228

(1) Any legal or natural person who provides incorrect data during the procedure for issuance of the authorisation for entry or import of a medicinal product which has not obtained the marketing authorisation in the Republic of Croatia shall be liable to a fine between HRK 50,000.00 and HRK 70,000.00 (Article 129, paragraph 1).

(2) For a misdemeanour from paragraph 1 of this Article, a responsible person of the legal person shall be also liable to a fine between HRK 5,000.00 and HRK 7,000.00.

(3) A medical doctor or a dental medicine doctor who prescribes a medicinal product in respect of which the marketing authorisation has not been granted in the Republic of Croatia, contrary to Article 129, paragraph 1 and the ordinance referred to in Article 129, paragraph 2, of this Act, shall be liable to a fine between HRK 5,000.00 and HRK 7,000.00.

Article 229

(1) Natural and legal persons shall be liable to a fine between HRK 30,000.00 and HRK 50,000.00 for the following misdemeanours:

1. for placing on the market a homeopathic medicinal product which is not labelled and does not have a package leaflet in accordance with the provisions of this Act (Article 70 and Article 71, paragraphs 1 and 2)

2. for failing to notify the Agency in writing about adverse reactions and the Agency and the Croatian Institute of Public Health in case of vaccines, in conformity with the provisions of this Act and regulations issued pursuant to this Act (Article 145, paragraphs 1, 2 and 3)

3. for failing to notify the Agency in writing about the incompliance of a medicinal product quality or suspected falsified medicinal product contrary to Article 181, paragraphs 1 and 2 of this Act and the ensuing ordinance.

(2) The responsible person of the legal person shall also be liable to a fine between HRK 3,000.00 and HRK 5,000.00 for a misdemeanour referred to in paragraph 1 of this Article.

VI. TRANSITIONAL AND FINAL PROVISIONS

Article 230

In accordance with Article 6 of this Act, the Agency shall issue a list of interchangeable medicinal products within 18 months from the day of entry into force of this Act.

Article 231

In the procedure for renewal of the marketing authorisation or the authorisation of variations to terms of the marketing authorisation, the Agency shall assign the number from Article 38 of this Act to medicinal products authorised until the day of entry into force of this Act.

Article 232

For medicinal products authorised pursuant to the Medicinal Products Act (Official Gazette 71/07, 45/09 and 124/11), whose marketing authorisations will cease to be valid in the period from 1 January 2014 to 31 March 2014, marketing authorisation holders shall file an application for renewal of the marketing authorisation with the Agency not later than six months prior to the expiry of its validity.

Article 233

For medicinal products authorised in the Republic of Croatia before the entry into force of this Act, Commission Regulation (EC) No 1234/2008 shall apply to applications for authorisation of variations submitted in the period from 1 July 2013 to the entry into force of the provisions of Commission Regulation (EU) No 712/2012 which are related to the authorisation of variations for medicinal products authorised under the national procedure.

Article 234

(1) On the day of entry into force of this Act, the Agency shall initiate the procedure for the revocation of marketing authorisations granted pursuant to the Medicinal Products Act (Official Gazette 71/07, 45/09 and 124/11) for medicinal products authorised in the European Union under the centralised procedure.

(2) A batch of the medicinal product from paragraph 1 of this Article, manufactured in line with the marketing authorisation granted prior to the entry into force of this Act, may be entered and marketed in the Republic of Croatia until the expiry of its shelf life or within a maximum of 12 months after the day of entry into force of this Act.

Article 235

(1) For a reference medicinal product for which an application for the first marketing authorisation under the centralised procedure was submitted before 20 November 2005, a ten-year data exclusivity period pursuant to Article 29, paragraph 1 of this Act shall apply and data exclusivity periods from Article 29, paragraphs 1, 2 and 3 of this Act shall not apply.

(2) For a reference medicinal product for which an application for the first marketing authorisation was submitted in an individual Member State of the European Union prior to the date defined as the data exclusivity period by the regulation of that EU Member State in accordance with Article 29, paragraphs 1, 2 and 3, of this Act, the data exclusivity period lasting six or ten years pursuant to the protection period from Article 29, paragraph 1 of this Act, shall apply depending on the regulation of an EU Member State valid at that time, while the data exclusivity periods form Article 29, paragraphs 1, 2 and 3 of this Act shall not apply.

Article 236

(1) On the day of entry into force of this Act, the Agency shall initiate the procedure for the revocation of marketing authorisations granted pursuant to the Medicinal Products Act (Official Gazette 71/07, 45/09 and 124/11) if the data exclusivity period for a reference medicinal product authorised in the European Union under the centralised procedure has not expired.

(2) A batch of the medicinal product authorised pursuant to the Medicinal Products Act (Official Gazette 71/07, 45/09 and 124/11) shall not be released on the market after the entry into force of this Act if the data exclusivity period pursuant to Article 29, paragraphs 2 and 3, of this Act for a reference medicinal product authorised in the European Union under the centralised procedure has not expired.

Article 237

(1) In accordance with the provisions of this Act, an application for marketing authorisation or for issuance of a decision shall be filed not later than six months following the day of entry into force of this Act for those homeopathic medicinal products for which the Agency has not granted marketing authorisations or issued decisions on the entry in the register pursuant to the Medicinal Products Act (Official Gazette 71/07, 45/09 and 124/11) as with the day of entry into force of this Act.

(2) Holders of the registration in the register of homeopathic medicinal products in accordance with the provisions of previous regulations shall procure, in the procedure for variation and renewal of the registration in the register of homeopathic medicinal products, a decision on the registration of the homeopathic medicinal product in accordance with this Act.

Article 238

Wholesale distributors and manufacturers of medicinal products, who are engaged in the manufacture and wholesale distribution of medicinal products on the day of entry into force of

this Act, shall harmonise their operations with the provisions of this Act and the ensuing regulations within 12 months after the entry into force of this Act.

Article 239

(1) Holders of marketing authorisations granted on the basis of the Ordinance on special conditions for placing medicinal products authorised in the Member States of the European Union on the market of the Republic of Croatia (Official Gazette 10/08) may institute the abbreviated repeated procedure not later than 12 months after the day of entry into force of this Act.

(2) Before the procedure from paragraph 1 of this Article has been instituted, marketing authorisation holders shall act in line with the provisions of the ordinance referred to in paragraph 1 of this Article.

Article 240

Legal persons that on the day of entry into force of this Act, perform the activity of import/export of medicinal products shall have to align their business operations with the provisions of this Act, within maximum 90 days from the day of entry into force of this Act.

Article 241

(1) Authorisation holders for the marketing of medicinal products included in the List of medicinal products in Appendix V to the Treaty of Croatia's Accession to the European Union, in the context of the process of the first renewal of the authorisation, shall have to submit to the Agency an application for an upgrade of the medicinal product dossier not later than three years from the day of accession of the Republic of Croatia to the European Union.

(2) The Agency shall revoke by a decision the marketing authorisation to any authorisation holder who fails to act in accordance with the provision of paragraph 1 of this Article, or who fails to upgrade the medicinal product dossier.

Article 242

(1) The Minister shall issue the ordinances referred to in Article 6, paragraph 4, Article 7, paragraph 2, Article 8, paragraph 3, Article 13, Article 18, paragraph 1, Article 26, paragraph 7, Article 43, paragraph 9, Article 52, paragraph 5, Article 53, paragraph 6, Article 56, paragraph 3, Article 60, paragraph 4, Article 62, paragraph 8, Article 63, paragraph 6, Article 69, paragraph 4, Article 73, paragraph 2, Article 74, paragraphs 2 and 3, Article 83, paragraph 5, Article 89, paragraph 2, Article 92, paragraph 2, Article 94, paragraph 5, Article 98, paragraph 5, Article 100, paragraph 4, Article 108, paragraph 3, Article 114, paragraph 2, Article 118, paragraph 4, Article 120, paragraph 3, Article 127, paragraph 2, Article 128, paragraph 3, Article 129, paragraph 2, Article 135, paragraph 4, Article 136, paragraph 4, Article 141, paragraph 2, Article 142, Article 145, paragraph 4, Article 173, paragraph 4, Article 180, paragraph 5, Article 181, paragraph 3, Article 184, paragraph 2, Article 188, paragraph 5, Article 190, paragraph 7, Article 196, paragraph 2 and Article 210, paragraph 2 of this Act, the adoption of which is by virtue of this Act entrusted to him, within 12 months from the day of entry into force of this Act.

(2) Ordinances related to safety feature of the medicinal product and sale at a distance shall be issued by the Minister after the issuance and the entry into force of the implementing

regulations regarding the safety feature of the medicinal product and sale at a distance in the European Union.

Article 243

Until the entry into force of ordinances from Article 242 of this Act, the following regulations shall remain in force:

1. Ordinance on the procedure and the method for granting marketing authorisations for medicinal products (Official Gazette 113/08 and 155/09)

2. Ordinance on special conditions for placing medicinal products authorised in the Member States of the European Union on the market of the Republic of Croatia (Official Gazette 10/08)

3. Ordinance on the licensing requirements for specialised stores for retail sale of medicinal products (Official Gazette 134/08 and 119/10)

4. Ordinance on the conditions and the procedure for establishing requirements of good manufacturing practice and the procedure for issuing manufacturing authorisations and certificates of good manufacturing practice (Official Gazette 74/09)

5. Ordinance on the manner of advertising medicinal products and homeopathic medicinal products (Official Gazette. 118/09 and 140/09)

6. Ordinance on pharmacovigilance (Official Gazette 125/09)

7. Ordinance on the criteria for the classification of medicinal products and on the prescription and dispensation of prescription medicinal products (Official Gazette 82/10)

8. Ordinance on the marketing, labelling and advertising of traditional herbal medicinal products (Official Gazette 89/10)

9. Ordinance on clinical trials of medicinal products and good clinical practice (Official Gazette 14/10 and 127/10)

10. Ordinance on quality control methods for medicinal products (Official Gazette 56/05)

11. Ordinance on the method for monitoring of deficiencies in medicinal products quality (Official Gazette 36/05)

12. Ordinance on the type of data and reporting on the distribution of finished medicinal products (Official Gazette 29/05)

13. Ordinance on the conditions of manufacture, placing on the market, quality control methods and keeping the register of homeopathic medicinal products (Official Gazette 62/05)

14. Ordinance on good practice in the wholesale distribution of medicinal products (Official Gazette 29/05)

15. Ordinance on the conditions and the procedure of obtaining the authorisation for the wholesale distribution of medicinal products and the import and export of medicinal products (Official Gazette 29/05)

16. Ordinance on good laboratory practice (Official Gazette 73/12)

17. Ordinance on bioavailability and bioequivalence studies of medicinal products (Official Gazette 71/99)

18. Ordinance on the pricing criteria in the wholesale distribution of medicinal products and on methods for reporting on wholesale prices (Official Gazette 155/09 and 22/10)

19. Ordinance on the criteria for the inclusion of medicinal products into the basic and the supplementary reimbursement lists of medicinal products of the Croatian Institute for Health Insurance (Official Gazette 155/09).

Article 244

The Medicinal Products Act (Official Gazette 71/07, 45/09 and 124/11) shall cease to have effect on the day of entry into force of this Act.

Article 245

This Act shall be enter into force on the eighth day after the day of its publication in the Official Gazette, with the exception of Articles 1 to 25, Article 26, paragraphs 1 to 6, Articles 27 to 42, Article 43, paragraphs 1 to 8, Articles 44 to 51, Article 52, paragraphs 1 to 4, Article 53, paragraphs 1 to 5, Articles 54 and 55, Article 56, paragraphs 1 and 2, Articles 57 to 59, Article 60, paragraphs 1 to 3, Articles 61 to 68, Article 69, paragraphs 1 to 3, Articles 70 to 72, Article 73, paragraph 1, Article 74, paragraph 1, Articles 75 to 82, Article 83, paragraphs 1 to 4, Articles 84 to 88, Article 89, paragraph 1, Articles 90 to 93, Article 94, paragraphs 1 to 4, Articles 95 to 97, Article 98, paragraphs 1 to 4, Article 99, Article 100, paragraphs 1 to 3, Articles 101 to 107, Article 108, paragraphs 1 and 2, Articles 109 to 113, Article 114, paragraph 1, Articles 115 to 119, Article 120, paragraphs 1 and 2, Articles 121 to 126, Article 127, paragraph 1, Articles 128 to 144, Article 145, paragraphs 1 to 3, Articles 146 to 187, Article 188, paragraphs 1 to 4, Article 189, Article 190, paragraphs 1 to 6 and Articles 191 to 244, which shall enter into force on the day of accession of the Republic of Croatia to the European Union, and Article 55, paragraphs 4 and 5 which shall enter into force on 28 October 2013.

Class: 022-03/13-01/122

Zagreb, 14 June 2013

THE CROATIAN PARLIAMENT

President

of the Croatian Parliament

Josip Leko, m.p.