

THE CROATIAN PARLIAMENT

2181

Pursuant to Article 88 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 21 June 2007.

Class: 011-01/07-01/59
Reg. No.: 71-05-03/1-07-2
Zagreb, 27 June 2007

The President
of the Republic of Croatia
Stjepan Mesić, m.p.

MEDICINAL PRODUCTS ACT

I GENERAL PROVISIONS

Article 1

With a view to ensure efficacy, quality and safety of medicinal products as products of special importance for the protection of human health, this Act lays down the procedures for testing, placing on the market, manufacture, labelling, classification, distribution, pharmacovigilance, advertising and information, supervision, and quality control of medicinal products.

This Act also establishes conditions and methods for placing on the market and control of homeopathic medicinal products.

Article 2

For the purposes of this Act, the following definitions apply:

1. *Medicinal product* means any substance or combination of substances intended for treating or preventing disease in human beings; or any substance or combination of substances which may be 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 making a medical diagnosis,
2. *Substance* referred to in item 1 of this Article may be of the following origins:
 - human, e.g. human blood and human blood products;
 - animal, e.g. micro-organisms, animals, parts of organs, animal secretions, toxins, extracts, blood product;
 - vegetable, e.g. micro-organisms, plants, parts of plants, vegetable secretions, vegetable extracts;

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

3. *Active substance* means any substance conferring a drug product action,

4. *Excipient* means any substance that instead of conferring a drug product action:

– assists in giving a pharmaceutical form to a drug product;

– protects, supports and improves stability, bioavailability and tolerance of a medicinal product;

– assists in drug product identification,

5. *Raw material* means any substance of specified quality intended for a drug product manufacture,

6. *Drug product* means any medicinal product that is industrially manufactured in order to be placed on the market,

7. *Galenic preparation* means any medicinal product of verified quality, manufactured in a galenic laboratory of a pharmacy according to the procedure provided in the current pharmacopoeia or the relevant literature and GMP (Good Manufacturing Practice) standards for galenic laboratories,

8. *Officinal formula* means any medicinal product prepared in a pharmacy in accordance with a prescription for an individual patient,

9. *Name of the medicinal product* means 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 manufacturer or the marketing authorisation holder. The invented name shall be different from and shall not be liable to confusion with the common name,

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

11. *Immunological medicinal product* means any medicinal product that is or consists of vaccines, toxins, serums or allergen products.

Vaccines, toxins and serums shall cover in particular:

– agents used to produce active immunity, such as vaccines against cholera, BCG, polio, small pox;

– agents used to diagnose the state of immunity, including in particular tuberculin and tuberculin PPD, toxins for Schick and Dick tests, brucellin;

– agents used to produce passive immunity, such as diphtheria antitoxin, globulin against small pox, antilymphocytic globulin.

Allergen product means any medicinal product that 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* means medicinal products based on blood constituents including, in particular, albumin, coagulating factors and immunoglobulins of human origin,

13. *Radiopharmaceutical* means any medicinal product that contains one or more radionuclides (radioactive isotopes), intended for medical use,

14. *Radionuclide generator* means 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* means any radioactive substance in a tightly sealed container used for external radiation treatment,

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

17. *Radionuclide precursor* means any radionuclide produced for the radiolabelling of another substance prior to administration,
18. *Homeopathic medicinal product* means any medicinal product prepared from substances or combination of 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 Member States; a homeopathic medicinal product may contain a number of principles,
19. *Herbal medicinal product* means 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* means a herbal medicinal product whose efficacy and safety can be recognised on the basis of its long-term use in the Republic of Croatia or the European Union, and that fulfils the conditions laid down in this Act,
21. *Herbal substances* means whole or fragmented or cut plants, plant parts, algae, lichen, fungi, in a dried or fresh form; 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* means preparations obtained by subjecting herbal substances to treatments such as fractionation, extraction, fermentation, distillation, purification, concentration. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates,
23. *Quality of the medicinal product* means the acceptable physical, chemical, biological, pharmaceutical and technological, as well as any other property of a medicinal product,
24. *Safety of the medicinal product* means the acceptable relation between efficacy and harmfulness of a medicinal product,
25. *Efficacy of the medicinal product* means the ability of a medicinal product verified in clinical trials conducted in compliance with this Act,
26. *Risks related to the use of the medicinal product* means:
- any risk relating to the quality, safety or efficacy of the medicinal product as regards patients' health or public health;
 - any risk of undesirable effects on the environment,
27. *Risk-benefit balance* means an evaluation of the positive therapeutic effects of the medicinal product in relation to the risks as defined in item 26 of this Article,
28. *Testing of the medicinal product* means the procedure for establishing quality, safety and efficacy of a medicinal product,
29. *Clinical trial* means any investigation in human subjects which is carried out in line with the protocol and which is intended to discover or verify the pharmacokinetic and pharmacodynamic properties of one or more investigational medicinal product(s); and/or to discover any adverse reactions to one or more investigational medicinal product(s) or their interactions; for the purpose of defining its (their) safety and/or efficacy,
30. *Protocol* means a document that describes the objective(s), design, methodology, statistical considerations and organisation of a trial. The term protocol refers to the protocol, successive versions of the protocol and protocol amendments,
31. *Sponsor* means any legal or natural person which takes responsibility for the initiation, management and/or financing of a clinical trial,
32. *Clinical trial applicant* means a sponsor seated in the Republic of Croatia or any legal person seated in the Republic of Croatia and registered for the performance of mediation activities relating to clinical trials who, on behalf of the sponsor and by virtue of a power of attorney, files the application for a clinical trial,

33. *Investigational medicinal product* means a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation 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,
34. *Testing of safety of the medicinal product after its placing on the market* means any pharmaco-epidemiologic or clinical trial conducted in line with the marketing authorisation and intended to determine or measure any possible safety risk of the authorised medicinal product,
35. *Non-interventional trial* means a study where the medicinal product(s) is (are) prescribed in the usual manner 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 medicine is clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures shall be applied to the patients and epidemiological methods shall be used for the analysis of collected data,
36. *Non-interventional trial applicant* means a holder of the marketing authorisation,
37. *Pharmaceutical testing of the medicinal product* means any physicochemical, biological and/or microbiological testing to determine the quality of the medicinal product,
38. *Sample of the medicinal product* means any quantity of the drug product requisite for pharmaceutical testing,
39. *Reference standard* means any material or substance whose property or properties is used in pharmaceutical testing,
40. *Pre-clinical test* means any toxicological and pharmacological testing to determine pharmacodynamic, pharmacokinetic and toxicological properties of the medicinal product in animals and other appropriate models,
41. *The Central Ethics Committee* means an independent body consisting of medical professionals and other non-medical members whose responsibility is to ensure the protection of rights, safety and well-being of clinical trial subjects and to provide assurance of that protection by, among other things, giving opinions on trial protocols, suitability of investigators, legal persons on whose premises trials are conducted, equipment, methods and documents to be used for informing the trial subjects and obtaining their informed consents. The minister in charge of health shall appoint the Central Ethics Committee (hereinafter: “the Minister”),
42. *Bioavailability* means the rate and the degree of availability of the active substance from a drug product (dosage form) determined according to the concentration-time curve in general circulation or excretions,
43. *Bioequivalent medicinal products* means pharmaceutical equivalents or pharmaceutical alternatives whose bioavailability after administration of the same molar dose is similar to the extent that it may be expected to produce basically the same effect, including efficacy and safety,
44. *Bioequivalence* means that two medicinal products, which are pharmaceutical equivalents or pharmaceutical alternatives, have similar bioavailability when administered at the same molar dose to the extent that basically the same effect, including efficacy and safety, can be expected,
45. *Pharmaceutical equivalents* means drug products containing the same active substance(s) in the same quantity and of the same dosage form, administered by the same route and complying with the same or comparable standards,

46. *Pharmaceutical alternatives* means drug products containing the same active substance but in the form of a different salt, ester and the like, or in a different pharmaceutical form or of a different strength,
47. *Good laboratory practice* means a quality system related to organisational processes and conditions which must be observed for designing, conducting, controlling, reporting and documentation of pre-clinical tests related to safe administration with respect to human health and the environment,
48. *Good clinical practice* means a set of internationally recognised ethical and scientific requirements which must be observed for designing, conducting, recording and reporting clinical trials,
49. *Informed consent* means a signed and dated consent of a trial subject given in writing, which proves the subject's willingness to participate in a clinical trial, after having received appropriately documented information on the nature and significance, as well as involved consequences and risks. If a subject is incapable of giving such a consent or is a minor, his legal representative or a guardian may sign an informed consent,
50. *Immediate packaging* means the container or other form of packaging immediately in contact with the medicinal product,
51. *Outer packaging* means a packaging into which the immediate packaging is placed,
52. *Summary of the Product Characteristics* means expert information on a drug product approved in an authorisation procedure and intended for physicians, dental medicine doctors and pharmacists. Also used as a source of information for drawing up package leaflets for end users, labelling of medicinal products, and for verification of advertising,
53. *Labelling* means any set of data provided on the immediate or outer packaging,
54. *Package leaflet* means a leaflet containing information for the user, which accompanies the medicinal product,
55. *Original medicinal product* means the first world-wide version of a medicinal product authorised for placing on the market on the grounds of complete efficacy, safety and quality documentation which complies with requirements in force,
56. *Reference medicinal product* means a medicinal product authorised in the Republic of Croatia or in the European Union on the basis of the complete documentation on efficacy, safety and quality in line with valid requirements,
57. *Generic medicinal product* means 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. 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; the various immediate-release oral pharmaceutical forms shall be considered to be one and the same pharmaceutical form,
58. *Medicinal product with a well-established medicinal use* means a medicinal product containing active substance or substances that has or have had a well-established medicinal use with recognised efficacy and an acceptable level of safety for at least ten years following the first systematic and documented use in the Republic of Croatia or the European Union,
59. *Biological medicinal product* means a medicinal product in which the active substance is a biological substance; biological substance means 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,
60. *Biosimilar medicinal product* means a medicinal product which has similar quality, safety and efficacy as the original biological medicinal product,

61. *Counterfeit medicinal product* means a medicinal product whose identity and/or the source is deliberately and fraudulently mislabelled, and it can contain proper or wrong ingredients, with or without active substances, or contain a wrong quantity of active substances in a fake or counterfeit packaging. Counterfeiting can apply to both brand name and generic products,
62. *Marketing authorisation* means an authorisation issued by the Agency that completes the procedure for establishing that a medicinal product meets the quality, efficacy and safety requirements,
63. *Marketing authorisation holder* means a legal person seated in the Republic of Croatia holding an authorisation for the marketing of a drug product in the Republic of Croatia,
64. *Manufacturing authorisation* means a document issued by the Agency confirming that the manufacturer meets the conditions imposed on premises, equipment and staff of a drug product manufacturing plant(s) and applies principles and guidelines of Good Manufacturing Practice in accordance with this Act and the ensuing regulations or the valid regulations of the European Union for manufacturers outside the Republic of Croatia,
65. *Manufacturer of the medicinal product* means a legal person responsible for production and development as well as quality, safety and efficacy of a medicinal product, regardless of whether it was manufactured by him or some other person on his behalf,
66. *Manufacturer with respect to manufacturing site* means a legal person holding the manufacturing authorisation for a plant or plants for drug product manufacturing,
67. *Manufacture of medicinal products* comprises the whole process or individual parts of the process, such as pharmaceutical and technological preparation of a drug product, production of a substance by synthesis or further processing of procured substances and materials, technological processing and packaging as well as quality control, storage and delivery,
68. *Good Manufacturing Practice* means the part of the quality assurance system which ensures that medicinal products are consistently produced and controlled in accordance with the relevant quality standards and in line with their purpose,
69. *Qualified person for medicinal product manufacture* means a master of pharmacy specialised in pharmaceutical technology or with at least five years of experience in the manufacture of medicinal products, unless otherwise specified by special regulations,
70. *Qualified person for release of a medicinal product batch* means a master of pharmacy specialised in testing and control of medicinal products or with at least five years of experience in medicinal products quality control, unless otherwise specified by special regulations,
71. *Pharmacovigilance* means activities comprising detection, assessment, understanding and prevention of adverse reactions and acting in the event of their occurrence as well as new knowledge about any unsafe administration of medicinal products,
72. *Responsible person of the marketing authorisation holder responsible for pharmacovigilance* means a medical doctor specialised in clinical pharmacology or a medical doctor or a dental medicine doctor or a master of pharmacy with at least two years of experience in pharmacovigilance or two years of experience in the relevant field with the appropriately documented training in pharmacovigilance,
73. *Adverse reaction* means any harmful and unintended reaction which occurs at authorised doses used for the prophylaxis or treatment of disease in humans or to restore, correct or modify a physiological function or make a diagnosis; in clinical trials, all untoward and unintended responses to an investigational medicinal product related to any dose administered,
74. *Unexpected adverse reaction* means an adverse reaction, the nature, severity or outcome of which is not consistent with a summary of product characteristics for an authorised product or investigator's brochure for investigational products in clinical trials,

75. *Adverse event* means any noxious and undesired sign, symptom or disease (including changes in laboratory findings) that coincides with the use of a medicinal product, and which does not necessarily imply the causal relationship with the administration of a medicinal product,

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

77. *Wholesale* shall cover procurement, acceptance, storage, sale, delivery, other than delivery to end users, and import and export of a medicinal product,

78. *Wholesaler* means a legal person holding the authorisation for the performance of wholesale activities issued by the Agency,

79. *Importer/exporter of medicinal products* means a legal person authorised by the Agency for import/export of medicinal products,

80. *Retail sale* shall cover ordering, keeping and dispensing of Rx and over-the-counter medicinal products, as well as the preparation and dispensing of official formulas and galenical preparations,

81. *Dispensing of a medicinal product* means the sale of a medicinal product to end users in retail outlets, with the consultation of a master of pharmacy,

82. *Good practice in wholesale of medicinal products* means the standard for storage and transportation of medicinal products which ensures organisation, performance and control over storage in line with prescribed conditions, as well as transport to the wholesale user,

83. *Qualified person in wholesale of medicinal products* means a master of pharmacy with five years of experience in the wholesale of medicinal products,

84. *Specialised stores for retail sale of medicinal products* means a store selling over-the-counter medicinal products in line with this Act and the ensuing regulations,

85. *Croatian pharmacopoeia* means a regulation that lays down requirements for preparation of medicinal products and homeopathic medicinal products, as well as their quality and quality control procedures, and is appropriately referenced to and harmonised with the European Pharmacopoeia,

86. *Agency for Medicinal Products and Medical Devices* means a legal person established pursuant to the Act on Medicinal Products and Medical Devices (Official Gazette 121/03), hereinafter „the Agency“, whose scope of activities in the field of medicinal products and homeopathic medicinal products is governed by this Act.

Article 3

Testing, production, distribution and quality control of medicinal and homeopathic medicinal products may be performed by legal and natural persons who meet the special conditions for performing these activities.

The Minister shall issue an ordinance establishing the special conditions referred to in paragraph 1 of this Article.

II MEDICINAL PRODUCTS

1. TESTING OF MEDICINAL PRODUCTS

Article 4

For the purpose of placing on the market, the quality, efficacy and safety of each drug product shall be established.

Article 5

Testing of a medicinal product shall include pharmaceutical and pre-clinical tests and clinical trials.

Tests and trials referred to in paragraph 1 of this Article shall be conducted in line with ordinances issued by the Minister.

Article 6

Medicinal products shall be tested on the premises of legal persons who fulfil the conditions laid down by the ordinance referred to in Article 3 of this Act.

Clinical trial can be conducted only by a legal person authorised by the Minister.

Medicinal products shall be tested on the premises of the legal persons referred to in paragraph 1 of this Article at the expense and at the request of the legal person requiring such testing as well as at the request of the Minister or the Agency.

Article 7

Pre-approval of the Minister shall be required for conducting clinical trials of:

1. a drug product without a marketing authorisation in the Republic of Croatia, but holding a marketing authorisation in another country;
2. a drug product without a marketing authorisation in the Republic of Croatia or any other country;
3. a drug product that is authorised for marketing in the Republic of Croatia, but needs to be tested for new indications, new methods of administration, newly proposed active substance combinations and different dosage regimens compared with those previously approved, or for the purpose of gaining new clinical experience required;
4. a drug product whose bioavailability will be tested either in comparison with the bioavailability of any product already authorised for marketing in the Republic of Croatia or in comparison with that of a product that has not been authorised for marketing in the Republic of Croatia;
5. a drug product intended for gene therapy, treatment with somatic cells, including xenogenic cells and treatment with medicinal products containing genetically modified organisms.

The Minister shall grant or refuse the pre-approval referred to in paragraph 1 of this Article by the decision that cannot be appealed, but against which administrative proceedings can be instituted.

The Minister shall grant or refuse the pre-approval for clinical trials of the medicinal product referred to in paragraph 1, items 1, 3 and 4 of this Article within 30 days from the receipt of the application and documentation to be established in an ordinance issued by him.

The Minister shall grant or refuse his pre-approval for clinical trials of the medicinal product referred to in paragraph 1, item 2 of this Article within 60 days from the receipt of an application and documentation to be prescribed by him.

The Minister shall grant or refuse his pre-approval for clinical trials of the medicinal product referred to in paragraph 1, item 5 of this Article within 90 days from the receipt of an application and documentation to be prescribed by him.

By way of derogation from paragraph 5 of this Article, there shall be no limitation to the period for granting pre-approval for xenogenic drugs.

The pre-approval referred to in paragraph 1 of this Article shall be granted only after establishing:

1. that previous tests were performed according to current knowledge about medicinal products testing,

2. that the prescribed documentation was submitted and that the trial protocol was approved by the Central Ethics Committee.

Should the Minister fail to grant or refuse the pre-approval within the term referred to in paragraphs 3, 4 and 5 of this Article, the pre-approval shall be considered granted.

A clinical trial of a drug product shall not start before the pre-approval has been granted, except in the cases referred to in paragraph 8 of this Article, or without a favourable opinion of the Central Ethics Committee.

The Minister shall issue an ordinance establishing the procedure for delivery of the opinion by the Central Ethics Committee.

Article 8

Each clinical trial shall be subject to obtaining informed consent from the trial subject.

Children may be subjects of a clinical trial only if tests on adults cannot produce appropriate results.

In exceptional cases, informed consent shall be granted by a legal representative or a guardian of a person who is unconscious, has severe mental difficulties, is incapable of working or is a minor.

Clinical trials shall not be conducted if potential risks of a drug product use outweigh medical justification, as assessed by the Minister.

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

Article 9

The principles of medical ethics as well as compulsory protection of subjects' privacy and data shall be observed during clinical trials of medicinal products, in line with an ordinance on clinical trials of medicinal products and an ordinance on good clinical practice issued by the Minister.

Clinical trials of medicinal products shall take place only on the premises of legal persons referred to in Article 6, paragraph 1 of this Act, who have entered into agreements with clinical trial applicants.

The agreement from paragraph 2 of this Article shall specify total costs of the clinical trial and the costs to be incurred by a clinical trial sponsor or applicant, including costs of medical and other services incurred by a legal person from Article 6, paragraph 1 of this Act and compensations to investigators and subjects.

The clinical trial applicant or sponsor shall pay compensations for investigators and subjects from paragraph 3 of this Article to a legal person with whom he concluded the agreement on a clinical trial of the medicinal product.

Article 10

Pre-clinical tests shall be conducted in accordance with the ordinance on good laboratory practice issued by the Minister.

2. PLACING DRUG PRODUCTS ON THE MARKET

Article 11

The granting of a marketing authorisation marks the completion of the procedure for establishing the quality, efficacy and safety of a drug product.

The marketing authorisation shall also be required for radionuclide generators, radionuclide

kits, radiopharmaceuticals, radionuclide precursors, and industrially prepared radiopharmaceuticals.

The marketing authorisation referred to in paragraphs 1 and 2 of this Article shall be issued by the Agency for a period of five years.

If the drug product has not been on the market in the Republic of Croatia for three consecutive years following the issuance of the marketing authorisation, the Agency shall revoke the marketing authorisation for such a product.

By way of derogation from paragraph 4 of this Article and subject to the approval by the Minister, the Agency shall not revoke the marketing authorisation for the drug product when this is necessary to protect public health or when the validity of the marketing authorisation in the Republic of Croatia is the prerequisite for the issuance and/or renewal of the marketing authorisation in other countries.

The marketing authorisation holder shall notify the Agency in writing about the date of placing of the drug product on the market within 15 days following its placing on the market.

By virtue of an ordinance, the Minister may lay down special conditions for placing on the Croatian market a drug product that has obtained a marketing authorisation in the EU Member States.

Article 12

By way of derogation from Article 11 of this Act, a marketing authorisation shall not be required for:

- raw materials used in manufacture of drug products,
- officinal formula,
- galenical preparation,
- medicinal products intended for *in vitro* developmental research,
- 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,
- radiopharmaceuticals prepared exclusively from approved radionuclide generators, radionuclide kit or radionuclide precursor according to the manufacturer's instructions at the time of its use by a natural or legal person authorised for such activity.

Galenical preparations and officinal formulas shall be manufactured and placed on the market in line with special regulations.

Article 13

The Agency may temporarily entrust individual tasks from the procedure for granting marketing authorisation to professional institutions, i.e. institutions engaged in scientific or scientific and educational activities, and to certain experts in the field of medicinal products.

Persons referred to in paragraph 1 of this Article shall keep confidential all data that come to their knowledge while carrying out the entrusted tasks.

Article 14

Legal persons seated in the Republic of Croatia shall submit applications for marketing authorisation to the Agency.

The following data and documents shall accompany applications referred to in paragraph 1 of this Article:

- a) name and address of the applicant, and if necessary also of the manufacturer,
- b) name of the medicinal product,
- c) qualitative and quantitative particulars of all medicinal product constituents, including an international non-proprietary name or in the absence thereof, some other common name,
- d) assessment of potential environmental impacts of medicinal products, done on a case-by-case basis, and designing special procedures for containment of those risks,
- e) description of the manufacturing method,
- f) therapeutic indications, contraindications and adverse reactions,
- g) dosing, pharmaceutical form, method and route of administration, and expected shelf life,
- h) if necessary, reasons for any precautionary and safety measures to be taken for the storage of the medicinal product, its administration to patients and for the disposal of waste products, together with an indication of potential risks presented by the medicinal product for the environment,
- i) description of the quality control methods employed by the manufacturer (qualitative and quantitative analyses of active substances, excipients and drug product, any special tests),
- j) results of:
 - pharmaceutical tests (physicochemical, biological and/or microbiological tests);
 - pre-clinical tests;
 - clinical trials,
- k) a detailed description of the pharmacovigilance and, where appropriate, of the risk-management system which the applicant intends to implement,
- l) a statement to the effect that clinical trials carried out outside the Republic of Croatia meet the ethical requirements of good clinical practice,
- m) the summary of the product characteristics, proposal for labelling of outer and immediate packaging and the package leaflet,
- n) the manufacturing authorisation,
- o) copies of any authorisation obtained in other states together with a list of states in which the authorisation procedure is underway; copies of the summary of the product characteristics approved in other states or proposed in the authorisation procedure currently underway in other states; copies of the package leaflet approved in other states or proposed in the authorisation procedure currently underway in other states; details of and reasons for any decision to refuse a marketing authorisation in other states,
- p) evidence that the applicant uses services of a qualified person responsible for pharmacovigilance and fulfils the condition to report on any suspected adverse reaction detected either in the Republic of Croatia or in any other country,
- q) a copy of any designation of the medicinal product as an orphan medicinal product, if applicable.

In addition to the application for marketing authorisation, at the Agency's request the applicant shall submit the samples of the medicinal product, as well as prescribed reference standards requisite for pharmaceutical testing.

The Minister shall issue an ordinance defining in greater detail the contents of the data and documents referred to in paragraph 2 of this Article, as well as the procedure and method of granting a marketing authorisation.

Documentation received by the Agency shall be considered confidential.

The costs for the granting, renewal, amendments and transfer of the marketing authorisation shall be defined by the Agency, subject to the approval by the Minister, and incurred by the applicant.

Article 15

The marketing authorisation applicant referred to in Article 14 of this Act shall not be required to enclose results of pre-clinical tests or the results of clinical trials if he can demonstrate that:

- a) the drug product is essentially similar to the reference medicinal product, provided that the reference product was granted marketing authorisation in the Republic of Croatia or any EU Member State more than six years ago for any strength, pharmaceutical form, method of administration or packaging, or
- b) the medical use of active substance or active substances of the drug product has been well-established in the European Union or the Republic of Croatia for at least ten years, with recognised efficacy and safety, as determined on the basis of a detailed scientific bibliography, or that
- c) the manufacturer of a reference product and the holder of marketing authorisation for that reference product authorised in the Republic of Croatia or the European Union have agreed to use from their files the pharmaceutical, pre-clinical and clinical data on the reference product for the purpose of assessment of documentation enclosed to application for obtaining the marketing authorisation for another medicinal product with the same qualitative and quantitative composition in active substances and of the same pharmaceutical form.

Article 16

In the event referred to in Article 15 item a) of this Act, if a reference medicinal product has no marketing authorisation in the Republic of Croatia, the applicant shall specify the EU Member State in which the marketing authorisation was issued for the reference medicinal product and the year of issue of the first marketing authorisation, in an application for marketing authorisation of a generic product.

Article 17

The marketing authorisation applicant referred to in Article 14 of this Act shall provide the results of the appropriate pre-clinical tests or clinical trials:

- a) where the medicinal product does not fully fall within the definition of a generic medicinal product or where the bioequivalence cannot be demonstrated through bioavailability studies or in case of changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration, vis-à-vis the reference medicinal product,
- b) where a biological medicinal product is similar to a reference biological product (biosimilar) which does not comply with the definition of a generic medicinal product, owing to raw materials or differences in the manufacturing processes of biosimilar and the reference biological medicinal product.

In the case of medicinal products containing active substances used in the composition of medicinal products authorised in the Republic of Croatia or the European Union, but not hitherto used in combination for therapeutic purposes, the marketing authorisation applicant referred to in Article 14 of this Act shall provide the results of new pre-clinical tests or new clinical trials relating to that combination, but shall not be required to provide scientific references for every active substance.

The Minister shall issue an ordinance on methods for bioequivalence testing.

Article 18

A medicinal product shall be designated as an orphan medicinal product in the Republic of Croatia if it is authorised as an orphan medicinal products in the European Union in line with the requirements set in the European Union and if:

- it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand persons in the Community or
- it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and it is unlikely to be placed on the market without incentives due to high development costs, and
- there exists no satisfactory method of diagnosis, prevention or treatment of the conditions in question or, if such method exists, the medicinal product will be of significant benefit to those affected by those conditions.

Article 19

In order to obtain traditional-use registration, the applicant shall submit the appropriate data and documents referred to in Article 14 of this Act.

Instead of results of pre-clinical tests and clinical trials, the applicant from paragraph 1 of this Article shall submit:

- bibliographical or expert evidence to the effect that the medicinal product in question, or a corresponding product has been in medicinal use throughout a period of at least 30 years preceding the date of the application, including at least 15 years in the Republic of Croatia or the Community,
- a bibliographic review of safety data together with an expert report, and where required by the Agency, upon additional request, data necessary for assessing the safety of the medicinal product.

A corresponding product, as referred to in paragraph 2, subparagraph 1 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 medicinal product applied for.

The procedure for granting of marketing authorisation for traditional herbal medicinal products can be conducted for medicinal products satisfying the following requirements:

- (a) they have indications exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner,
- (b) they are exclusively intended for administration in accordance with a specified strength and posology,
- (c) they are an oral, external and/or inhalation preparation,
- (d) the period of traditional use complies with paragraph 2, subparagraph 1 of this Article,
- (e) the data on the traditional use of the medicinal product are sufficient; in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-standing use and experience.

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

Within the procedure for granting of marketing authorisation for traditional herbal medicinal products, the Agency can establish that the product satisfies the requirements from Article 15

item b) or Article 107 of this Act for the placing of the drug product or the homeopathic medicinal product on the market, in which case the provisions of this Article shall not apply. The Minister shall issue an ordinance establishing the form and the contents of documentation to be submitted for the procurement of marketing authorisation for traditional herbal medicinal products, requisite evidence about their medicinal use over a 30-year period, and rules for labelling and advertising of traditional herbal medicinal products.

Article 20

The Agency shall grant or refuse a marketing authorisation within 210 days from the receipt of a valid application.

An application referred to in paragraph 1 of this Article shall be deemed valid if within a maximum of 30 days from its receipt the Agency verifies that all the data and documents referred to in Articles 14, 15, 16, 17, and 19 of this Act have been submitted, about which the Agency shall keep records and shall inform the applicant.

Should the Agency require the applicant to supplement the application, the time limit referred to in paragraph 1 of this Article shall be suspended until such time as the required supplementary information has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant for giving a verbal or written explanation.

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

The list of marketing authorisations shall be published in the Official Gazette.

Along with the decision on granting the marketing authorisation, the Agency shall send the approved summary of the product characteristics, the approved package leaflet and the approved labelling, which are integral parts of the decision on granting the marketing authorisation, to the authorisation holder.

The marketing authorisation holder shall be responsible for the conformity of the summary of the product characteristics, the package leaflet and the labelling with the summary, the leaflet and the labelling accepted at the time of issuing the marketing authorisation or at the time of any subsequently approved amendments.

The Agency shall draw up a report on the relevant documentation and the tests performed.

The report on documentation and tests shall be updated with any new information of importance for assessment of the quality, safety or efficacy of the drug product concerned. Based on collected data, the Agency may change the decision on the marketing authorisation.

Article 21

In accordance with Article 14, paragraph 2, item i), of this Act and in order to examine a marketing application, the Agency may decide to test the product, its raw materials and, if applicable, its intermediate products or other constituents, for the purpose of checking the compliance of quality control procedures used and described by the manufacturer in the data supporting his application referred to in Article 6, paragraph 3, of this Act.

Article 22

The Agency shall refuse marketing authorisation if, after checking the data and documents referred to in Articles 14, 15, 16, 17, and 19 of this Act, it establishes:

- a) that the drug product is harmful under normal conditions of use, or
- b) that its therapeutic efficacy is lacking or is insufficiently substantiated by the applicant, or
- c) that its quantitative and/or qualitative composition is not as declared, or

d) that labelling or package leaflets are not in accordance with the provisions of Articles 41 through 47 of this Act or with the data provided in the summary of the product characteristics. The Agency shall likewise refuse the marketing authorisation if relevant data and documents submitted alongside the application do not comply with Articles 14, 15, 16, 17, and 19 of this Act.

Article 23

No later than 180 days before the expiry of the marketing authorisation referred to in Article 11, paragraph 3, of this Act, an application for the renewal of the marketing authorisation may be submitted to the Agency.

The marketing authorisation can be renewed for a five-year period.

The marketing authorisation can be issued for an indefinite period of time after the Agency re-evaluates the risk-benefit balance and if the marketing authorisation holder has submitted the documentation supplemented with the updated data on quality, safety and efficacy of the drug product, including all amendments as from the date of obtaining the marketing authorisation, for the purpose of renewal of the marketing authorisation.

Following the renewal of the marketing authorisation pursuant to paragraph 3 of this Article, the marketing authorisation shall be valid for an indefinite period of time, unless the Agency requires the procedure for authorisation renewal to be reinstated pursuant to paragraph 3 of this Article due to reasons relating to pharmacovigilance.

The Agency shall grant or refuse the renewal of the marketing authorisation within 180 days from the receipt of a valid application.

If an application is not valid, the Agency shall invite the applicant in writing to rectify deficiencies explicitly stated in the written notification, and submit the requested data and documents within a maximum of 30 days.

Should the Agency require the applicant to supplement the application, the time limit referred to in paragraph 5 of this Article shall be suspended until such time as the required supplementary information has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant for giving a verbal or written explanation.

The Minister shall issue an ordinance detailing the contents of the documentation referred to in paragraph 3 of this Article, submitted for the purpose of renewal of the marketing authorisation.

Article 24

After obtaining a marketing authorisation, its holder shall be obliged to keep abreast of the latest scientific and technical developments from the field of production procedures and quality control, and implement necessary changes which would ensure that the medicinal product is manufactured and its quality controlled in line with generally accepted scientific methods.

Since implementation of changes referred to in paragraph 1 of this Article may require amendment to the marketing authorisation or documentation accepted in the procedure of the marketing authorisation issuance, the holder of the marketing authorisation shall beforehand submit an application to the Agency for the approval of such changes.

He shall forthwith inform the Agency of any other new information which might influence the amendments to the documentation accepted within the procedure for granting of the marketing authorisation, and in particular any other new information which might influence the evaluation of the risk-benefit balance and of the degree of prohibition or restriction measures imposed by other countries in which the medicinal product was placed on the market.

The marketing authorisation holder shall enclose data and documents to the application for amendment, in accordance with the type of relevant changes.

The amended authorisation from paragraph 9 of this Article shall remain in force until the expiry of the original authorisation.

If the application from paragraph 4 of this Article is not valid, the Agency shall invite the applicant in writing to amend or supplement the application within the term of 30 days.

Should the Agency invite the applicant to supplement the application, the time limit referred to in paragraph 9 of this Article shall be suspended until such time as the required supplementary information has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant to provide verbal or written explanation.

If the approved amendment requires amendment to the decision on the marketing authorisation or its integral parts, the Agency shall issue a decision on such amendment. The Agency's decision cannot be appealed, but administrative proceedings can be instituted against it.

The Agency shall approve or refuse an amendment to the decision on the marketing authorisation or the approved amendment, depending on the type of change, within maximum 90 days of receipt of a valid application.

The Minister shall issue an ordinance specifying the acceptance procedures and contents of documentation to be submitted for the purpose of the marketing authorisation amendment.

Article 25

The marketing authorisation holder can apply for transfer of the marketing authorisation to another legal person seated in the Republic of Croatia.

The Minister shall issue an ordinance specifying the procedure, time limits and contents of documentation to be submitted for transfer of the marketing authorisation.

Article 26

Should a marketing authorisation holder decide to discontinue production of a medicinal product or withdraw it from the market before the expiry of its marketing authorisation, he shall accordingly inform the Agency six months in advance, except in the event of an urgent recall.

In the event referred to in paragraph 1 of this Article, the Agency shall revoke the marketing authorisation upon the holder's request.

The decision from paragraph 2 of this Article cannot be appealed. However, the administrative proceedings can be instituted.

Article 27

The marketing authorisation holder shall take emergency precautions if he obtains any new safety information which calls for restriction in medicinal product administration as compared to the valid authorisation.

The emergency precaution shall imply an amendment to the package leaflet related to one or more parts of the summary of the product characteristics as follows:

- therapeutic indications,
- posology and method of administration,
- contra-indications,
- special warnings and precautions for use,
- target group, and
- recall period, based on any new data which affect safe use of the medicinal product.

The marketing authorisation holder shall forthwith inform the Agency in writing about any emergency precaution. The emergency precaution shall be deemed accepted if the Agency

does not require any additional precautions within 24 hours from the receipt of a written notification.

Within 15 days from the date of implementation of emergency precautions, the marketing authorisation holder shall file an application for amendment to the marketing authorisation pursuant to Article 24 of this Act.

On account of new data affecting the safety of the medicinal product, the marketing authorisation holder shall take all emergency precautions required by the Agency and shall file an application for the marketing authorisation amendment in line with the required emergency precautions and within the time limit set by the Agency.

Article 28

The emergency recall shall be conducted by the Agency *ex officio* or upon the request of a pharmaceutical inspector from the ministry competent for health (hereinafter: „the Ministry“). The measures for recall of the medicinal product or a batch of a medicinal product shall be carried out if established that:

- the medicinal product is harmful under usual conditions of use, or
- it lacks therapeutic effect, or
- the risk-benefit balance is unfavourable with respect to the authorised use, or
- the qualitative and quantitative composition of the medicinal product is not as declared, or
- the medicinal product is not manufactured in line with its manufacturing authorisation.

Article 29

A marketing authorisation shall be revoked before the expiry of its five-year term if found that:

- the drug product was placed on the market contrary to the provisions of this Act,
- the drug product is unacceptably harmful or lacking therapeutic efficacy under provided conditions of use, or that the risk-benefit balance is unfavourable under provided conditions of use,
- the quantitative and qualitative composition of the drug product is not as declared in the documentation supporting the application for granting either the marketing authorisation or the authorisation for its amendment,
- inaccurate data have been provided in the drug product documentation,
- inaccurate data have been provided about the marketing authorisation holder,
- the drug product has not been on the market of the Republic of Croatia for three consecutive years following the issuance of the marketing authorisation in accordance with Article 11, paragraph 4, of this Act.

The decision on revoking of the marketing authorisation cannot be appealed, but administrative proceedings can be instituted.

The list of decisions on revoking of marketing authorisations shall be published in the Official Gazette on an annual basis.

The costs of the procedure for revoking a marketing authorisation shall be defined by the Agency subject to the approval by the Minister, and incurred by the marketing authorisation holder.

3. MANUFACTURING AUTHORISATION

Article 30

Manufacture of a medicinal product within the territory of the Republic of Croatia shall be allowed only to a legal person holding a manufacturing authorisation.

The manufacturing authorisation referred to in paragraph 1 of this Article shall be issued by the Agency.

The manufacturing authorisation shall be required equally for the entire and for partial manufacture of the medicinal product.

The manufacturing authorisation shall be issued for a plant or plants manufacturing a pharmaceutical form or a medicinal product or a group of medicinal products.

Pursuant to this Act, preparation of an officinal formula or galenical preparation shall not be considered as manufacture.

Article 31

A legal person seated in the Republic of Croatia shall submit an application for obtaining the manufacturing authorisation to the Agency.

Along with the application from paragraph 1 of this Article and the evidence about the fulfilment of good manufacturing practice requirements from Article 34 of this Act, the applicant shall enclose the following data and documents:

- full name and head office of the legal person,
- evidence of entry in the court register,
- evidence of entry of the activity in the court register,
- evidence of professional competencies and employment contract with a qualified person,
- evidence of professional competencies and employment contract with a person responsible for production,
- evidence of professional competencies and employment contract with a person responsible for distribution,
- personal data of the person responsible for production, quality control and distribution,
- description of the whole or a part of the relevant manufacturing procedure,
- a list of relevant medicinal products and pharmaceutical forms,
- full name and address of the manufacturing and quality control plants.

Article 32

The Agency shall issue a decision on granting or refusing a manufacturing authorisation within 90 days from the day of receipt of a valid application.

An application referred to in paragraph 1 of this Article shall be deemed valid if within 30 days from its receipt the Agency verifies that all the data and documents referred to in Article 31 of this Act have been submitted.

If the application is not valid, the Agency shall invite the applicant in writing to rectify deficiencies explicitly stated in the written notification and submit the requested data and documents within 30 days.

Should the Agency require the applicant to supplement the application, the time limit referred to in paragraph 1 of this Article shall be suspended until such time as the required supplementary information has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant for giving a verbal or written explanation.

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

Article 33

In the procedure for evaluating conditions for granting the manufacturing authorisation,

besides the data and documents referred to in Article 31 of this Act, the Agency's Expert Commission shall establish whether the GMP guidelines have been observed during the manufacture of a medicinal product or a group of medicinal products, while a pharmaceutical inspector from the Ministry shall deliver the relevant opinion.

Article 34

An applicant shall be deemed to observe the principles of Good Manufacturing Practice if:

1. given the scope and complexity of manufacture of either one or a group of medicinal products, he has the adequate number of qualified persons with a university diploma in pharmacy, chemistry, biology, biochemistry, biotechnology, chemical technology, medicine, dental medicine, veterinary medicine or other corresponding professions,
2. he has at his disposal the services of a qualified person for the release of a medicinal product batch who should be permanently available,
3. he has at his disposal the services of a qualified person for drug product manufacture and distribution,
4. he has at his disposal suitable premises and equipment requisite for the manufacture, quality control, storage and delivery of medicinal products,
5. he observes the principles and guidelines of Good Manufacturing Practice,
6. he uses only active substances manufactured in line with good manufacturing practice as raw materials, as well as excipients, when laid down by special regulations,
7. he enables the qualified person to carry out his activities independently, and ensures all requisite resources.

The Minister may prescribe that persons engaged in the manufacture of specific medicinal products and specific pharmaceutical forms have other degrees of qualification or other fields of specialisation.

The Minister shall issue an ordinance detailing the GMP requirements to be fulfilled by manufacturers of medicinal products as well as the procedure for defining such requirements.

Article 35

The manufacturing authorisation shall be issued for a period of five years.

If established that an applicant has failed to comply with any of the prescribed conditions, the Agency may issue a temporary authorisation and set a time limit for rectifying the established deficiencies. 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 paid by the applicant or the manufacturing authorisation holder.

Article 36

In the event of any amendment to the data and documents on the basis of which the manufacturing authorisation was issued, a manufacturing authorisation holder shall file an application with the Agency for approval of any such amendment.

If the amendments refer to the data and documents from Articles 31 and 34 of this Act, the required procedure and decision shall be completed within a maximum of 30 days from the date of receipt of a valid application. In exceptional cases the time limit may be extended to 90 days.

If the application from paragraph 1 of this Article is not valid, the Agency shall require the applicant in writing to rectify deficiencies explicitly given in a written notification, and submit the requested data and documents within a maximum of 15 days.

Should the Agency require the applicant to supplement the application, the time limit referred

to in paragraph 2 of this Article shall be suspended until such time as the required supplementary information has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant for giving a verbal or written explanation.

Article 37

A manufacturing authorisation holder seated in the Republic of Croatia may file an application for the issuance of the certificate of good manufacturing practice with the Agency, which establishes whether good manufacturing requirements have been met.

The certificate of the implementation of good manufacturing practice shall be issued by the Agency.

The minister shall issue an ordinance laying down the procedure for issuance of the certificate of good manufacturing practice.

Article 38

The Agency shall revoke a manufacturing authorisation if established that a manufacturer has failed to comply with requirements laid down by this Act and the ensuing regulations.

The decision to revoke the manufacturing authorisation cannot be appealed, but administrative proceedings can be instituted against such a decision.

Article 39

The Agency shall verify whether manufacturers with manufacturing sites outside of the Republic of Croatia are capable of manufacturing and performing quality control of medicinal products in the manner laid down by this Act, the ensuing regulations and the regulations of the European Union.

The costs of verification referred to in paragraph 1 of this Article shall be determined by the Agency subject to the approval by the Minister and paid by a foreign manufacturer or by a marketing authorisation holder.

Article 40

A valid manufacturing authorisation shall be also compulsory for foreign manufacturers.

The manufacturing authorisation referred to in paragraph 1 of this Article shall be deemed valid if issued by a competent authority of another state in accordance with requirements complying with those laid down by this Act and the ensuing regulations or regulations of the European Union.

4. LABELLING AND PACKAGE LEAFLET

Article 41

The following particulars shall appear on the outer and immediate packaging of a drug product or, where there is no outer packaging, only on the immediate packaging:

- the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, 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, the common name,
- the qualitative and the quantitative composition in active substances, using common names, for each presentation of the medicinal product, or depending on the pharmaceutical form per volume or weight,
- the pharmaceutical form and content in weight, volume or units of dosage,
- list of excipients of known action or efficacy, and in the event of medicinal products

administered as injections or topically or ophthalmologic medicinal products, all excipients shall be indicated,

- the method of administration and, if necessary, the route of administration; space shall be provided for the prescribed dose to be indicated,
- a special warning that the medicinal product must be stored out of the reach and sight of children,
- specific precautions, if necessary,
- expiry date (month and year),
- special storage precautions, if applicable,
- special precautions for disposal of unused medicinal products or waste materials derived from such medicinal products, if appropriate, along with instructions for the appropriate system for their collection,
- name and address of the marketing authorisation holder,
- number of the marketing authorisation,
- batch number,
- in case of over-the-counter medicinal products, the instructions for use of such medicinal products.

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

Where the immediate packaging takes the form of a blister and it is placed in the outer packaging which complies with requirements from paragraph 1 of this Article, it shall contain at least the following information:

- name of the drug product in line with paragraph 1 of this Article,
- name or a designation of the manufacturer or the marketing authorisation holder,
- expiry date,
- batch number.

In the event of a small immediate packaging that cannot contain all data from paragraph 1 of this Article, it shall contain at least the following:

- name of the drug product in line with paragraph 1 of this Article and, if necessary, administration route,
- method of administration,
- expiry date,
- batch number,
- content in weight, volume or units of dosage.

The Minister shall issue an ordinance regulating in greater detail labelling of medicinal products.

Article 42

The data given on the outer and immediate packaging shall be easily legible, comprehensible, indelible and written in the Croatian language and Latin script.

The name of the medicinal product from Article 41, paragraph 1, subparagraph 1, 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.

If so required during the process of granting the marketing authorisation and if approved by the Agency, the data on the immediate blister packaging and on the small container shall not have to be provided in the Croatian language.

Article 43

The Minister may require that certain other data also appear on the packaging of a medicinal product, such as those referring to:

- the price of the medicinal product,
- reimbursement by obligatory health insurance,
- dispensing (on prescription, or over-the-counter),
- identification and authenticity of the packaging.

Article 44

A package leaflet with information for the user shall be inserted into each medicinal product packaging.

By way of exception, the package leaflet shall not be obligatory where all the required information is directly conveyed on the outer packaging or on the immediate packaging of a medicinal product.

Article 45

The package leaflet shall be clear and comprehensible to the user and written in the Croatian language and Latin script.

Alongside Croatian and Latin script, other languages and scripts may also be used provided that the conveyed data are identical.

Article 46

The summary of the 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 constituents of the excipient, 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 precautions for disposal of a used medicinal product or waste materials derived from such medicinal product,
 7. name and address of the marketing authorisation holder,
 8. marketing authorisation number(s),
 9. date of the first authorisation or renewal of the authorisation,
 10. date of revision of the text,
 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.
- The Minister shall issue an ordinance specifying the contents and manner of inserting the summary of the product characteristics.

Article 47

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

- for the identification of the medicinal product:

(1) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for babies, children or adults. The common name shall be included where the product contains only one active substance and if its name is an invented name;

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

- the therapeutic indications;

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

(1) contra-indications;

(2) appropriate precautions for use;

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

(4) special warnings;

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

- (1) the dosage,
 - (2) the method and, if necessary, route of administration;
 - (3) the frequency of administration, specifying if necessary the appropriate time at which the medicinal product may or must be administered; and, as appropriate, depending on the nature of the product:
 - (4) the duration of treatment, where it should be limited;
 - (5) the action to be taken in case of an overdose (such as symptoms, emergency procedures);
 - (5) what to do when one or more doses have not been taken;
 - (6) indication, if necessary, of the risk of withdrawal effects;
 - (8) a specific recommendation to consult the doctor or the pharmacist, as appropriate, for any clarification on the use of the product;
- 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 doctors or pharmacist about any adverse reaction which is not mentioned in the package leaflet;
 - a reference to the expiry date indicated on the label, with:
 - (1) a warning against using the product after expiry date;
 - (2) where appropriate, special storage precautions;
 - (3) if necessary, a warning concerning certain visible signs of deterioration;
 - (4) the full qualitative composition (in active substances and excipients) and the quantitative composition in active substances, using common names, for each presentation of the medicinal product;
 - (5) for each presentation of the product, the pharmaceutical form and content in weight, volume or units of dosage;
 - (6) the name and address of the marketing authorisation holder,
 - (7) the name and address of the manufacturer;
 - (8) the date on which the package leaflet was last revised.

The package leaflet shall take into account the particular conditions of certain categories of users (children, pregnant or breastfeeding women, the elderly, persons with specific pathological conditions) and indicate, if appropriate, possible effects on the ability to drive vehicles or to operate machinery. It shall also list those excipients knowledge of which is important for safe and effective use of the medicinal product.

The list of excipients that may affect safety and efficacy of medicinal products shall be issued by the Minister.

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

Article 48

The Minister shall issue an ordinance specifying the contents and manner of inserting the package leaflet.

Article 49

Medicinal properties of a medicinal product shall be given neither on the outer nor on the immediate packaging if such a medicinal product does not have a marketing authorisation as a medicinal product or a homeopathic medicinal product, or if it is not entered in the Agency's register as a homeopathic medicinal product.

The prohibition from paragraph 1 of this Article shall not apply to galenical preparations and official formulas.

5. CLASSIFICATION OF MEDICINAL PRODUCTS

Article 50

Dispensation of medicinal products shall be regulated in the decision on marketing authorisation of drug products.

With respect to dispensation, medicinal products fall into two categories:

1. Medicinal products subject to medical prescription,
2. Medicinal products not subject to medical prescription.

The Minister shall issue an ordinance establishing more detailed criteria for classification of medicinal products.

Article 51

Medicinal products shall be dispensed only on medical prescription if they:

- are likely to present either direct or indirect hazard, even when used correctly, if taken without medical supervision, or
- are frequently and to a great extent used incorrectly, and as a result likely to present direct or indirect hazard to human health, or
- contain substances or preparations whose activity and/or adverse reactions require further investigation, or
- are usually prescribed by a doctor for parenteral administration.

Medicinal products not governed by the criteria from paragraph 1 of this Article may be dispensed without medical prescription.

The Minister shall issue an ordinance regulating in greater detail the dispensation of medicinal products on medical prescription.

Article 52

For the purpose of marketing authorisation renewal or when new facts are brought to its attention, the Agency shall examine current classification of medicinal products by applying the criteria listed in Article 51, paragraph 1, of this Act.

6. DISTRIBUTION OF MEDICINAL PRODUCTS

Article 53

Distribution of drug products in the territory of the Republic of Croatia shall be subject to the possession of the marketing authorisation.

Data listed in Articles 41 and 42 of this Act shall be indicated on the outer and immediate packaging of drug products referred to in paragraph 1 of this Article, with the exception of key medicinal products for hospital use whose annual import is limited.

On Agency's proposal, the Minister shall issue an annual list of medicinal products referred to in paragraph 2 of this Article by 31 January of every year.

By way of derogation from the provision of paragraph 1 of this Article, a batch of manufactured or imported drug product with a valid shelf life may stay in circulation up to 18 months after expiry of its marketing authorisation.

Article 54

In order to prevent any changes in quality or misuse of medicinal products, all legal and natural persons and government bodies coming in possession of medicinal products shall ensure their transportation, holding and storage in conformity with prescribed conditions. The Minister shall issue an ordinance on good practice in wholesale distribution of medicinal products.

Article 55

Wholesale distribution of medicinal products shall be carried out by:

- legal persons holding the Agency's authorisation for wholesale distribution of medicinal products (wholesale distributors of medicinal products),
- manufacturers of medicinal products seated in the Republic of Croatia, for products they manufacture and products whose marketing authorisations they hold,
- The Croatian National Institute of Public Health for wholesale distribution of sera and vaccines, and
- The Croatian Institute for Transfusion Medicine for wholesale distribution of blood and blood components.

Article 56

Wholesale distributors shall be allowed to procure medicinal products directly from manufacturers, or from importers or from other wholesale distributors.

Article 57

Pursuant to Article 53 of this Act, wholesale distributors and manufacturers shall be allowed to supply medicinal products to:

- pharmacies and pharmacy depots,
- healthcare institutions and companies engaging in pharmacy business,
- other wholesale distributors,
- private surgeries in quantities required for treatment of acute conditions.

The Minister shall issue the list and the required quantities of medicinal products allowed to the surgeries referred to in paragraph 1, subparagraph 4, of this Article.

The Croatian National Institute of Public Health shall supply infusion solutions, vaccines and sera to healthcare institutions and private surgeries.

The Croatian Institute for Transfusion Medicine shall supply blood and blood components to healthcare institutions.

Pursuant to this Act and the ensuing regulations, in exceptional cases, wholesale distributors may supply other legal and natural persons with medicinal products for which the Agency has granted approval on the basis of marketing authorisations.

The importer shall supply medicinal products to wholesalers only.

Article 58

Wholesale distribution of medicinal products shall be carried out only by legal persons holding the Agency's wholesale distribution authorisation.

Applicants for the authorisation referred to in paragraph 1 shall meet at least the following conditions:

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

2. have adequate staff, and in particular qualified persons responsible for wholesale distribution of medicinal products as well as for documentation review,
3. observe the principles of good practice in wholesale distribution of medicinal products,
4. maintain the documentation in a manner which would enable urgent recall of medicinal products from the market as ordered by the Agency or in co-operation with the manufacturer or marketing authorisation holder.

The Minister shall issue an ordinance specifying conditions, procedures, documents and data for obtaining the wholesale distribution authorisation for medicinal products.

Article 59

The Agency shall process an application for the distribution authorisation referred to in Article 58, paragraph 1 within 90 days of receipt of a valid application.

Should the applicant fail to submit a valid application, i.e. required data and documents, the Agency shall invite the applicant in writing to rectify deficiencies explicitly stated in the notification and furnish the requested data before the expiry of 30 days of the invitation receipt.

Should the Agency invite the applicant to supplement the application, the time limit referred to in paragraph 1 of this Article shall be suspended until such time as the required supplementary information has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant to give a verbal or written explanation.

The authorisation for wholesale distribution of medicinal products shall be granted by a decision which cannot be appealed, but against which administrative proceedings can be instituted.

The Agency, subject to the approval by the Minister, shall determine the costs of issuance, denial, amendment or revoking of wholesale distribution authorisation. The costs shall be settled by applicants or holders of wholesale distribution authorisations.

Article 60

The Agency shall revoke a wholesale distribution authorisation where the data or documents provided with the application are inaccurate or where the authorisation holder no longer fulfils the conditions based on which the authorisation was granted.

The wholesale distribution authorisation shall be revoked by a decision which cannot be appealed, but against which administrative proceedings can be instituted.

The wholesale distribution authorisation and the decision on its revoking shall be published in the Official Gazette.

Article 61

Holders of wholesale distribution authorisations shall notify the Agency in writing about all changes in conditions, documentation and data based on which the authorisation for wholesale distribution was granted.

The Agency shall issue the decision on amendment to the wholesale distribution authorisation within 90 days of receipt of a valid application.

Where an application is not valid, i.e. required data and documents are not submitted, the Agency shall invite the applicant to rectify deficiencies, i.e. to submit the required documents and data within 30 days of receipt of the written invitation.

Should the Agency invite the applicant to supplement the application, the time limit referred to in paragraph 2 of this Article shall be suspended until such time as the required supplementary information has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant to give a verbal or written explanation.

Amendment to the authorisation for the wholesale distribution of medicinal products shall be granted by a decision which cannot be appealed, but against which administrative proceedings can be instituted.

Article 62

Wholesale distributors and importers of drug products shall carry out the import and export of medicinal products.

Only the legal persons holding the Agency's wholesale distribution authorisation or import and export licence for medicinal products shall be allowed to engage in import and export of medicinal products.

The Minister shall issue an ordinance laying down the conditions to be met by legal persons applying for the licence for import and export of medicinal products.

The Agency, subject to the approval by the Minister, shall determine the costs of issuance, denial, amendment or revoking of the import and export licences. The costs shall be settled by applicants or licence holders.

Article 63

The legal persons referred to in Article 62 shall not be required to apply for the import licence of:

- drug products with marketing authorisations,
- substances referred to in Article 2, paragraph 1, items 2, 4 and 5, of this Act,
- partially technologically processed substances and various pharmaceutical forms of medicinal products whose technological processing (with the exception of packaging) has been completed, and which are used for further technological processing or packaging by the Croatian manufacturers of medicinal products.

Provision of paragraph 1 shall not apply to granting the import licence for:

- blood, blood components and blood products,
- substances used for the manufacture of immunological medicinal products,
- radiopharmaceuticals.

Article 64

The Agency may exceptionally allow import of drug products which do not have authorisation for marketing in the Republic of Croatia, provided that there is an urgent medically justified need, as for example:

- for purposes of research,
- for clinical trials,
- for pharmaceutical testing,
- for pre-clinical tests,
- in case of natural disasters or other emergencies,
- for emergency treatments of individual patients with a drug product prescribed by a medical doctor or dental medicine doctor in charge.

The Minister shall issue an ordinance establishing more detailed conditions for granting the import licence referred to in paragraph 1.

Provisions of a special Act on Combating Narcotics Abuse shall apply to import, export, transportation and transit of narcotics, substances for their manufacture and drug products containing narcotics.

Article 65

Retail sale of medicinal products shall be carried out by legal and natural persons with authorisation to engage in pharmacist activities granted under a separate Act, as well as

specialised retail stores holding the Agency's authorisation for retail sale of medicinal products.

The Minister shall issue an ordinance specifying detailed conditions for retail sale of medicinal products.

In accordance with Article 50, paragraph 2, of this Act, products issued on medical prescription may be dispensed only by pharmacies, while over-the counter dispensation is also allowed in specialised retail stores for medicinal products in conformity with the Agency's decision on the marketing authorisation for drug products.

The Agency may impose restriction on strengths and package sizes of medicinal products dispensed through specialised retail stores.

The Minister shall issue an ordinance specifying conditions for granting authorisations to specialised retail stores.

Article 66

The Agency shall grant the authorisation referred to in Article 65, paragraph 1 within 90 days of receipt of the valid application.

In case the application referred to in paragraph 1 is not valid, i.e. required data and documents are not submitted, the Agency shall invite the applicant in writing to rectify deficiencies explicitly stated in the invitation and furnish required data and documents within 30 days of receipt of the invitation.

Should the Agency invite the applicant to supplement the application, the time limit referred to in paragraph 1 of this Article shall be suspended until such time as the required supplementary information has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant to give a written or verbal explanation.

The authorisation for the retail sale of medicinal products shall be granted by a decision which cannot be appealed, but against which administrative proceedings can be instituted.

The Agency, subject to the approval by the Minister, shall determine the costs of issuance, denial, amendment or revoking of retail sale authorisations. The costs shall be settled by applicants or holders of retail sale authorisations.

Article 67

The Agency shall revoke the authorisation granted to a specialised retail store if the data supporting the application are found to be inaccurate and if the authorisation holder no longer fulfils the conditions based on which the authorisation was issued.

The authorisation for the retail sale of medicinal products shall be revoked by a decision which cannot be appealed, but against which administrative proceedings can be instituted.

Article 68

All legal persons engaging in wholesale distribution of medicinal products, as well as legal and natural persons engaging in retail sale of medicinal products, shall submit a report on distribution of medicinal products to the Agency, at least on a yearly basis.

The Minister shall issue an ordinance specifying the type of data and the method of preparing the report referred to in paragraph 1 of this Article.

Article 69

The Minister shall issue an ordinance on conditions and method for wholesale distribution of blood, blood components and blood products, as well as immunological medicinal products and radiopharmaceuticals.

The Minister shall also issue an ordinance on wholesale distribution and retail sale of narcotics, substances for their preparation, and drug products containing narcotics.

Article 70

Medicinal products that are no longer usable shall be disposed of at the expense of their owners.

Regulations in force applicable to the disposal of hazardous waste shall also apply to the disposal of medicinal products referred to in paragraph 1 of this Article.

7. PHARMACOVIGILANCE

Article 71

Healthcare professionals coming in contact with users of medicinal products and manufacturers of medicinal products or marketing authorisation holders shall notify the Agency in writing about adverse reactions, in particular about serious and unexpected adverse reactions, while in case of vaccines they shall also notify the Croatian National Institute of Public Health. Healthcare professionals shall report serious and unexpected adverse reactions within the shortest possible time.

Healthcare professionals who participate in clinical trials as investigators shall forthwith report all serious adverse reactions to the clinical trial sponsors and to the Agency.

Article 72

Marketing authorisation holders shall be required to:

1. appoint a pharmacovigilance expert who shall be at their disposal at all times,
2. maintain detailed records of all suspected adverse reactions occurring either in the Republic of Croatia or any other country,
3. report promptly to the Agency, and no later than 15 days following the receipt of the information, all suspected adverse reactions which occurred in the territory of the Republic of Croatia and which are brought to their attention by a health-care professional,
4. report promptly to the Agency, and no later than 15 days following the receipt of the information, all other suspected serious adverse reactions occurring in the territory of the Republic of Croatia and any suspected transmission via a medicinal product of any infectious agent that falls under the reporting obligation,
5. ensure that all suspected serious unexpected adverse reactions and any suspected transmission via a medicinal product of any infectious agent occurring in the territory of any other country are reported promptly to the Agency, and no later than 15 days following the receipt of the information,
6. submit reports of all adverse reactions to the Agency in the form of a Periodic Safety Update Report, immediately upon request or periodically. The Periodic Safety Update Reports shall include an evaluation of the risk-benefit balance of the medicinal product.

Clinical trial sponsors shall:

1. keep detailed records of all adverse events reported by investigators, and send the data to the Agency and the Central Ethics Committee,
2. ensure that all data on suspected serious unexpected adverse reactions, which are either fatal or life threatening, are immediately reported to the Agency and the Central Ethics Committee, and no later than seven days following the receipt of the information (follow-up report to be submitted within the next eight days),
3. report unexpected adverse reactions to the Agency and the Central Ethics Committee immediately, and no later than 15 days following the receipt of the information,
4. notify investigators about all suspected serious unexpected adverse reactions,
5. submit the aggregate annual report for the previous year with the list of all suspected serious adverse reactions recorded during the reporting period, as well as the report on safety

of trial subjects, to the Agency and the Central Ethics Committee by 31 March of the current year.

Article 73

The Minister shall issue an ordinance on pharmacovigilance.

Article 74

Healthcare professionals coming in contact with medicinal products or their users, as well as legal and natural persons engaging in manufacture or distribution of medicinal products, shall notify the Agency in writing about any incompliance of medicinal products quality that they learn about.

In case of suspected counterfeit medicinal products, the persons referred to in paragraph 1 of this Article shall within 24 hours notify the Agency and the marketing authorisation holder about such suspicion.

An ordinance on the method of monitoring the quality incompliance of medicinal products shall be issued by the Minister.

8. QUALITY CONTROL OF MEDICINAL PRODUCTS

Article 75

Within the meaning of this Act, quality control shall imply the procedure for establishing conformity of medicinal product quality with predetermined quality requirements in accordance with this Act and the ensuing regulations.

Quality control can be performed:

- on a regular basis,
- in exceptional cases,
- in distribution, and
- in special cases.

The Minister shall issue an ordinance on the quality control method referred to in paragraph 2 of this Article.

Article 76

Regular quality control shall apply to:

- every batch of a manufactured or imported drug product,
- every batch of a substance whether in original manufacturer's packaging or placed on the market by a wholesale distributor in his packaging.

A drug product manufacturer seated in the Republic of Croatia and holding a marketing authorisation for every manufactured batch of the drug product shall be obliged to subject every batch of the drug product to regular quality control.

Wholesale distributors of imported drug products, or importers of drug products, shall subject every single batch of an imported drug product for regular quality control to the Agency.

By way of derogation from paragraph 3 of this Article, where the quality control of a batch has been performed in the European Union, wholesale distributors distributing imported drug products and importers of drug products shall submit to the Agency the manufacturer's quality control certificate for every batch of imported drug product, in evidence of performed quality control in the European Union.

In addition to the certificate referred to in paragraph 4 of this Article, wholesale distributors and importers shall submit samples of drug products to the Agency who will check the data indicated on outer and immediate packaging and package leaflets.

Based on received certificates and samples referred to in paragraph 5 of this Article, the Agency shall grant authorisation for marketing of imported drug product batches.

The Agency shall either grant or refuse an authorisation within 8 days of receipt of the certificate referred to in paragraph 4 of this Article.

In case of any doubt, the Agency shall be entitled to carry out quality control of the imported drug product batch referred to in paragraph 4 of this Article, and for this purpose wholesale distributors or importers shall supply the Agency with sufficient quantity of samples for analysis and reference standards.

The costs of regular quality control referred to in paragraph 1 of this Article and of granting an authorisation referred to in paragraph 6 shall be settled by the manufacturer seated in the Republic of Croatia, or a holder of marketing authorisation if the drug product comes from import, or the wholesale distributor, or the importer.

Where the initial doubt proves to be ungrounded after quality control of the imported drug-product batch referred to in paragraph 8, the costs referred to in paragraph 9 shall be covered by the Agency.

Article 77

Exceptional quality control shall apply to:

- first batch of every drug product following the issuance of marketing authorisation,
- every batch of drug product from blood or plasma and of immunological medicinal product,
- other medicinal products specified by the Minister on the Agency's proposal.

The Agency shall perform the exceptional quality control.

The Agency shall complete the quality control within 30 days of receipt of the samples.

Costs of quality control referred to in paragraph 1 shall be settled by manufacturers seated in the Republic of Croatia, or in case of imported drug products, they shall be settled by holders of the marketing authorisation, or wholesale distributors or importers if medicinal products do not have marketing authorisations.

Article 78

Quality control from distribution shall apply to drug products and galenical preparations taken from distribution by the Ministry's pharmaceutical inspectorate in accordance with inspection plan, and it shall be performed for every pharmaceutical form and strength of a drug product at least once in five years.

The Agency shall perform quality control of samples of medicinal products taken from distribution.

The Agency shall complete the quality control from distribution within 30 days of receipt of samples of medicinal products or galenical preparations.

Costs of the first quality control in five years and samples of medicinal products or galenical preparations referred to in paragraph 1 shall be settled by:

- holders of marketing authorisations for medicinal products, and in absence of marketing authorisation, the importing wholesale distributors or importers,
- healthcare institution or pharmacy that has manufactured the relevant galenical preparation.

Costs of the second and all subsequent quality controls over the five year period shall be settled by:

- the Ministry if the relevant medicinal product or galenical preparation proves to be compliant;
- a marketing authorisation holder, and in absence of the marketing authorisation the importing wholesale distributor or importer, if the relevant medicinal product is non-compliant or if its package leaflet and labelling are not in conformity with those approved;
- legal or natural person whose incorrect activities in production or distribution have resulted in non-compliant medicinal product quality,

–healthcare institution or pharmacy which manufactured the relevant galenical preparation, if it proves to be incompliant.

Article 79

Special quality control shall be conducted on request of the Ministry or the Agency in case of any unusual or suspicious signs relevant to the quality of a medicinal product. The Agency shall carry out the special quality control.

The Agency shall complete the special quality control within 30 days of receipt of the sample and of the minutes providing data on suspected product quality.

Costs of the quality control referred to in paragraph 1 shall be settled by:

- proposer of special quality control i.e. the Ministry or the Agency if the medicinal product is compliant;
- marketing authorisation holder, and in absence of the marketing authorisation the importing wholesale distributor or importer if the relevant medicinal product is of poor quality or if the package leaflet and labelling are not in conformity with those approved,
- legal or natural person whose incorrect activities in production or distribution have resulted in incompliant medicinal product quality.

Article 80

Quality control shall be carried out in line with procedures laid down in the accepted medicinal product documentation accompanying the application for the marketing authorisation or in the absence thereof, the procedures adopted by the Agency.

The scope of quality control of individual medicinal products shall be determined by the Agency.

The quality of a medicinal product or raw materials for its manufacture, including raw materials for outer and 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 medicinal product is not included in either Croatian or European Pharmacopoeia, its quality shall comply with a pharmacopoeia recognised in the European Union or with other internationally recognised standards.

Following the Agency's proposal, the Minister shall adopt the Croatian Pharmacopoeia.

Article 81

Manufacturers, wholesale distributors and all importers of medicinal products shall keep registers on performed regular, exceptional and special quality controls.

The Agency shall keep the register of performed quality control.

Registers referred to in paragraphs 1 and 2 shall be kept for a year after expiry of shelf life of the relevant medicinal product.

The Minister shall issue an ordinance on the contents and maintenance of the register referred to in paragraphs 1 and 2 of this Article.

9. INFORMATION AND ADVERTISING

Advertising of Medicinal Products

Article 82

Within the meaning of this Act, advertising of medicinal products shall imply any form of communication designated to promote prescription, dispensing, sale and consumption of medicinal products, be it in written, pictorial, audio, oral, electronic, digital or any other form.

Article 83

Advertising of medicinal products referred to in Article 50, paragraph 2, items 1 and 2, of this Act shall be allowed in technical literature, at professional and scientific meetings, and to healthcare professionals.

Advertising of medicinal products referred to in Article 50, paragraph 2, item 2, of this Act to the general public shall be allowed.

Advertising of medicinal products referred to in Article 50, paragraph 2, item 1, of this Act to the general public shall be prohibited.

The prohibition referred to in paragraph 3 shall not apply to public-health activities promoting immunisation, seroprophylaxis and chemoprophylaxis according to the programme passed by the Minister in compliance with the Act on Protection of Population from Infectious Diseases. Advertising of drug products without marketing authorisation shall be prohibited, with the exception of advertising at professional and scientific meetings and in technical literature, but only if the procedure for obtaining the marketing authorisation has been initiated and if the common name of the relevant medicinal product is used without any reference to the manufacturer. These restrictions shall not apply to international gatherings held in the Republic of Croatia.

Article 84

Advertising of medicinal products shall be objective, it shall promote rational pharmacotherapy, and it shall not be misleading.

The Minister shall issue an ordinance establishing the methods of advertising.

Article 85

Product advertisements shall not refer to therapeutic properties of medicinal or homeopathic medicinal products which have no marketing authorisation or, in case of homeopathic medicinal products, which are not entered in the Agency's register.

The prohibition referred to in paragraph 1 shall not apply to galenical preparations.

Information about Medicinal Products

Article 86

The provision of information about medicinal products referred to in Article 50, paragraph 2, items 1 and 2, of this Act shall be allowed.

Within the meaning of this Act, information shall imply:

- informative release of facts and technical information concerning, for example, package changes, adverse reaction warnings and precautions, trade catalogues and price lists, provided that they do not contain any statements about medicinal products,
- informative release of clinical trial results, and
- any unbiased, objective information about diseases, prevention and available methods of treatment, released to the general public.

The Minister shall issue an ordinance specifying methods of providing information about medicinal products.

10. SUPPLY OF CROATIAN MEDICINAL PRODUCTS MARKET

Article 87

The Agency shall monitor the consumption of medicinal products in the Republic of Croatia.

The Agency shall submit reports on the consumption of medicinal products referred to in paragraph 1 of this Article and shall propose measures for supervising the consumption of medicinal products to the Minister.

Article 88

The Minister shall issue an ordinance on price calculation criteria for medicinal products.

Article 89

The Croatian Institute for Compulsory Health Insurance shall adopt a reimbursement list of medicinal products in compliance with a separate Act.

Criteria for inclusion of medicinal products on the reimbursement list referred to in paragraph 1 of this Article shall be specified in an ordinance issued by the Minister.

11. SUPERVISION

Article 90

The Ministry's pharmaceutical inspectorate shall supervise testing, manufacture and preparation, distribution, quality control, pharmacovigilance, advertising and provision of information on medicinal products.

The Minister shall issue an ordinance specifying the methods of supervision referred to in paragraph 1 of this Article.

Article 91

In the framework of inspectional supervision referred to in Article 90 of this Act, a pharmaceutical inspector shall have the following rights and obligations:

1. order engagement in activities in compliance with conditions laid down in this Act and other regulations,
2. order rectifying of detected irregularities and defects within a specified limit of time,
3. prohibit activities which are contrary to this Act and other regulations,
4. temporarily prohibit work of legal or natural persons who fail to observe requirements related to employees, equipment and premises,
5. prohibit work of legal or natural persons engaged in testing, manufacture and preparation, distribution and quality control of medicinal products without an authorisation of the Agency,
6. prohibit placing of a medicinal product on the market and submit to the Agency an application for its recall in the following cases:
 - where proven that a medicinal product could be harmful under normal conditions of use, or
 - that it lacks therapeutic efficacy, or
 - where its qualitative and/or quantitative composition is not identical to the composition declared in the application for marketing authorisation, or
 - where quality control of a drug product and/or the contained raw materials was not carried out, or
 - where shelf life of a drug product has expired, or
 - where any other requirement or condition for granting the marketing authorisation has not been met,
7. submit an application to the Agency for the recall of medicinal products batches which do not meet the conditions laid down in this Act and other regulations,
8. declare that a product established as incompliant represents hazardous waste and order its disposal,
9. prohibit work and propose to the Agency to revoke the operating licence in cases where non-compliance with conditions defined in this Act or other regulations could be hazardous to human life and health,
10. prohibit the sale of medicinal products and homeopathic medicinal products which do not have marketing authorisation, or of homeopathic medicinal products which are not entered in

the Agency's register of homeopathic medicinal products, in cases where therapeutic properties are indicated on outer or immediate packaging,

11. propose to the Agency revoking of the marketing authorisation if its holder does not have an established pharmacovigilance system and a qualified person responsible for pharmacovigilance, or fails to meet other obligations laid down in Article 72 of this Act,

12. order other measures falling under his competence pursuant to this Act and other regulations.

Article 92

Where established during inspection that a sampled medicinal product is non-compliant, the costs of quality control, recall or disposal shall be covered either by legal persons responsible for its placing on the market or import, or legal or natural persons responsible for the product deterioration on account of their incorrect product storage or handling.

Article 93

Besides rights and obligations referred to in Article 91 of this Act, pharmaceutical inspectors shall also have the following rights and obligations:

- temporarily suspend marketing authorisation decisions for all medicinal products and dosage forms covered by a manufacturing authorisation, if any of requirements specified in Articles 34, 39 and 40 of this Act was not fulfilled,
- temporarily suspend marketing authorisation decisions on account of breach of provisions from Article 76, paragraphs 2, 3 and 4 and Article 77 of this Act.

Article 94

Pharmaceutical inspectors are persons with university degree in medical or other related fields, and five-year experience on corresponding jobs, who have passed the state examination and who fulfil other requirements to be laid down in an ordinance issued by the Minister.

Article 95

Pharmaceutical inspectors shall have official identity cards in evidence of their official capacity, identity and authority.

The Minister shall issue an ordinance establishing the form and contents of official identity cards as well as the manner of issuance and maintenance of the register of issued official identity cards.

Article 96

Where during supervision a pharmaceutical inspector discovers that misdemeanour or criminal act was committed by breach of regulations, he shall immediately, within maximum 15 days after supervision, submit a claim or report to the competent authority.

The competent authority to which the claim or report referred to in paragraph 1 was submitted shall inform the Ministry about the outcome of the relevant proceedings.

Article 97

Legal and natural persons shall enable pharmaceutical inspectors to carry out supervision, and shall provide a required quantity of samples for quality control as well as necessary data and information.

Article 98

During inspectional supervision, pharmaceutical inspectors shall examine business premises, buildings, equipment, facilities and documentation.

Article 99

In carrying out supervision, pharmaceutical inspectors shall observe confidentiality regulations with respect to business, state, military, official and professional secrets. Legal and natural persons concerned shall inform pharmaceutical inspectors about definition of secret under their by-laws.

Article 100

Pharmaceutical inspectors shall pass verbal decisions in the following cases:

1. where threat to human health or life requires immediate implementation of a certain measure,
2. where some evidence could be hidden, replaced or destroyed unless a measure is immediately taken;

Pharmaceutical inspectors may order immediate execution of a verbal decision. The decision shall be entered into the supervision report.

Pharmaceutical inspectors shall draw up a written communication of verbal decision within eight days of passing the verbal decision.

Article 101

Decisions of pharmaceutical inspectors cannot be appealed, but administrative proceedings can be instituted instead.

Article 102

Pharmaceutical inspectors shall draw up reports on completed supervision, established status and taken or ordered measures, as well as on performed activities.

Pharmaceutical inspectors shall send a copy of the report to a natural person or a qualified employee of the legal person whose premises were inspected.

Article 103

Activities of pharmaceutical inspectors shall be governed by the provisions of the Act on General Administrative Procedure, unless otherwise regulated by this Act.

Article 104

Pharmaceutical inspectors shall keep registers of performed inspectional supervisions. The method of register keeping shall be prescribed by the Minister.

Article 105

Pharmaceutical inspectors shall be responsible for:

1. any failure to take or order measures under their competence,
2. exceeding their authorities,
3. any failure to submit a claim or report to competent authorities on established irregularities or defects.

III HOMEOPATHIC MEDICINAL PRODUCTS

THE PLACING OF HOMEOPATHIC MEDICINAL PRODUCTS ON THE MARKET

Article 106

Only homeopathic medicinal products with marketing authorisations granted by the Agency or entered in the Agency's register in accordance with this Act and the ensuing regulations shall be placed on the market.

Article 107

Applications for obtaining marketing authorisations for homeopathic medicinal products shall be submitted to the Agency. Applications shall be accompanied with data and documents required in line with conditions for placing medicinal products on the market, referred to in Articles 14 and 15 of this Act.

Article 108

The marketing authorisation shall not be required for homeopathic medicinal products entered in the Agency's register if they meet the following conditions:

- they are intended for oral or external administration,
- there is no reference to their therapeutic indications on the packaging or in the product documentation,
- they are sufficiently diluted to guarantee safe use; in particular, such 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 require medical prescription.

Article 109

For register entry, the Agency shall specify dispensing classification of the products. An ordinance on the register contents and maintenance shall be issued by the Minister. No evidence of therapeutic effect shall be required for homeopathic medicinal products referred to in Article 108 of this Act.

Article 110

An application for entry in the Agency's register may comprise product batches derived from the same homeopathic stock or stocks.

In order to demonstrate the pharmaceutical quality and batch-to-batch homogeneity of the products concerned, the application shall be supported with the following:

- scientific name or other pharmacopoeial name of homeopathic stock or stocks, and description of diverse administration methods, pharmaceutical forms and dilutions,
- documentation showing how homeopathic stock or stocks are obtained and tested and providing evidence on its/their homeopathic nature on the basis of the relevant bibliography,
- manufacture and quality control file for every pharmaceutical form and description of the dilution and potentiation method,
- manufacturing authorisation for individual products,
- evidence of register entries or marketing authorisations obtained for the same product in other states,
- a specimen of outer and immediate packaging of the product for which the authorisation is applied for,
- product stability data.

Article 111

The Agency shall grant or refuse the marketing authorisation within 210 days of receipt of the valid application.

An application referred to in paragraph 1 of this Article shall be deemed valid if within 30 days of its receipt the Agency establishes that all the data and documents referred to in Article 107 have been submitted, about which the Agency shall keep records and notify the applicant.

The marketing authorisation shall be issued for a period of 5 years.

For reasons referred to in Article 22, the marketing authorisation for homeopathic medicinal

product shall not be granted.

Not less than 180 days before expiry of a marketing authorisation for homeopathic medicinal products, an application for its renewal may be submitted to the Agency.

Provisions of Article 11, paragraphs 4, 5, 6 and 7 shall also apply to homeopathic medicinal products.

The Minister shall issue an ordinance specifying the contents of data and documents required for renewal of the marketing authorisation.

Provisions of Article 29 shall appropriately apply to withdrawal of marketing authorisations for homeopathic medicinal products before expiry of their validity.

Article 112

Provisions of Article 20, paragraphs 3, 4 and 5 shall also appropriately apply to homeopathic medicinal products.

2. LABELLING AND PACKAGE LEAFLET

Article 113

Provisions of Articles 41 to 47 shall also appropriately apply to homeopathic medicinal products requiring the marketing authorisation.

Homeopathic nature shall be clearly and legibly indicated on the product's outer and immediate packaging.

Article 114

In addition to a clear label reading "homeopathic medicinal product", the following information shall appear on outer and immediate packaging and, if necessary, package leaflets of homeopathic medicinal products referred to in Article 113:

- scientific name of homeopathic stock or stocks and indication of dilution using pharmacopoeial symbols,
- name and address of the legal person seated in the Republic of Croatia who is the holder of the marketing authorisation for homeopathic medicinal products and, if necessary, the manufacturer's name and address,
- method of administration and, if required, route of administration,
- shelf life,
- pharmaceutical form,
- product composition,
- special storage instructions, where applicable,
- special warnings, where applicable,
- batch number,
- entry number in the Agency's register,
- label reading »homeopathic medicinal product without proven therapeutic indications«,
- a warning instructing patients to consult a physician if symptoms fail to disappear during use of the product.

3. ADVERTISING AND INFORMATION

Article 115

Prohibitive provisions from Article 83, paragraph 5 and Article 85, paragraph 1 shall appropriately apply to advertising of homeopathic medicinal products.
The Minister shall issue an ordinance on the method for advertising of homeopathic medicinal products.

Article 116

Provisions of Article 86 shall appropriately apply to providing information about homeopathic medicinal products.

Article 117

The Minister shall issue an ordinance on providing information about homeopathic medicinal products.

4. OTHER PROVISIONS

Article 118

Manufacture, wholesale distribution, retail sale and quality control of homeopathic medicinal products shall be more closely defined in an ordinance issued by the Minister.

Article 119

Provisions of this Act concerning supervision of medicinal products shall also appropriately apply to homeopathic medicinal products.

Pharmacovigilance provisions of this Act shall also appropriately apply to homeopathic medicinal products with marketing authorisations.

IV. AGENCY FOR MEDICINAL PRODUCTS AND MEDICAL DEVICES

Article 120

The Agency shall engage in the following activities:

- granting of marketing authorisations for medicinal products and homeopathic medicinal products,
- maintaining the register of homeopathic medicinal products,
- providing expert assessment of quality, efficacy and safety of medicinal products and homeopathic medicinal products,
- conducting pharmaceutical testing of medicinal products and homeopathic medicinal products,
- keeping records of clinical trials conducted in the Republic of Croatia, filing final reports, analysing information about adverse reactions of tested medicinal products,
- performing quality control of medicinal products and homeopathic medicinal products and issuing quality control certificates,
- drawing up the Croatian pharmacopoeia,
- issuing manufacturing authorisations to manufacturers of medicinal products and homeopathic medicinal products,
- issuing Good Manufacturing Practice (GMP) certificates,
- issuing wholesale distribution authorisation for medicinal products and homeopathic medicinal products,
- issuing retail sale authorisation to stores specialised in retail sale of medicinal products,
- issuing import and export licences for medicinal products,

- giving approvals for import and export of medicinal products,
- monitoring adverse reactions and incompliances of medicinal products,
- carrying out urgent recall procedures for drug products
- monitoring the consumption of medicinal products and promoting their rational use,
- proposing measures to supervise consumption of medicinal products to the Minister,
- engaging in waste management activities (for its own needs),
- engaging in training and providing information on medicinal products,
- offering expert advice from its scope of activities,
- proposing harmonisation of medicinal products regulations with those of the European Union as well as with regulations and guidelines of international institutions,
- establishing international cooperation in the field of medicinal products,
- maintaining the register of medical devices,
- providing expert assessment of quality or conformity and safety of medical devices,
- conducting laboratory testing medical devices,
- supervising clinical trials of medical devices, keeping records of clinical trials of medical devices carried out in the Republic of Croatia, filing final reports, analysing information on adverse reactions of tested medical devices,
- issuing manufacturing authorisations to manufacturers of medical devices,
- issuing wholesale distribution authorisation for medical devices,
- issuing retail sale authorisations to stores specialised in retail sale of medical devices,
- issuing import and export licences for medical devices,
- giving approval for import and export of medical devices,
- monitoring adverse reactions and incompliances of medical devices,
- providing information on medical devices,
- establishing international cooperation in the field of medical devices,
- carrying out other tasks from the area of medicinal products and homeopathic medicinal products in accordance with this Act and the ensuing regulations.

Article 121

The Agency shall have a Statute which shall regulate its organisational structure, authorities and decision making process of its individual bodies as well as conditions and procedure for appointing the manager and other issues of importance for the Agency's activities and operations in accordance with this Act.

The Agency's Administrative Council shall adopt the Statute subject to approval by the Government of the Republic of Croatia.

Article 122

Besides the Statute, the Agency shall have its by-laws in line with this Act and other regulations.

Rights and obligations of the Agency's employees and other employment-related issues shall be regulated by the Labour Relations By-law.

The Administrative Council shall adopt the Labour Relations By-law and other by-laws of the Agency, unless this Act and the Statute require their adoption by the Agency's manager.

Article 123

The bodies of the Agency shall comprise: the Administrative Council, the Manager, the Expert Council and other bodies defined by the Statute.

Article 124

The Agency shall be managed by the Administrative Council.

The Administrative Council shall have 5 members.

The president and members of the Administrative Council shall be appointed by the Government of the Republic of Croatia on proposal of the Minister.

Members of the Administrative Council shall be appointed for a period of four years.

Article 125

The Government of the Republic of Croatia may relieve a member of the Agency's Administrative Council before the expiry of his term of office in the following cases:

- if the member himself demands to be relieved from duty,
- if in his work he seriously or repeatedly breaches the law and other regulations relevant to the Agency's operations and activities,
- if in his work he causes damage to the Agency,
- in other cases defined by the law and the Statute.

Article 126

The Administrative Council shall:

- adopt the Agency's Labour Relations By-law and other by-laws,
- adopt the Agency's business and financial plan,
- adopt the Agency's annual accounts and business reports,
- appoint and relieve from duty the Agency's manager,
- make decisions on the Agency's internal organisational structure,
- make decisions on other issues defined in the Agency's Statute.

Article 127

The Agency's manager shall manage the Agency's operations.

The Agency's manager shall be appointed for the term of four years. After the expiry of his term of office, the manager may be re-appointed without restrictions on the number of his terms of office.

Article 128

The Agency's manager shall:

- run and manage the Agency's operations,
- act as the Agency's agent and representative,
- propose the adoption of acts under his competence to the Administrative Council,
- decide on other matters defined by the Statute.

Article 129

The Administrative Council shall relieve the manager from duty before the expiry of his term of office if he:

- requests to be relieved,
- fails to observe the Agency's regulations and by-laws,
- unjustifiably refuses to implement decisions of the Agency's Administrative Council made within the scope of the Council's competence,
- causes substantial damage to the Agency through unconscientious and inaccurate work,
- frequently neglects or unconscientiously performs his duties thus causing difficulties in the Agency's operations.

Article 130

The Agency's assets shall consist of operating funds which shall be provided by its founder, or acquired by rendering services, or from other sources.

The funds for the Agency's activities shall be provided from:

- the Agency's operating revenues (from rendering services and from annual fees)
- other sources in accordance with this Act or other regulations.

The Agency shall specify the amount of annual fees subject to the approval by the Minister. Annual fees shall be paid by holders of marketing authorisations for drug products and holders of entry in the register of homeopathic medicinal products.

Article 131

Legal aspects of the Agency's operations shall be supervised by the Ministry.

Article 132

The Agency shall submit annual reports to the Minister and to the Government of the Republic of Croatia.

Article 133

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.

The Act on Public Servants' Salaries shall not apply to the Agency.

V PENAL PROVISIONS

Article 134

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 provisions of this Act and the ensuing regulations (Article 4; Article 5, paragraph 2; Article 6, paragraph 3; Articles 7, 8, 9 and 10),
2. for paying fees to investigators and trial subjects contrary to the provision of Article 9, paragraph 4 of this Act,
3. for placing medicinal products on the market in the Republic of Croatia without the required marketing authorisation (Article 11 and Article 53, paragraph 1),
4. for providing incorrect data in the documentation accompanying the marketing authorisation application (Article 14, paragraph 2 and Article 15),
5. if qualitative and quantitative composition of medicinal products does not comply with the composition provided in the documentation accompanying the application for marketing

authorisation or application for its amendment, or if proven that the drug product is unacceptably harmful, or insufficiently effective under prescribed conditions of use (Article 29, paragraph 1),

6. for manufacturing a medicinal product in the Republic of Croatia without the manufacturing authorisation (Article 30, paragraph 1),

7. for providing incorrect data in the application for manufacturing authorisation and for failing to inform the Agency about changes of data on the grounds of which the manufacturing authorisation was issued (Article 31 and 36, paragraph 1),

8. for engaging in wholesale and retail sale of medicinal products without authorisation (Article 55 and Article 65, paragraph 1),

9. for engaging in import and export without import or export licence (Article 62, paragraph 2),

10. for carrying out quality control of medicinal products contrary to provisions of this Act and the ensuing regulations (Articles 75 to 81),

11. for advertising and providing information about medicinal products contrary to provisions of this Act and the ensuing regulations (Articles 82 to 86),

12. for calculating a medicinal product price contrary to criteria from Article 88 of this Act,

13. for failing to act in due course in accordance with legally valid ruling of a pharmaceutical inspector which prescribes certain measures or prohibits work (Article 91),

14. for failing to enable a pharmaceutical inspector to carry out supervision in accordance with provisions of this Act and the ensuing regulations (Article 97),

15. for placing homeopathic medicinal products on the market without the Agency's authorisation or entry in the Agency's register (Articles 106 and 108),

16. for providing incorrect data in the documentation accompanying the application for entry in the register of homeopathic medicinal products (Article 110).

For misdemeanour referred to in paragraph 1, natural persons and qualified employees of legal persons shall be liable to a fine between HRK 10 000.00 and HRK 15 000.00.

Article 135

Legal persons shall be liable to a fine between HRK 70 000.00 and HRK 100 000.00 for the following misdemeanours:

1. for carrying out tests and quality control of products covered by this Act without meeting the conditions laid down in this Act and the ensuing regulations (Article 3),

2. for conducting unauthorised clinical trials of medicinal products (Article 7),

3. for conducting or allowing clinical trials contrary to provisions of Article 9, paragraph 2, of this Act,

4. for distribution of drug products subject to marketing authorisations that are not valid in the Republic of Croatia (Article 11, paragraph 3 and 4, and Article 53, paragraph 1),

5. for placing on the Croatian market drug products that are unlabelled or without package leaflet in compliance with provisions of this Act and the ensuing regulations (Article 41 and 44),

6. for dispensing drug products in a manner and at the place contrary to the issued marketing authorisation (Article 50),

7. for failing to ensure transportation and storage of medicinal products in accordance with storage conditions indicated on products (Article 54),

8. for providing incorrect data in documentation accompanying the application for wholesale distribution authorisation and marketing authorisation for medicinal products (Article 58),

9. for importation of medicinal products without prescribed import licence (Article 64),

10. for failing to submit data on medicinal products distribution to the Agency (Article 68, paragraph 1),

11. for failing to meet the obligation from Article 72 herein,
12. for failing to subject every batch of manufactured or imported drug product to regular quality control, contrary to Article 76 of this Act,
13. for failing to supply the Agency with sufficient quantity of samples (Article 76, paragraph 8),
14. for failing to subject a drug product to exceptional quality control (Article 77),
15. 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, do not comply with the Croatian pharmacopoeia or other pharmacopoeia as referred to in Article 80, paragraph 3 herein,
16. for failing to maintain register of regular, exceptional and special quality control in accordance with provisions of this Act and the ensuing regulations (Article 81),
17. for failing to put data required by this Act on outer and immediate packaging (Article 113 and Article 114),
18. for advertising homeopathic medicinal products referred to in Article 115, paragraph 1 herein.

For misdemeanour referred to in paragraph 1, natural persons and qualified employees of legal persons shall be liable to a fine between HRK 7 000.00 and HRK 10 000.00.

Article 136

Any legal person who provides incorrect data during the procedure of import licence issuance for a medicinal product without marketing authorisation in the Republic of Croatia shall be liable to a fine between HRK 50 000.00 and HRK 70 000.00 (Article 64, paragraph 1).

For misdemeanour from paragraph 1, a responsible person of the legal person shall be also liable to a fine between HRK 5 000.00 and HRK 7 000.00.

A medical doctor or a dental medicine doctor who prescribes a medicinal product that does not have marketing authorisation in the Republic of Croatia, contrary to Article 64, paragraph 1 and the ordinance referred to in Article 64, paragraph 2, of this Act, shall be liable to a fine between HRK 5 000.00 and HRK 7 000.00.

Article 137

Legal or physical persons shall be liable to fine between HRK 30 000.00 and HRK 50 000.00 in the following cases:

1. for disposing of unusable medicinal products contrary to provisions of this Act and valid regulations (Article 70),
2. for failing to notify the Agency in writing about adverse reactions, or the Croatian National Institute of Public Health in case of vaccines, in conformity with provisions of this Act and the ensuing regulations (Article 71),
3. for failing to notify the Agency in writing about incompliance of a medicinal product or suspected counterfeit, contrary to Article 74 herein and the ensuing ordinance,
4. for placing on the market a homeopathic medicinal product which is not labelled in accordance with provisions of this Act (Article 113 and 114).

A qualified employee of the legal person shall be liable to a fine between HRK 3 000.00 and HRK 5 000.00 for misdemeanour referred to in paragraph 1 herein.

VI TRANSITIONAL AND FINAL PROVISIONS

Article 138

The Minister shall issue the ordinances placed under his competence by this Act within a year from the date of entry into force of this Act.

Article 139

Until the entry into force of ordinances referred to in Article 138 of this Act, the following ordinances shall remain in force:

1. Ordinance on monitoring adverse drug reactions to medicinal products and medical devices (Official Gazette-29/05),
2. Ordinance on advertising and providing information on medicinal products, homeopathic medicinal products and medical devices (Official Gazette 62/05),
3. Ordinance on good laboratory practice (Official Gazette 51/06.),
4. Ordinance on clinical trials and good clinical practice (Official Gazette 175/03 and 55/04),
5. Ordinance on classification, prescribing and dispensation of medicinal products (Official Gazette 123/05 and 112/06),
6. Ordinance on quality control of medicinal products (Official Gazette 56/05),
7. Ordinance on pharmacovigilance (Official Gazette 36/05),
8. Ordinance on testing bioavailability and bioequivalence of medicinal products (Official Gazette 71/99),
9. Ordinance on the licensing requirements specialised stores for retail sale of medicinal products and medical devices (Official Gazette 29/05, 81/06 and 5/07),
10. Ordinance on good manufacturing practice related to medicinal products (Official Gazette 40/05),
11. Ordinance on the procedure and method of granting marketing authorisations for drug products (Official Gazette 143/98.),
12. Ordinance on the type of data and reporting on the distribution of finished medicinal products (Official Gazette 29/05),
13. Ordinance on special conditions for placing on the market of the Republic of Croatia drug products with a marketing authorisation in EU Member States (Official Gazette 86/04.),
14. Ordinance on good practice in wholesale distribution of medicinal products (Official Gazette 29/05),
15. Ordinance on the conditions and the procedure of obtaining the for the wholesale distribution of medicinal products and the import and export of medicinal products (Official Gazette 29/05),
16. Ordinance on the criteria for wholesale pricing of medicinal products and the methods for reporting wholesale prices (Official Gazette 91/06),
17. Ordinance on identity cards of pharmaceutical inspectors (Official Gazette 19/05),
18. Ordinance on the conditions of manufacture, placing on the market, quality control and the register of homeopathic medicinal products (Official Gazette 62/05).

Article 140

Procedures for granting, amending and renewal of drug product marketing authorisations, for issuing manufacturing authorisations, authorisation for wholesale distribution and retail sale of medicinal products, licences for import and export of medicinal products, which have been initiated before the entry into force of this Act, shall be completed in conformity with provisions of the Act on Medicinal Products and Medical Devices (Official Gazette 121/03 and 177/04).

Article 141

Legal persons holding manufacturing authorisation on the date of entry into force of this Act shall harmonise their work and operations with provision of Article 34 of this Act within one year from its entry into force.

Article 142

Marketing authorisations issued on the grounds of regulations valid until the entry into force of this Act shall remain in force till expiry of their original term.

Article 143

Legal persons holding marketing authorisations for drug products on the date of entry into force of this Act shall harmonise their work and operations with Article 72 of this Act within a year from its entry into force.

Article 144

Legal persons who hold marketing authorisations for drug products shall harmonise labelling and package leaflet as well as the summary of the product characteristics with provisions of this Act and the ensuing ordinances within six months of the entry into force of ordinances referred to in Article 41 paragraph 5, Article 46 paragraph 2 and Article 48 herein.

Article 145

The Agency shall harmonise its work and operations with provisions of this Act within three months of its entry into force.

Article 146

The following ordinances shall remain effective till the date of the entry into force of a separate act on medical devices:

1. Ordinance on classification, placing on the market, essential requirements, conformity assessment procedures and the register of medical devices (Official Gazette 54/05), and
2. Ordinance on good practice and conditions for issuing authorisations for distribution of medical devices (Official Gazette 54/05).

Article 147

Provisions of the Act on Medicinal Products and Medical Devices (Official Gazette 121/03 and 177/04) shall cease to have effect on the date of entry into force of this Act, with the exception of provisions of Article 43 paragraph 1, Article 51 paragraphs 4, 5, 6, 7 and 8, Article 52, Articles 76 to 86, in the part which concerns medical devices as well as Articles 99 to 123. The Act on Medicinal Products and Medical Devices shall cease to have effect one year from entry into force of this Act.

Article 148

This Act shall enter into force on 1 October 2007, with the exception of provisions of Article 23, paragraphs 3 and 4, Article 42, paragraph 2 and Article 47, paragraph 4, which shall enter into force on the date of accession of the Republic of Croatia to the European Union.

Class: 530-08/07-01/01

Zagreb, 21 July 2007

THE CROATIAN PARLIAMENT
The President of the Croatian Parliament
Vladimir Šeks, m.p.

PROVISIONAL TRANSLATION