

# THE CROATIAN PARLIAMENT

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Pursuant to Article 88 of the Constitution of the Republic of Croatia, I hereby pass the

## DECISION

### PROMULGATING THE

### ACT ON MEDICINAL PRODUCTS AND MEDICAL DEVICES

I hereby promulgate the Act on Medicinal Products and Medical Devices adopted by the Croatian Parliament at its session on 17 July 2003.

No: 01-081-03-2668/2

Zagreb, 23 July 2003

The President of the Republic of Croatia

**Stjepan Mesić, m.p.**

## ACT

### ON MEDICINAL PRODUCTS AND MEDICAL DEVICES

#### I. GENERAL PROVISIONS

##### Article 1

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

This Act also regulates conditions and methods for market placement and control of homeopathic products.

##### Article 2

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

1. **Medicinal product:** Any substance or combination of substances intended for treatment or prevention of human diseases as well as any substance or combination of substances which may be administered to human beings with a view of restoring, correcting or modifying their physiological functions or 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. microorganisms, including genetically modified organisms, animals, parts of organs, animal secretions, toxins, extracts, blood products,
- vegetable, e.g. plants, parts of plants, vegetable secretions, extracts,
- chemical, e.g. elements, naturally occurring chemical materials and chemical products obtained by a chemical change or synthesis,

3. **Active substance:** Any matter conferring a drug product action,

4. **Excipient:** 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:** Any substance of specified quality intended for a drug product manufacture,

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

7. **Galenic preparation:** Any medicinal product from the List of Galenic Preparations issued by the Minister for Health, manufactured in a galenic laboratory according to the procedure provided in the current pharmacopoeia and GMP (Good Manufacturing Practice) standards for galenic laboratories,

8. **Magistral formula:** Any medicinal product prepared in a pharmacy from active substances and excipients of prescribed and verified quality, in accordance with a prescription for an individual patient,

9. **Name of the medicinal product:** 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. The invented name shall not be liable to confusion with the common name,

10. **Common name:** 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:** 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,
- agents used to diagnose the state of immunity,
- agents used to produce passive immunity.

“Allergen product” means any medicinal product that is intended to identify or induce a specific acquired alteration in the immunological response to an allergizing agent.

12. **Medicinal products derived from human blood or human plasma:** Medicinal products based on blood constituents including, in particular, albumin, coagulating factors and immunoglobulin,

13. **Radiopharmaceutical:** Any medicinal product that contains one or more

radionuclides,

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

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

17. **Radiopharmaceutical precursor:** Any radionuclide produced for the radiolabelling of another substance prior to administration,

18. **Medical device:** Any product used for the purpose of making a medical diagnosis, prevention, monitoring, treatment or alleviation of disease and compensation for an injury or handicap; for investigation, replacement or modification of the anatomy or of a physiological process; for administration of medicinal products and control of conception.

Medical devices do not achieve their principal intended action in or on the human body by pharmacological, metabolic or immunological means, although in their function they may be assisted by such means,

19. **Homeopathic medicinal product:** Any medicinal product prepared from substances or compositions of substances used as homeopathic stocks, in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or by other currently used pharmacopoeias in the EU Member States,

20. **Quality of the medicinal product:** The acceptable physical, chemical, biological, pharmaceutical and technological, as well as other property of a medicinal product,

21. **Safety of the medicinal product:** The acceptable relation between efficacy and harmfulness of a medicinal product.

22. **Efficacy of the medicinal product:** The ability of a medicinal product verified in clinical trials conducted in compliance with this Act,

23. **Testing of the medicinal product:** The procedure for establishing quality, safety and efficacy of a medicinal product which is performed for the purpose of obtaining a marketing authorisation,

24. **Clinical trial:** Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic activities of one or more investigational medicinal product(s); and/or to discover any adverse reactions to one or more investigational medicinal product(s); and/or to study absorption, distribution, metabolism and excretion of one or more investigational product(s) for the purpose of defining its (their) safety and/or efficacy.

Clinical trials may be conducted at one or several places,

25. **Laboratory testing of medicinal products:** The testing by which the quality of a medicinal product is determined,

26. **Pharmacological and toxicological testing of medicinal products:** The testing of pharmacodynamic, pharmacokinetic and toxicological properties of a medicinal product on animals and other appropriate models,

27. **The Central Ethics Committee:** 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 for Health shall appoint the Central Ethics Committee,

28. **Bioavailability:** 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,

29. **Bioequivalent drugs:** Pharmaceutical equivalents or pharmaceutical alternatives whose bioavailability after administration of the same molar dose is to such extent similar that it may be expected to produce basically the same effect, including efficacy and safety,

30. **Pharmaceutical equivalents:** 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,

31. **Pharmaceutical alternatives:** Drug products containing the same active substance but in the form of a different salt, ester and the like, or in the same pharmaceutical form but of a different strength,

32. **Good Laboratory Practice:** The standard for organising, designing, conducting, monitoring, reporting and documenting of laboratory studies,

33. **Good Clinical Practice:** The standard for designing, conducting, completing, monitoring, analysing, reporting and documenting human clinical trials, which ensures that the trials are scientifically and ethically founded and that clinical properties of the medicinal product tested for diagnostic, treatment or prevention purposes have been appropriately documented,

34. **Informed consent:** 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 consent or is a minor, his legal representative or a guardian may sign an informed consent,

35. **Immediate packaging:** The container or other form of packaging immediately in contact with the medicinal product,

36. **Outer packaging:** The packaging into which the immediate packaging is placed,

37. **Summary of product characteristics:** Expert information on a drug product approved in an authorisation procedure and intended for physicians, stomatologists 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,

38. **Labelling:** Any set of data provided on the immediate or outer packaging,

39. **Package leaflet:** A leaflet containing information for the user, which accompanies the medicinal product,

40. **Original medicinal product:** 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,

41. **Essentially similar medicinal product:** A drug product which has the same active amount of the active substance in the same dosage, form as well as equal bioavailability/bioequivalence as the original product. A medicinal product of a different dosage form than another product of the same composition (capsules/tablets) intended for oral administration is also considered to be an essentially similar medicinal product, with the exclusion of dosage forms with controlled active substance release,

42. **Marketing authorisation:** An authorisation issued by the competent authority of the Republic of Croatia after completion of the procedure for establishing that a medicinal product meets the quality, efficacy and safety requirements,

43. **Marketing authorisation holder:** A legal person seated in the Republic of Croatia holding an authorisation for the marketing of a drug product in the Republic of Croatia,

44. **Manufacturing authorisation:** A document issued by the competent authority 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 regulations derived therefrom,

45. **Manufacturer of the medicinal product:** 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,

46. **Manufacturer with respect to manufacturing site:** A legal person holding the manufacturing authorisation for a plant or plants for drug product manufacturing,

47. **Manufacture of medicinal products:** Comprises the whole process or individual parts of pharmaceutical and technological preparation of a drug product, including production of a substance or acceptance of substances and materials, technological processing and packaging as well as quality control, storage and delivery,

48. **Good Manufacturing Practice:** The part of the quality assurance system which ensures that medicinal products are consistently produced and controlled in accordance with requirements and procedures relevant to the marketing authorisation issuance,

49. **Qualified person for medicinal products manufacture:** A master of pharmacy specialised in pharmaceutical technology or with at least five years of experience in the manufacture of medicinal products,

50. **Qualified person for release of a medicinal product batch:** 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,

51. **Pharmacovigilance:** Activities comprising detection, assessment, understanding and prevention of adverse reactions as well as other reactions caused by medicinal products,

52. **Responsible person of the marketing authorisation holder responsible for pharmacovigilance:** A physician specialised in clinical pharmacology or having at least five years of experience in the field,

53. **Adverse reaction:** Any noxious and unintended response to a medicinal product taken at normal and correctly administered doses for an approved indication,

54. **Unexpected adverse reaction:** Any adverse reaction that is not consistent with the summary of product characteristics,

55. **Adverse event:** Any noxious and undesired sign, symptom or disease (including changes in laboratory findings) that coincides with the use of a medicinal product or a medical device,

56. **Serious adverse event:** Any adverse event or adverse reaction that is fatal, life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, congenital anomaly/birth defect,

57. **Wholesale distribution of medicinal products and medical devices:** All activities including procurement, storage, supply or import/export of a medicinal product or medical device,

58. **Good practice in wholesale distribution of medicinal products and medical devices:** The standard for storage and transportation of medicinal products and medical devices which ensures organisation, performance and control over storage in line with prescribed conditions, as well as transport from the manufacturer to the end user,

59. **Qualified person for acceptance, storage and supply of medicinal products and medical devices in wholesale:** A master of pharmacy holding the necessary authorisation to operate independently,

60. **Specialised stores for retail sale of medicinal products and medical devices:** A store

selling medicinal products in line with this Act and regulations derived therefrom,

61. *Croatian pharmacopoeia*: A regulation that lays down requirements for preparation of medicinal products and medical devices, as well as their quality and quality control procedures, and is appropriately referenced to and harmonised with the European Pharmacopoeia,

62. *Agency*: A legal person established by the Republic of Croatia whose competencies in the field of medicinal products, medical devices and homeopathic products are regulated by this Act.

### Article 3

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

The Minister for Health shall pass an ordinance laying down 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 must be established.

#### Article 5

Testing of a medicinal product includes laboratory, pharmacological and toxicological tests as well as clinical trials.

Tests and trials referred to in paragraph 1 of this Article shall be conducted in line with regulations passed by the Minister for Health.

#### Article 6

Medicinal products shall be tested on the premises of legal persons who fulfil the conditions referred to in Article 3 of this Act, based on the previous approval of the Minister for Health.

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 for Health or the Agency for Medicinal Products and Medical Devices (hereinafter referred to as: the Agency).

#### Article 7

Pre-approval of the Minister for Health 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 the ones earlier 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 one already authorised for marketing in the Republic of Croatia or in comparison with the one 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 for Health 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 prescribed by him.

The Minister for Health 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 for Health 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 4 of this Article, there shall be no limitation to the period for granting pre-approval for xenogenic drugs.

The pre-approval for clinical trials referred to in paragraph 1 item 2 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 Ethics Committee responsible for clinical trials,

3. that the Ethics Committee of the relevant health institution approved the protocol of a trial carried out in only one health institution of the Republic of Croatia, i.e. that the Central Ethics Committee approved the trial protocol in case of a multicentric trial.

Should the Minister for Health fail to grant or refuse the pre-approval within the term referred to in paragraphs 2, 3 and 4 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 7 of this Article, or without a favourable opinion of the competent Ethics Committee.

## Article 8

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

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

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

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

#### 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 Good Clinical Practice passed by the Minister for Health.

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.

#### Article 10

Laboratory as well as pharmacological and toxicological tests shall be conducted in accordance with the Ordinance on Good Laboratory Practice passed by the Minister for Health.

## 2. MARKETING AUTHORIZATION

#### 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, radiopharmaceutical 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.

The Minister for Health may lay down special conditions for placing on the Croatian market a drug product that has obtained an authorisation to be placed on the markets of 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 drug products' manufacture,
- magistral formula,
- galenical preparation,
- medicinal products intended for in vitro development and research,
- intermediate products intended for further processing by an authorised manufacturer,
- whole blood, plasma or blood cells of human origin,
- radionuclides in a sealed radiation source,
- radiopharmaceuticals prepared exclusively from approved radionuclide generators, radionuclide kit or radiopharmaceutical precursor according to the manufacturer's instructions at the time of its use by a natural or legal person authorised for such activity.

#### Article 13



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

Institutions 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

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

The following data and documents shall accompany the application 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, using an international non-proprietary name or in the absence of the same, some other common name for the constituents,
- d) description of the manufacturing method,
- e) therapeutic indications, contra-indications and adverse reactions,
- f) posology, pharmaceutical form, method and route of administration, and expected shelf life,
- g) where applicable, explanation of any special precautionary measures required during medicinal products storage, administration to patients, as well as disposal as waste accompanied by an indication of all potential environmental risks that the medicinal product presents,
- h) description of the manufacturer's control methods (qualitative and quantitative analysis of active substances, excipients and drug product, any special tests),
  - i) results of:
    - physico-chemical, biological and/or microbiological tests,
    - toxicological and pharmacological tests,
    - clinical trials,
  - j) the summary of the product characteristics, proposal for labelling of outer and immediate packaging or one or more specimens of the outer packaging and immediate packaging as well as the package leaflet,
  - k) the manufacturing authorisation,
  - l) 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 underway in other states; copies of the package leaflet approved in other states or proposed in the authorisation procedure underway in other states; details of and reasons for any decision to refuse a marketing authorisation in other states.

The Minister for Health shall pass 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 filed in the Agency shall be considered confidential.

The costs of the procedure for obtaining a marketing authorisation shall be determined by the Agency and paid 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 toxicological and pharmacological tests or the results of clinical trials if he can demonstrate that:

a) the drug product is essentially similar to the original manufacturer's drug product which is already on the market of the Republic of Croatia or the market of an EU Member State, or

b) the active substance or active substances of the drug product has/have a well-established medicinal use, with recognised efficacy and safety, as determined on the basis of a detailed scientific bibliography, or that

c) the drug product is essentially similar to the drug product of the original manufacturer and that both the original manufacturer and the holder of the marketing authorisation in the Republic of Croatia have agreed to use the toxicological, pharmacological and/or clinical data on the original medicinal product from their files during examination of the submitted applications.

## Article 16

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 Article 14 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 oral or written explanation.

The authorisation referred to in paragraph 1 of this Article shall be granted or refused by means of a decision, against which a complaint shall not be allowed, but an administrative dispute may be initiated.

The marketing authorisation shall be published in the Official Gazette.

Alongside with the decision on granting the marketing authorisation, the Agency shall deliver the approved summary of the product characteristics to the authorisation holder.

The authorisation holder shall be responsible for the conformity of the summary of the product characteristics with the summary 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 quality assessment, safety or efficacy of the drug product concerned. Based on collected data, the Agency may change the decision on the marketing authorisation.

## Article 17

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 submitted in line with Article 6 paragraph 2 of this Act, in accordance with Article 14 paragraph 2 subparagraph h) of this Act.

## Article 18

The marketing authorisation shall be refused if, after checking the data and documents referred to in Articles 14 and 15 of this Act, the following is established:

- 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 31 through 37 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 and 15 of this Act.

## Article 19

No later than 90 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 Agency shall grant or refuse the renewal of the marketing authorisation within 90 days from the receipt of a valid application.

An application referred to in paragraph 2 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 paragraph 9 of this Article have been submitted, about which the Agency shall keep records and shall notify the applicant.

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 oral or written explanation.

For any change to the documentation on the basis of which the Agency had granted the marketing authorisation for a medicinal product, the authorisation holder shall submit to the Agency an application for the amendment of the authorisation.

The Agency shall grant or refuse an amendment to a marketing authorisation within 90 days from the receipt of a valid application.

An application referred to in paragraph 6 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 paragraph 9 of this Article have been submitted, about which the Agency shall keep records and shall notify the applicant.

Should the Agency require the applicant to supplement the application, the time limit referred to in paragraph 6 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 oral or written explanation.

The Minister for Health shall pass an ordinance detailing the contents of the documentation referred to in paragraphs 1, 3 and 7 of this Article, submitted for the purpose of renewing or amending the marketing authorisation.

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 case of an urgent withdrawal.

An urgent withdrawal of a drug product from the market referred to in paragraph 10 of this Article shall be ordered by means of a decision passed by a pharmaceutical inspector of the Agency.

#### Article 20

A marketing authorisation shall be revoked before the expiry of its five-year validity 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,
- 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 revoking of a marketing authorisation shall be published in the Official Gazette.

### 3. MANUFACTURING AUTHORIZATION

#### Article 21

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 granted or refused by issuing a decision against which a complaint shall not be allowed, but an administrative dispute may be instituted.

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 the manufacturing site of a pharmaceutical form or a medicinal product or a group of medicinal products.

Within the meaning of this Act, preparation of a magistral or a galenical formula shall not be considered as manufacture.

#### Article 22

An application for obtaining the manufacturing authorisation submitted to the Agency shall contain:

- a description of the whole or a part of the relevant manufacturing procedure,
- a list of relevant medicinal products and pharmaceutical forms,
- the manufacturer's seat and the exact location of the manufacturing site,
- the legal person's seat and the exact location of the quality control premises,
- personal data on qualified persons in charge of manufacture, quality control and sales.

### Article 23

The Agency's procedure for granting or refusing a manufacturing authorisation shall not exceed 90 days from the day of the 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 22 of this Act have been submitted, about which the Agency shall keep records and shall notify 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 an oral or written explanation.

The manufacturing authorisation referred to in paragraph 1 of this Article shall be granted or refused by issuing a decision against which a complaint shall not be allowed, but an administrative dispute may be initiated.

### Article 24

In the procedure for evaluating conditions for granting the manufacturing authorisation, besides the data and documents referred to in Article 22 of this Act an opinion of the Agency's pharmaceutical inspector shall also be required on whether the GMP guidelines have been observed during the manufacture of a medicinal product or a group of medicinal products.

### Article 25

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 at his disposal the services of an adequate number of qualified persons with a university diploma in one of the following scientific disciplines: pharmacy, chemistry, chemical technology, medicine, stomatology, veterinary medicine or other corresponding professions,
2. he has at his disposal the services of a qualified person for drug product manufacture,
3. he has at his disposal the services of a qualified person for the release of a medicinal product batch,
4. he has at his disposal suitable premises, equipment and requisites for the manufacture, quality control, storage and delivery of medicinal products,
5. he observes the principles and guidelines of Good Manufacturing Practice.

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

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

### Article 26

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 timelimit for eliminating the established deficiencies. The costs of issuing a manufacturing authorisation shall be determined by the Agency and paid by the applicant.

#### Article 27

A manufacturing authorisation holder shall notify the Agency in advance in writing about all the changes he plans to make to the data on the basis of which the manufacturing authorisation was issued.

If the changes refer to the data and documents referred to in Article 22 subparagraphs 3 and 4 or Article 25 paragraph 1 item 4 of this Act, the required procedure and decision shall be completed within a maximum of 30 days from the day of receipt of a valid application. In exceptional cases the time limit may be extended to 90 days.

A valid application referred to in paragraph 2 of this Article shall imply that alongside the application, all data and documents have been submitted, from which the contents and scope of change can be undoubtedly ascertained in relation to the data on the basis of which the manufacturing authorisation was issued.

#### Article 28

A manufacturing authorisation shall be revoked if established that a manufacturer has failed to comply with requirements laid down by this Act and regulations derived therefrom.

#### Article 29

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

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

#### Article 30

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 regulations derived therefrom or regulations of the European Union.

### 4. LABELLING AND PACKAGE LEAFLET

#### Article 31

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 drug product,
- the pharmaceutical form and the dose of a medicinal product if there are several forms and doses,
- the qualitative and quantitative composition of active substances,
- the list of excipients prescribed by the Minister for Health,
- the method and the route of administration, if necessary,

- special warnings, if necessary,
- the expiry date (month and year),
- special storage precautions, if any,
- special precautions for disposal of unused medicinal products or their waste materials, if appropriate,
- the name and address of the marketing authorisation holder,
- the number of the marketing authorisation ,
- the batch number,
- in case of self-medication, the instructions on use of the medicinal product without medical supervision.

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

Labelling of medicinal products shall be regulated in greater detail by an ordinance of the Minister for Health.

#### Article 32

Particulars appearing on the outer and immediate packaging of a medicinal product shall be easily legible, comprehensible, indelible and written in the Croatian language.

#### Article 33

The Minister for Health 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 health insurance,
- dispensation (on prescription, or over-the-counter),
- identification and authenticity of the packaging.

#### Article 34

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

By way of exception, the packaging 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 35

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

Alongside Croatian, other languages may also be used under the condition that the conveyed data are identical.

#### Article 36

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

- data for identification of the medicinal product,

- therapeutic indications,
- information that must be given to the user before taking the medicinal product
- necessary and usual instructions for the proper use of the medicinal product,
- the description of possible adverse reactions under normal conditions of use,
- a reference to the expiry date indicated on the packaging,
- the date on which the package leaflet was last revised.

#### Article 37

The Minister for Health shall by means of an ordinance specify the contents and manner of inserting the package leaflet.

### 5. CLASSIFICATION OF MEDICINAL PRODUCTS

#### Article 38

The dispensation of a medicinal product shall be regulated by the marketing authorisation. With respect to dispensation, medicinal products fall into two categories:

1. Medicinal products dispensed on medical prescription,
2. Medicinal products dispensed without medical prescription.

More detailed criteria for classification of medicinal products shall be prescribed by an ordinance of the Minister for Health.

Medicinal products referred to in paragraph 2 item 1 of this Article shall be dispensed exclusively through pharmacies, while medicinal products referred to in paragraph 2 item 2 may also be dispensed through stores specialised in the retail sale of medicinal products and medical devices according to the decision on granting a marketing authorisation.

#### Article 39

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

- are likely to present a direct or indirect hazard, even when used correctly, if utilised without medical supervision,
- are frequently and to a great extent used incorrectly, and are as a result likely to present a direct or indirect hazard to human health,
- contain substances or preparations thereof, the activity and/or adverse reactions of which require further investigation, or
- are normally prescribed by a doctor to be administered parenterally.

Medicinal products to which the criteria referred to in paragraph 1 of this Article do not apply may be dispensed without a medical prescription.

The Minister for Health shall pass an ordinance by which the prescription and dispensation of medicinal products shall be regulated in greater detail.

#### Article 40

A list of medicinal products authorised for placing on the market shall be published by the Agency in the Official Gazette at least once a year.

#### Article 41

On the occasion of the marketing authorisation renewal or when new facts are brought to



its knowledge, the Agency shall re-examine the current medicinal product classification by applying the criteria referred to in Article 39 item 1 of this Act.

## 6. DISTRIBUTION OF MEDICINAL PRODUCTS

### Article 42

Distribution of medicinal products in the territory of the Republic of Croatia shall be subject to the possession of an authorisation.

The data referred to in Articles 31 and 32 of this Act shall appear on the outer and immediate packaging of each drug product placed on the market, with the exclusion of medicinal products for hospital use whose annual import is limited.

Before 31 January of each year, the Minister for Health shall issue an annual list and the largest quantities of drug products referred to in paragraph 2 of this Article.

### Article 43

All legal and natural persons as well as government bodies coming in possession of medicinal products in whatever way shall ensure their transport, holding and storage in accordance with the prescribed requirements, in order to prevent any deterioration of quality or misuse of medicinal products.

The Minister for Health shall pass an ordinance on good practice in wholesale distribution of medicinal products.

### Article 44

Wholesale distribution of medicinal products shall be carried out by:

- legal persons holding an authorisation of the Agency for wholesale distribution of medicinal products,
- manufacturers of medicinal products seated in the Republic of Croatia, for medicinal products of their manufacture and for which they hold marketing authorisations,
- 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 constituents,

### Article 45

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

### Article 46

Pursuant to Article 42 of this Act, wholesale distributors and manufacturers shall be allowed to supply medicinal products to:

- pharmacies,
- health institutions and companies engaging in pharmaceuticals business,
- other wholesalers,

– private surgeries, in quantities required for the treatment of acute conditions.

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

The Croatian National Institute for Public Health may supply health institutions and private surgeries with vaccines and sera.

The Croatian Institute for Transfusion Medicine may supply health institutions with blood and blood constituents.

Pursuant to this Act and regulations derived therefrom, wholesalers may be exceptionally allowed to supply other legal and natural persons with medicinal products subject to the Agency's approval granted on the grounds of a marketing authorisation.

#### Article 47

Import and export of medicinal products shall be carried out by legal persons holding an import and export licence granted by the Agency.

The Minister for Health shall lay down conditions to be met by legal persons applying for a licence for import and export of medicinal products.

The legal persons referred to in paragraph 1 of this Article shall not be required to obtain an import licence for:

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

The provision of paragraph 3 of this Article does not apply to the import of:

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

Provisions of a special Act on Combating Drug Abuse shall apply to import, export, transportation and transit of narcotics and drug products containing narcotics.

#### Article 48

By way of exception, in case of an urgent medically justified need the Agency may allow import of a drug product for which the marketing authorisation was not granted, for the following purposes:

- research,
- clinical trials,
- laboratory tests,
- pharmacological and toxicological tests,
- in case of natural disaster or other emergencies,
- individual patient needs and on his responsibility, in accordance with a medical prescription.

The Minister for Health shall pass an ordinance regulating in detail the import of drug products referred to in paragraph 1 of this Act.

#### Article 49

Retail trade in medicinal products shall be carried out by the legal and natural persons authorised for pharmaceuticals business under a special act, as well as specialised stores for retail sale of medicinal products holding the Agency's authorisation.

The Minister for Health shall by way of an ordinance lay down conditions for granting the retail sale authorisation to specialised stores.

The costs of granting the retail sale authorisation referred to in paragraph 2 of this Article shall be determined by the Agency and paid by the applicant.

The Agency shall grant the retail sale authorisation for medicinal products referred to in paragraph 2 of this Article within 90 days from receiving a valid application.

The application referred to in paragraph 4 of this Article shall be deemed valid if supported by all documents and data prescribed by the Minister for Health.

The retail sale authorisation referred to in paragraph 2 of this Article shall be granted by a decision against which a complaint shall not be allowed, but an administrative dispute may be instituted.

#### Article 50

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 requirements on the basis of which the authorisation was granted.

#### Article 51

Only wholesalers holding the Agency's wholesale distribution authorisation shall be entitled to carry out the wholesale distribution of medicinal products.

In order to obtain the authorisation, applicants shall fulfil the following minimum requirements:

1. to have at their disposal suitable premises, installations and equipment ensuring proper storage and wholesale distribution of medicinal products,
2. to meet the conditions related to the staff employed, particularly in relation to the qualified person responsible for acceptance, storage and delivery of medicinal products as well as for documentation review,
3. to observe the principles of good practice in wholesale distribution of medicinal products,
4. to maintain the documentation in a manner that will enable urgent withdrawal of a medicinal product from the market subject to the Agency's decision or an agreement with the manufacturer or the marketing authorisation holder.

The Minister for Health shall by way of an ordinance specify the conditions and the procedure for granting distribution authorisations for the wholesale of medicinal products.

The costs of granting the distribution authorisation referred to in paragraph 1 of this Article shall be determined by the Agency and paid by the applicant.

The Agency shall grant the distribution authorisation referred to in paragraph 1 of this Article within 90 days from the day of receiving a valid application.

An application referred to in paragraph 5 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 paragraph 8 of this Article have been submitted, about which the Agency shall keep records and shall notify the applicant.

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 supplementary information required has been provided. Likewise, the time limit shall be suspended for the time allowed to the applicant for giving oral or written explanation.

The Minister for Health shall by way of an ordinance specify the documents and data referred to in paragraph 6 of this Article.

#### Article 52

Authorisations for the wholesale distribution of medicinal products shall be given by means of a decision against which a complaint shall not be allowed, but an administrative dispute may be instituted.

The Agency shall revoke the wholesale distribution authorisation where the data supporting the application are found to be inaccurate and where the authorisation holder no longer fulfils the conditions on the basis of which the authorisation was granted.

Authorisations for the wholesale distribution of medicinal products and decisions on their revoking shall be published in the Official Gazette.

#### Article 53

At least once a year, all legal and natural persons engaged in the wholesale or retail sale of medicinal products shall submit to the Agency the data on medicinal products distribution.

The type of data and manner of drawing up the report referred to in paragraph 1 of this Article shall be regulated by an ordinance of the Minister for Health.

#### Article 54

The Minister for Health shall pass an ordinance on the conditions and distribution method of blood, blood cells and blood products, as well as immunological medicinal products and radiopharmaceuticals.

Provisions of a special Act on Combating Drug Abuse shall apply to the wholesale distribution of narcotics and drug products containing narcotics.

#### Article 55

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

Regulations 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 56

Health care professionals coming in contact with users of medicinal products, manufacturers of medicinal products and the 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 the Croatian National Institute of Public Health shall also be notified.

#### Article 57

A marketing authorisation holder shall be required to:

1. appoint a qualified person responsible for pharmacovigilance,
2. maintain detailed records of all suspected adverse reactions in the Republic of Croatia and in other countries,
3. immediately report to the Agency all suspicions about serious adverse reactions brought to his attention by a health care professional,
4. report to the Agency all other suspected serious adverse reactions meeting the reporting criteria, about which he can reasonably be expected to have knowledge,
5. ensure that all suspicions about serious and unexpected adverse reactions occurring in another state are reported to the Agency,
6. submit to the Agency periodic safety reports, either immediately upon request or periodically as regulated by an ordinance of the Minister for Health.

An ordinance on pharmacovigilance shall be passed by the Minister for Health.

#### Article 58

Health care professionals coming in contact with a medicinal product or its user as well as the legal and natural person engaging in manufacture or sale of the medicinal product shall notify the Agency in writing about any observed deterioration of the medicinal product quality.

An ordinance on the method of monitoring the deterioration of medicinal product quality shall be passed by the Minister for Health.

### 8. QUALITY CONTROL OF MEDICINAL PRODUCTS

#### Article 59

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

Quality control may be:

- regular,
- special,
- from distribution, and
- extraordinary.

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

#### Article 60

The regular quality control shall apply to:

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

A drug product manufacturer seated in the Republic of Croatia and holding a marketing authorisation for each manufactured batch of the drug product shall have the obligation to

subject each batch of the drug product to regular quality control.

Wholesalers distributing imported drug products, i.e. importers, shall subject every single batch of an imported drug product to the regular quality control of the Agency.

The costs of the regular quality control referred to in paragraph 1 of this Article shall be paid by a manufacturer seated in the Republic of Croatia, or the marketing authorisation holder of an imported product, or a wholesaler, or a substance importer.

#### Article 61

The special quality control shall apply to:

- the first batch of each drug product after obtaining the marketing authorisation,
- each batch of a drug product from blood or plasma and of an immunological medicinal product,
- other drug products specified by the Minister for Health on the Agency's proposal.

The special quality control shall be carried out by the Agency.

The Agency shall perform quality control within 60 days from the day of receiving the relevant sample.

The costs of quality control referred to in paragraph 1 of this Article shall be paid by the manufacturer seated in the Republic of Croatia, or the marketing authorisation holder in case of imported drug products.

#### Article 62

The quality control from distribution shall apply to all medicinal products taken from distribution by the Agency's pharmaceutical inspectorate, and drug products shall be subject to this quality control at least once during the validity of the marketing authorisation.

The quality control of medicinal products' samples taken from distribution shall be performed by the Agency.

The costs of quality control referred to in paragraph 1 of this Article shall be paid by:

- the holder of the drug product distribution authorisation,
- the health care institution or the pharmacy that has prepared the magistral formula or the galenical preparation,
- the substance producer seated in the Republic of Croatia or the substance importer for imported substances.

The costs of sampling for the purpose of quality control shall be paid by the legal or natural person on whose premises the sampling took place.

#### Article 63

An extraordinary quality control shall be carried out on request of the Ministry of Health or the Agency in case of any unusual or suspicious signs relevant to the quality of a certain medicinal product. The extraordinary quality control shall be performed by the Agency.

The costs of quality control from paragraph 1 of this Article shall be paid by the Ministry for Health or the Agency if the suspicions are not confirmed, and otherwise by the legal or natural person whose irregular manufacturing procedure, preparation or distribution of the medicinal product led to quality deterioration.

#### Article 64

Quality of medicinal products and raw materials for their production, including materials

used for immediate packaging, shall comply with requirements of the Croatian Pharmacopoeia, or if not included in the pharmacopoeia, with other recognised international standards.

The Croatian Pharmacopoeia shall be adopted by the Minister for Health on proposal of the Agency.

The quality control of a medicinal product shall be conducted in accordance with the procedures specified in the accepted documentation accompanying the relevant application for a marketing authorisation, or in absence of such documentation, the procedures adopted by the Agency shall apply.

The Agency shall determine the scope of quality control for individual medicinal products.

#### Article 65

Manufacturers, wholesalers and each importer of medicinal products shall keep a register on the regular, extraordinary and special quality controls performed.

The Agency shall keep a register on quality controls performed.

Registers referred to in paragraphs 1 and 2 of this Article shall be kept for one year longer than the shelf life of the relevant medicinal product.

The contents and manner of maintaining the register referred to in paragraphs 1 and 2 of this Article shall be prescribed by an ordinance of the Minister for Health.

### 9. ADVERTISING AND PROVIDING INFORMATION ON MEDICINAL PRODUCTS

#### Article 66

Within the meaning of this Act, advertising and providing information on medicinal products shall include any form of information designated to promote the prescription, dispensation, sale and consumption of medicinal products, be it in written, figurative, audio, verbal, electronic, digital or any other form.

#### Article 67

Advertising and providing information on medicinal products referred to in Article 38 paragraph 2 items 1 and 2 of this Act shall be allowed in technical literature, at professional and scientific meetings on the subject of medicinal products, and towards health care professionals.

Advertising and providing information on medicinal products referred to in Article 38 paragraph 2 item 2 of this Act to the general public shall be allowed.

Advertising and providing information on medicinal products referred to in Article 38 paragraph 2 item 1 of this Act to the general public shall be prohibited.

It is prohibited to advertise or provide information on a drug product without a marketing authorisation, except 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 medicinal product is used without any reference to its manufacturer. These limitations shall not apply to international meetings held in the Republic of Croatia.

#### Article 68

Advertising and providing information on a medicinal product shall be objective, shall

promote rational pharmacotherapy and shall not be misleading.

The Minister for Health shall by way of an ordinance regulate advertising and providing information on drug products.

## 10. SUPPLY OF CROATIAN MEDICINAL PRODUCTS MARKET

### Article 69

Supervision over the Croatian market supply of medicinal products shall fall within the competence of the Ministry of Health.

The Agency shall monitor the consumption of medicinal products in accordance with the National Policy on Medicinal Products.

The Government of the Republic of Croatia shall adopt the National Policy on Medicinal Products on the proposal of the Minister for Health.

The Agency shall propose measures of supervision over the consumption of medicinal products to the Minister for Health, in accordance with the National Policy on Medicinal Products.

### Article 70

In order to achieve an optimal supply of the market with medicinal products for public health protection, care shall be taken to adjust their prices according to the social structure of the Republic of Croatia.

In accordance with the objectives referred to in paragraph 1 of this Article, the Minister for Health shall issue an ordinance on pricing criteria for medicinal products as well as the price reporting method.

On the Agency's request, a marketing authorisation holder shall set a medicinal product price in accordance with the criteria referred to in paragraph 2 of this Article.

### Article 71

The Minister for Health may demand price negotiations, in case the high price of a medicinal product stands in the way of normal market supply.

A marketing authorisation holder shall at the Agency's request enable inspection of the price structure of the medicinal product which he has proposed to the market.

## 11. SUPERVISION

### Article 72

The Agency's pharmaceutical inspectorate shall supervise the testing, manufacture and preparation, sales, quality control as well as advertising and providing information on medicinal products.

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

### Article 73

In carrying out the supervision referred to in Article 72 of this Act, a pharmaceutical inspector shall have the right and duty to:



1. order that activities be carried out in accordance with the conditions laid down under this Act and other regulations,
2. order that established irregularities and defects be remedied within a certain time limit,
3. prohibit activities contrary to this Act and other regulations,
4. temporarily prohibit the work of a legal or natural person who fails to meet requirements related to staff, equipment and premises,
5. prohibit the work of legal and natural persons engaged in testing, manufacture and preparation, distribution and quality control of medicinal products without an authorisation of the Agency,
6. prohibit placing on the market and order withdrawal from the market of a medicinal product:
  - proven to be harmful under normal conditions of use, or
  - lacking in therapeutic efficacy, or
  - whose qualitative and/or quantitative composition is not as declared in the application for obtaining the marketing authorisation, or
  - if quality control of the product and/or raw materials from its composition has not been performed, or
  - if the second requirement or condition for granting the marketing authorisation has not been fulfilled,
7. order withdrawal from distribution of a medicinal product batch that fails to meet the conditions laid down by this Act and other regulations,
8. declare that a product established to be defective is hazardous waste and order its disposal,
9. prohibit the work and propose to the Agency to revoke an operating license in case the failure to observe conditions laid down by this Act and other regulations could result in a threat to human life or a health hazard,
10. order taking other measures within his authority under this Act and other regulations.

The costs of quality control, withdrawal from the market, or disposal of a product which was found to be defective during supervision, shall be paid by the legal person who placed the product on the market or imported the defective product or by the legal and natural person responsible for the deterioration of the product through irregular storage or handling.

#### Article 74

Besides the rights and duties referred to in Article 73 of this Act, a pharmaceutical inspector shall also have the right and duty to:

- temporarily suspend marketing authorisations of all medicinal products and dosage forms to which they apply in case of failure to observe any of the conditions provided in Articles 25, 29 and 30 of this Act,
- temporarily suspend a marketing authorisation due to the breach of Article 60 paragraph 2 and 3 and Article 61 of this Act.

#### Article 75

The tasks of a pharmaceutical inspector shall be performed by persons with a university degree in medicine or other appropriate fields, who have five years of experience in appropriate jobs and who meet other conditions to be prescribed by an ordinance of the Minister for Health.

#### Article 76

The Agency shall authorize recognised experts to perform individual tasks of the

pharmaceutical inspectorate for which special expertise is required.

#### Article 77

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

The Minister for Health shall pass an ordinance regulating the form and contents of the official identity card, as well as the manner of issuing and maintaining a register on the official identity cards issued.

#### Article 78

If a pharmaceutical inspector discovers during the supervision that a misdemeanour or criminal act was committed by breach of regulations, he shall without delay and no later than within 15 days from completing supervision submit the relevant application or report to the competent authority.

The authority to which the application or report as defined in paragraph 1 of this Article has been submitted shall inform the Agency about the outcome of the relevant proceedings.

#### Article 79

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

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

#### Article 80

In carrying out supervision, pharmaceutical inspectors shall observe regulations on keeping business, state, military, official and professional secrets.

Legal and natural persons shall inform the pharmaceutical inspector of what is considered as secret under their by-laws.

#### Article 81

Pharmaceutical inspectors shall be allowed to pass oral decisions in the following cases:

1. when a certain measure has to be taken without delay because human life or health is endangered,
2. where there is danger of proof being hidden, replaced or destroyed unless a measure is immediately taken.

A pharmaceutical inspector may order the immediate execution of his oral decision. The oral decision shall be entered into the supervision minutes.

The pharmaceutical inspector shall be obliged to make a copy of the decision within eight days.

#### Article 82

A complaint may be lodged to the Ministry of Health against the decision of the Agency's inspector.

No complaint against the decision of the Ministry of Health shall be allowed, however an administrative dispute may be instituted.

#### Article 83

A pharmaceutical inspector shall keep minutes on the supervision performed, status established, measures ordered and taken, and on activities carried out.

The inspector shall submit copies of the minutes to the natural person or to the responsible person within the legal person on whose premises the supervision took place.

#### Article 84

Provisions of the Act on General Administrative Procedure shall apply to the procedure of pharmaceutical inspectors, unless certain issues have been otherwise regulated by this Act.

#### Article 85

The pharmaceutical inspectors shall maintain records of the supervisions performed.

The Minister for Health shall pass an ordinance on the method of keeping the register.

#### Article 86

A pharmaceuticals inspector shall be responsible:

1. for failing to take or order measures that he was obliged to take or order during supervision,
2. for exceeding his authority,
3. for failing to submit an application or report to the competent authorities on irregularities or defects established.

### **III. HOMEOPATHIC PRODUCTS**

#### **1. PLACING HOMEOPATHIC PRODUCTS ON THE MARKET**

#### Article 87

A homeopathic product shall be placed on the market only if it has been issued a marketing authorisation by the Agency or entered into the Agency's register in accordance with this Act and regulations derived therefrom.

#### Article 88

For the purpose of obtaining the marketing authorisation, an application shall be submitted to the Agency. The application shall be accompanied by data and documents in line with conditions for placing a medicinal product on the market referred to in Articles 14 and 15 of this Act.

#### Article 89

Without obtaining the marketing authorisation, the homeopathic products which satisfy the following conditions shall be entered into the Agency's registry:

- that they are intended for oral or external administration,
- that no therapeutic indication appears on the packaging or documentation,
- that there is a sufficient degree of dilution to guarantee the safety of the products; in particular, such products may not contain more than one part per 10000 of the mother tincture or more than 1/100<sup>th</sup> of the smallest therapeutic dose of the active substance that would require a medical prescription.

#### Article 90

Upon entry into the register, the Agency shall designate the dispensing classification of the products. Contents and maintenance of the register shall be prescribed in an ordinance passed by the Minister for Health.

Evidence of therapeutic efficacy shall not be required for homeopathic products referred to in Article 89 of this Act.

#### Article 91

An application for entry into the Agency's register may cover batches of products derived from the same homeopathic stock or stocks.

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

- scientific name or other pharmacopoeial name for a homeopathic stock or stocks, description of various administration methods, pharmaceutical forms and degree of dilution,
- documentation describing how a homeopathic stock or stocks is/are obtained and controlled and justifying its/their homeopathic nature on the basis of the relevant bibliography,
- manufacturing and quality control file for each pharmaceutical form and description of the method of dilution and potentization,
- manufacturing authorisation for the individual product,
- evidence of entry into the register or the marketing authorisation obtained for the same product in other states,
- a specimen of the outer packaging and the immediate packaging of the product for which the marketing authorisation is requested,
- data on the stability of the product.

#### Article 92

The Agency shall grant or refuse the 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 30 days from its receipt the Agency verifies that all the data and documents referred to in Article 88 of this Act have been submitted, about which the Agency shall keep records and shall notify the applicant.

The marketing authorisation shall be issued for a term of 5 years. An application for renewal of a homeopathic product authorisation may be submitted to the Agency no later than 90 days before the expiry of its validity.

Provisions of Article 20 of this Act shall appropriately apply to the withdrawal of the homeopathic product's marketing authorisation prior to the expiry of its validity.

#### Article 93

Provisions of Article 16 paragraphs 3, 4 and 5 of this Act shall also appropriately apply to homeopathic products.

### 2. LABELLING AND PACKAGE LEAFLET

#### Article 94

Provisions of Articles 31 through 37 of this Act shall also appropriately apply to homeopathic products for which a marketing authorisation is required.

The homeopathic nature of the product shall be clearly and legibly indicated on the outer packaging as well as on the immediate packaging.

#### Article 95

Outer and immediate packaging and, if necessary, package leaflets of homeopathic products referred to in Article 89 of this Act shall in addition to a clear label "homeopathic medicinal product" bear only the following information:

- the scientific name of the homeopathic stock or stocks and indication of the degree of dilution using pharmacopoeial symbols,
- the name and address of the legal person seated in the Republic of Croatia to whom the marketing authorisation has been issued and, if necessary, the manufacturer's name and address,
- the method of administration and, if necessary, the route of administration,
- shelf life,
- pharmaceutical form,
- composition of the product,
- special storage precautions, if necessary,
- special warning, if necessary,
- the batch number,
- the entry number in the Agency's register,
- the label »a homeopathic product without proven therapeutic indications «,
- a warning in which patients are instructed to consult a physician if symptoms fail to disappear during use of the product.

### 3. ADVERTISING AND PROVIDING INFORMATION

#### Article 96

Advertising and providing information on homeopathic products referred to in Article 89 of this Act shall be prohibited.

The method of advertising and providing information on homeopathic products not subject to the prohibition referred to in paragraph 1 of this Article shall be regulated by an ordinance of the Minister for Health.

## 4. OTHER PROVISIONS

### Article 97

The manufacture, wholesale distribution and retail sale as well as quality control of homeopathic products shall be specified in an ordinance passed by the Minister for Health.

### Article 98

Provisions of this Act referring to the supervision over medicinal products shall also appropriately apply to homeopathic products.

## IV. MEDICAL DEVICES

### Article 99

Within the meaning of this Act, medical devices include: in vitro diagnostic medical devices including reagents, reagent kits, calibrators, control materials, instruments, apparatuses, equipment and systems.

The following products shall likewise be considered as medical devices:

- used exclusively with a certain medicinal product to improve its handling or use,
- custom-made for a certain user,
- intended for clinical trials.

The provisions of Articles 107 and 111 through 114 of this Act shall not apply to the medical devices referred to in paragraph 2 of this Article.

### Article 100

According to the degree of risk to its users, medical devices are classified as follows:

- I – medical devices presenting a low degree of risk to their users,
- IIa – medical devices presenting a higher degree of risk to their users,
- IIb – medical devices presenting a high degree of risk to their users,
- III – medical devices presenting the highest degree of risk to their users.

With respect to their nature, energy sources and other properties, medical devices fall into the following groups:

- non-invasive,
- invasive, and
- active.

More detailed conditions and methods of classification of individual medical devices as well as how and where they are dispensed with respect to their intended use and risks for the user, shall be regulated by an ordinance of the Minister for Health.

### Article 101

The method of advertising and providing information on medical devices shall be regulated by an ordinance of the Minister for Health.

## 1. REQUIREMENTS FOR MEDICAL DEVICES

### Article 102

The following general requirements for medical devices shall apply:

- they have to be designed, manufactured, installed, maintained and used under the

prescribed conditions and for their intended purpose in order to avoid potential health hazard to their users,

–the quality assurance system must be observed in their design and manufacture.

Special requirements for medical devices shall be determined with respect to their intended purpose.

The Minister for Health shall pass an ordinance laying down general and special requirements for medical devices.

## 2. CONFORMITY ASSESSMENT AND MARKING OF MEDICAL DEVICES

### Article 103

The conformity assessment is a procedure used to directly or indirectly establish whether a medical device meets the requirements set out in Article 102 of this Act.

### Article 104

Conformity of a medical device with the prescribed requirements shall be confirmed by issuing a conformity document (a declaration of conformity, testing report, a certificate or other conformity document).

### Article 105

The procedure for the assessment of medical device conformity with the prescribed requirements shall be carried out in accordance with the classes referred to in Article 100 paragraph 1 of this Act.

Manufacturers of class I medical devices shall assess whether they comply with the prescribed requirements and shall at their own risk issue a declaration of conformity.

Calibrators and sterile products belonging to class I shall be assigned to class II or III and shall not be subject to the provision set out in paragraph 2 of this Article.

The conformity of medical devices from classes II a, II b and III with the prescribed requirements shall be established by the Agency.

The procedure for conformity assessment of medical devices shall be regulated in greater detail by an ordinance of the Minister for Health.

### Article 106

The Agency shall recognise another state's conformity document and conformity marking if they comply with international agreements ratified by the Republic of Croatia.

The Agency may also recognise other conformity documents and conformity markings if issued on the grounds of applications similar to the applications defined in this Act as well as by another state's body with authorities corresponding to the authorities of the Agency.

### Article 107

Based on conformity documents, manufacturers shall be obliged to affix the prescribed conformity markings on their products.

The Minister for Health shall pass an ordinance prescribing the conformity marking and contents of the declaration of conformity.

Provisions of this Article shall not apply to medical devices intended for testing or medical devices custom-made for individual users.

### Article 108

It is prohibited to affix on medical devices any markings incompliant with the provisions of this Act.

### **3. MANUFACTURE OF MEDICAL DEVICES**

#### **Article 109**

A medical device manufacturer is a legal or natural person responsible for the design, manufacture, packaging, package leaflets and marking of medical devices prior to their placing on the market under his own name, regardless of whether the entire manufacture was carried out by himself or by another person on his behalf.

#### **Article 110**

A medical device manufacturer shall submit the required documentation to the Agency for the purpose of entering the medical device into the Agency's register.

A medical device manufacturer shall provide the conformity documents referred to in Article 105 of this Act.

The Minister for Health shall pass an ordinance defining the documentation contents and format in greater detail as well as the procedure for entering medical devices into the register referred to in paragraph 1 of this Article.

A medical device manufacturer shall notify the Agency about any change made to the data and documentation submitted for the purpose of entering the medical device into the register.

### **4. DISTRIBUTION OF MEDICAL DEVICES**

#### **Article 111**

Medical devices may be placed on the market or put into service, only if they fulfil the requirements provided in Article 102 of this Act, if their conformity is established in accordance with the prescribed procedure, if labelled as required, and if entered into the register.

Medical device distribution shall comprise wholesale and retail sale.

Manufacturers, legal and natural persons engaging in wholesale trade, pharmacies, and specialised retail sale stores shall be allowed to distribute medical devices.

Wholesale trade, legal and natural persons engaging in import or export, and specialised retail stores for medical devices shall possess the Agency's authorisation for distribution and/or import and export of medical devices.

Provisions of Article 51 paragraphs 4, 5, 6, 7 and 8 as well as Article 52 of this Act shall also apply to medical devices.

Wholesale trade and other legal and natural persons holding an import licence shall be allowed to import medical devices that are not entered into the Agency's register, subject only to the Agency's pre-approval.

The Agency shall maintain a register of persons engaged in the distribution of medical devices referred to in paragraph 3 of this Article, with the exclusion of pharmacies, as well as a register of medical devices allowed for sale in the Republic of Croatia.

The costs of register maintenance shall be determined by the Agency and paid by the persons referred to in paragraph 3 of this Article.

The contents and the method of register maintenance referred to in paragraph 7 of this Article shall be regulated by an ordinance of the Minister for Health.



#### Article 112

Conditions for granting an authorisation for distribution of a medical device shall be regulated by an ordinance of the Minister for Health.

#### Article 113

Provisions of Article 43 paragraph 1 of this Act shall also appropriately apply to medical devices.

#### Article 114

The Minister for Health shall pass an ordinance on good practice in wholesale distribution of medical devices.

### **5. CLINICAL TRIALS OF MEDICAL DEVICES**

#### Article 115

A clinical trial of a medical device shall be any trial conducted in order to establish or confirm a manufacturer's statement about the safety and efficacy of a medical device.

Clinical trials of medical devices shall be subject to obtaining an informed consent from each trial subject.

Clinical trials shall not be conducted if the potential risks of using a medical device outweigh the health care justification of the trial, as assessed by the Minister for Health.

Prisoners or persons that could be coerced into giving their consent to participate in a clinical trial shall not be clinical trial subjects.

Children may be clinical trial subjects only if appropriate results cannot be achieved in trials on adults.

#### Article 116

The principle of medical ethics and compulsory protection of privacy and personal data of trial subjects, in accordance with the Ordinance on Good Clinical Practice passed by the Minister for Health, shall be observed in conducting clinical trials of medical devices.

#### Article 117

A medical device manufacturer or a legal person on whose premises the clinical trial of a medical product is conducted shall possess a clinical trial authorisation issued by the Minister for Health as well as an agreement signed with the clinical trial applicant.

#### Article 118

The Minister for Health shall grant or refuse a clinical trial authorisation within 60 days from submission of a valid application.

An application referred to in paragraph 1 of this Act shall be deemed valid if within a maximum of 30 days from its receipt the Agency verifies that all the data and documents required by the Minister for Health have been submitted, about which the Agency shall keep records and shall notify 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 is provided. Likewise, the time limit shall be suspended for the time allowed to the applicant for giving oral or written explanation.

The costs of trials and authorisation issue shall be paid by the applicant.

The Minister for Health shall pass an ordinance regulating the procedure and conditions for testing medical devices.

## **6. PHARMACOVIGILANCE OF MEDICAL DEVICES**

### **Article 119**

Legal and natural persons as well as health care professionals coming in contact with users of medical devices shall report to the Agency in writing on adverse reactions or suspected adverse reactions.

The Minister for Health shall pass an ordinance regulating in greater detail the pharmacovigilance of medical devices.

### **Article 120**

Medical devices that are no longer fit for use shall be disposed of at the expense of their owners.

Regulations applicable to the disposal of hazardous waste shall also apply to the disposal of medical devices referred to in paragraph 1 of this Act.

## **7. SUPERVISION**

### **Article 121**

Compliance with the provisions of this Act and regulations derived therefrom related to medical devices, shall be supervised by the pharmaceutical inspectorate of the Agency.

### **Article 122**

In exercising supervision, a pharmaceutical inspector shall have the right and duty to:

- supervise the quality assurance system of a medical device manufacturer and, if necessary, premises of his suppliers or other contractual parties,
- request all the necessary information from the importer, manufacturer or wholesale trader as well as insight into the conformity documents issued and technical documentation,
- order the performing of appropriate tests and controls of medical devices in order to evaluate compliance with regulations even after placing a medical device on the market or after putting it into service,
- sample medical devices and order conducting the procedure for the assessment of compliance with the prescribed requirements,
- order the labelling of a medical device in accordance with regulations or the removal of an irregularly labelled medical device,
- prohibit, restrict or withdraw from distribution medical devices which fail to meet the prescribed requirements,
- prohibit, restrict or order discontinuation of use of medical devices which fail to meet the prescribed requirements,
- suspend any supply, dispensation or promotion of a medical device in case of a justified suspicion about its compliance with the prescribed requirements,
- order the destruction of non-compliant medical devices, where necessary for the protection of public health.

### **Article 123**

Provisions of Articles 76 through 86 of this Act, referring to the supervision over

medicinal products shall also appropriately apply to medical devices.

## **V. AGENCY FOR MEDICINAL PRODUCTS AND MEDICAL DEVICES**

### **Article 124**

The Agency for Medicinal Products and Medical Devices (hereinafter referred to as: “the Agency”) is a legal person whose organization and operating method are governed by this Act and regulations derived therefrom.

The Republic of Croatia shall be the founder of the Agency.

The Agency shall be entered into the Court Register.

The Agency shall be seated in Zagreb.

### **Article 125**

The Agency’s activities shall include:

- granting marketing authorisations for medicinal and homeopathic products,
- maintaining a register of medicinal and homeopathic products,
- providing expert evaluation of the quality, efficacy and safety of medicinal and homeopathic products as well as of the quality or compliance and safety of medical devices,
- performing laboratory testing of medicinal products, medical devices and homeopathic products,
- supervising clinical trials of medicinal products and medical devices, keeping records of clinical trials conducted in the Republic of Croatia, filing final reports, analysing information on untoward effects of medicinal products and medical devices tested,
- performing quality control of medicinal products, medical devices and homeopathic products,
- drawing up monographs for the Croatian pharmacopoeia,
- issuing manufacturing authorisations to the manufacturers of medicinal products, medical devices and homeopathic products,
- issuing authorisations for wholesale distribution of medicinal products, medical devices and homeopathic products,
- issuing retail sale authorisations to stores specialised in retail sale of medicinal products and medical devices,
- issuing import and export licences for medicinal products and medical devices,
- giving import and export approvals for medicinal products and medical devices,
- monitoring adverse reactions and defective medicinal products and medical devices,
- monitoring consumption and promoting rational use of medicinal products,
- supervising, through its pharmaceutical inspectorate, the implementation of this Act and regulations derived therefrom,
- proposing supervising measures for the consumption of medicinal products to the Minister for Health,
- proposing measures from the field of the National Policy on Medicinal Products,
- providing information on medicinal products and medical devices,
- proposing harmonisation of regulations on medicinal products and medical devices with EU regulations as well as with regulations and guidelines of international institutions,
- realizing international cooperation in the area of medicinal products and medical devices,

- performing other tasks in the area of medicinal products and medical devices in accordance with this Act and regulations derived therefrom.

#### Article 126

The Agency shall have a Statute which shall, in accordance with this Act, detail the organisation, authorities and decision making of individual bodies, the conditions and procedure for appointing the manager as well as other issues of importance for carrying out activities and business operations of the Agency.

The Agency's Administrative Council with the consent of the Government of the Republic of Croatia shall adopt the Statute.

#### Article 127

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

The rights and obligations of the Agency's employees shall be regulated by the Labour Ordinance.

The Labour Ordinance as well as other by-laws of the Agency shall be adopted by its Administrative Council, unless it is prescribed by this Act and the Statute that it be adopted by the Agency's manager.

#### Article 128

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

#### Article 129

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 on behalf of the Republic of Croatia by the Government of the Republic of Croatia, at the proposal of the Minister for Health.

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

#### Article 130

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,
- if in his work he seriously infringes or repeatedly infringes the law and other regulations relevant to operations and performance of the Agency's activities,
- if his work causes damage to the Agency,
- in other cases defined by law and the Statute.

#### Article 131

The Administrative Council shall:

- adopt the Labour Ordinance and other by-laws of the Agency,

- adopt a business and financial plan for the Agency,
- adopt annual accounts and business reports of the Agency,
- appoint and relieve of duty the Agency’s manager,
- decide on the internal organisation of the Agency,
- decide on other issues set out in the Agency’s Statute.

#### Article 132

The Agency’s manager shall run the Agency’s operations.

The Manager of the Agency shall be appointed for a period of four years. After the expiry of his term of office, a manager may be re-appointed without restrictions to the number of his terms of office.

#### Article 133

The Agency’s manager shall:

- run and manage the Agency’s operations,
- act as the Agency’s agent and representative,
- make proposals on acts under his competence to the Administrative Council,
- decide on other matters defined by the Statute,

#### Article 134

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

- requests to be relieved,
- fails to observe the Agency’s regulations and by-laws,
- refuses, without foundation, to carry out the decisions of the Agency’s Administrative Council that fall within its competence,
- causes substantial damage to the Agency through unconscientious and erroneous work,
- frequently neglects or unconscientiously carries out his duties thus causing difficulties to the operation of the Agency.

#### Article 135

The Agency’s property shall consist of operating funds provided by its founder, or acquired by rendering services or from other sources.

The funds necessary for the Agency’s business operations shall be provided from:

- revenues from the Agency’s operations (from service payments and annual fees)
- and other sources in line with this Act or other regulations.

#### Article 136

The Ministry of Health shall supervise the lawfulness of the Agency’s operation.

#### Article 137

The Agency shall submit an annual report on its operation to the Minister for Health and to the Government of the Republic of Croatia.

#### Article 138

General labour regulations and the collective agreement shall govern the legal status of the Agency's employees, employment conditions, salaries and other issues not regulated by this Act.

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

## VI. PENAL PROVISIONS

### Article 139

A legal person shall be fined for misdemeanours between HRK 70,000.00 and HRK 100,000.00 for:

1. placing a medicinal product on the market without previously performing tests or for testing a medicinal product contrary to the provisions of this Act and regulations derived therefrom (Article 4, Article 5 paragraph 2, Article 6 paragraph 2, Articles 7, 8, 9 and 10),
2. placing on the market of the Republic of Croatia a medicinal product for which the marketing authorisation was not previously obtained (Article 11 and Article 42 paragraph 1),
3. providing incorrect data in the documentation accompanying the application for obtaining a marketing authorisation (Article 14 paragraph 2 and Article 15),
4. a medicinal product whose qualitative and quantitative composition differs from the data accompanying the application for obtaining the marketing authorisation or an authorisation for its amendment, or if proven that a drug product is unacceptably harmful or lacking efficacy under the prescribed conditions of use (Article 20 paragraph 1),
5. manufacturing a medicinal product in the Republic of Croatia without the manufacturing authorisation issued by the Agency (Article 21 paragraph 1),
6. providing incorrect data in the application for obtaining the manufacturing authorisation or failing to notify the Agency that he changed the data on the basis of which the manufacturing authorisation was issued (Articles 22 and 27, paragraph 1),
7. engaging in wholesale distribution or retail sales of a medicinal product without a marketing authorisation issued by the Agency (Article 44 and Article 49 paragraph 1),
8. engaging in import and export of a medicinal product without an import or export license (Article 47 paragraph 1),
9. conducting quality control of a medicinal product contrary to the provisions of this Act and regulations derived therefrom (Article 59 through 65),
10. advertising and providing information on a medicinal product contrary to the provisions of this Act and regulations derived therefrom (Article 66 through 68),
11. pricing a medicinal product contrary to the criteria provided in Article 70 paragraph 2 of this Act (Article 70 paragraph 2)
12. failing to enable insight into a medicinal product price structure as required by the Agency (Article 71 paragraph 2),
13. failing to act timely in accordance with a final decision of a pharmaceutical inspector by which specific measures or actions are ordered or his work prohibited (Article 73),
14. failing to enable supervision by a pharmaceutical inspector in accordance with the provisions of this Act and regulations derived therefrom (Article 79),
15. placing a homeopathic product on the market without the Agency's pre-approval or entry into the Agency's register (Article 87 and 89),
16. providing incorrect data in the documentation accompanying an application for the entry of a homeopathic product into the register (Article 91),
17. advertising or providing information on a medical device contrary to this Act and

regulations derived therefrom (Article 101),

18. providing incorrect data in the documentation accompanying an application for the entry of a medical device into the register (Article 110),

19. placing on the market a medical device contrary to the provisions of Article 111 paragraph 1 of this Act (Article 111 paragraph 1),

20. engaging in the distribution or import and export of medical devices without the Agency's distribution authorisation or license for import and export of medical devices (Article 111 paragraph 4),

21. manufacturing a medical device in the Republic of Croatia without the Agency's manufacturing authorisation (Article 125).

For misdemeanours referred to in paragraph 1 of this Article, a natural person and a responsible person within a legal person shall be fined between HRK 7,000.00 and HRK 10,000.00.

#### Article 140

A legal person shall be fined for misdemeanours between HRK 50,000.00 and HRK 80,000.00 for:

1. failing to fulfil the conditions laid down by this Act and regulations derived therefrom in performing tests and quality control of products to which this Act applies (Article 3),

2. conducting clinical trials of a medicinal product or a medical device without an authorisation from the Minister for Health (Article 7 and Article 117),

3. distributing a drug product whose marketing authorisation is not valid in the Republic of Croatia (Article 11 paragraph 3 and Article 42 paragraph 1),

4. placing on the market of the Republic of Croatia a drug product without a label or a package leaflet or a medicinal product without a conformity assessment or without labelling in accordance with the provisions of this Act and regulations derived therefrom (Article 31, Article 34, paragraph 2 and 4 of Article 105, and Article 108),

5. dispensing a medicinal product in a manner and at a place contrary to the issued marketing authorisation (Article 38),

6. failing to ensure the transportation, holding and storage of a medicinal product or a medical device in accordance with the storage conditions provided on the label of the medicinal product or the medical device (Article 43 and Article 113),

7. importing or exporting a medicinal product or a medical device without the required approval (Article 48 and Article 111 paragraph 6),

8. providing inaccurate data in the documentation accompanying the application for obtaining an authorisation for the wholesale distribution of a medicinal product or a medical device (Article 51 and Article 111 paragraph 5),

9. failing to meet the obligation referred to in Article 57 of this Act (Article 57),

10. failing to submit every batch of a manufactured or imported drug product or every batch of substance, to the regular quality control before placing on the market (Article 60),

11. failing to submit a drug product to the special quality control (Article 61),

12. placing on the Croatian market a medicinal product whose quality, including the quality of all raw materials necessary for the manufacture and preparation of the medicinal product, as well as the quality of materials for immediate packaging, fails to comply with the Croatian pharmacopoeia or is not included in the same or is not in accordance with other internationally recognised standards (Article 64 paragraph 1),

13. failing to maintain a register on regular, extraordinary and special quality control in line with the provisions of this Act and regulations derived therefrom (Article 65),

14. failing to provide data in accordance with this Act on the outer packaging and immediate packaging of a homeopathic product (Article 94 and Article 95),

15. advertising and providing information on a homeopathic product referred to in Article 89 of this Act (Article 96),

16. dispensing medical devices in a manner and place contrary to this Act and regulations derived therefrom (Article 100 paragraph 3).

For misdemeanours referred to in paragraph 1 of this Article, a natural person and a responsible person within a legal person shall be fined between HRK 5,000.00 and HRK 8,000.00.

#### Article 141

A legal person shall be fined for misdemeanours between HRK 40,000.00 and HRK 60,000.00 for submitting an inaccurate piece of information in the process of obtaining approval for the import of a medicinal product or a medical device for which authorisation for marketing in the Republic of Croatia has not been granted (Article 48 and Article 111 paragraph 6).

For misdemeanours referred to in paragraph 1 of this Article a responsible person within a legal person shall be fined between HRK 4,000.00 and HRK 6,000.00.

#### Article 142

A legal or natural person shall be fined for misdemeanours between HRK 30,000.00 and HRK 50,000.00 for:

1. failing to timely inform the Agency about the intended withdrawal of a medicinal product from the market before the expiry of the relevant authorisation (Article 19 paragraph 10),

2. disposing of medicinal products or medical devices which are no longer fit for use in a manner that is contrary to the provisions of this Act and regulations in force (Articles 55 and 120),

3. failing to notify in writing the Agency, as well as the Croatian National Institute of Public Health in the case of vaccines, about adverse reactions to a medicinal product or a medical device in line with the provisions of this Act and regulations derived therefrom (Article 56, Article 57 and Article 119),

4. failing to notify the Agency in writing about any detected deterioration in the quality of a medicinal product in accordance with the provisions of this Act and regulations derived therefrom (Article 58),

5. advertising and providing information on a medicinal product in order to encourage prescribing, dispensing and consumption of a medicinal product for which a marketing authorisation was not granted in the Republic of Croatia or for failing to fulfil other conditions for its placing on the market (Article 67 paragraph 4),

6. placing on the market homeopathic products which are not labelled in accordance with the provisions of this Act (Article 94),

For misdemeanours referred to in paragraph 1 of this Act a responsible person within a legal person shall be fined between HRK 3,000.00 and HRK 5,000.00.

## VII. TRANSITIONAL AND FINAL PROVISIONS

#### Article 143



The Croatian National Institute for the Control of Medicinal Products and the Croatian National Institute for the Control of Immunobiologicals, both established under the Health Care Act (Official Gazette Nos 75/93, 11/94, 55/96, 1/97 – consolidated text, 111/97, 95/00 and 129/00) shall as of 1 October 2003 continue operating jointly as the Agency.

The Agency shall be the universal legal successor of the Croatian National Institute for the Control of Medicinal Products and the Croatian National Institute for the Control of Immunobiologicals.

#### Article 144

The Government of the Republic of Croatia shall appoint the Agency's Administrative Council and approve its Statute no later than the opening day of the Agency.

The Agency's Administrative Council shall adopt the Statute and appoint the Agency's manager no later than the opening day of the Agency.

#### Article 145

Employees of the Croatian National Institute for the Control of Medicinal Products and the Croatian National Institute for the Control of Immunobiologicals shall continue working as the Agency's employees when the Agency begins operating.

The Administrative Council shall propose the Agency's internal organisation and job classification, taking into account the required number of employees, no later than within 30 days from the opening day of the Agency.

#### Article 146

Legal persons manufacturing medicinal products shall harmonise their work and business operations with Article 25 of this Act within 3 years from its entry into force.

#### Article 147

Legal persons holding the marketing authorisation for a drug product shall harmonise the labelling and the package leaflet inserted into the product with the provisions of this Act within two years from the entry into force of the ordinance referred to in Articles 31 through 37 of this Act.

#### Article 148

Legal persons engaged in wholesale distribution of medicinal products shall harmonise their work and business operations with the provisions of this Act and ordinances derived therefrom within six months from the entry into force of the ordinance referred to in Articles 47, 51, 53 and 54 of this Act.

#### Article 149

Within two years from the entry into force of this Act, the foreign manufacturers of medicinal products shall ensure that their representative offices in the Republic of Croatia operate in compliance with the provisions of this Act, or shall otherwise entrust the right of a marketing authorisation holder to another legal person in the Republic of Croatia.

#### Article 150

The Minister for Health shall adopt the regulations under his competence within one year after this Act enters into force.

#### Article 151

Until the provisions referred to in Article 150 of this Act come into effect, the following

ordinances shall remain in force:

1. Ordinance on pharmacovigilance of medicinal products and medical devices (Official Gazette, No. 14/99),
2. Ordinance on blood and blood constituents (Official Gazette, No. 14/99),
3. Ordinance on Good Clinical Practice (Official Gazette, No. 143/98),
4. Ordinance on procedure and manner of granting marketing authorisations for drug products (Official Gazette, No. 143/98),
5. Ordinance on procedure and method of granting an authorisation for marketing of medical devices (Official Gazette, No. 92//99),
6. Ordinance on good practice in wholesale distribution of medicinal products and medical devices (Official Gazette, No. 124/98),
7. Ordinance on advertising and providing information on medicinal products and medical devices (Official Gazette, No. 143/98),
8. Ordinance on distribution of medicinal products and medical devices (Official Gazette, No. 143/98),
9. Ordinance on good manufacturing practice (Official Gazette, No. 71/99 and 118/99),
10. Ordinance on criteria of wholesale pricing of medicinal products and on methods of reporting about wholesale prices (Official Gazette, No. 84/01 and 129/02),
11. Ordinance on bioavailability and bioequivalence testing of medicinal products (Official Gazette, No. 71/99),
12. Ordinance on special conditions for placement of medicinal products on the Croatian market, for which marketing authorisations have been obtained in other states (Official Gazette, No. 55/99),
13. Ordinance on the method and procedure for granting a marketing authorisation (Official Gazette, No. 143/98),
14. Ordinance on identity cards of health inspectors (Official Gazette, No. 63/03).

#### Article 152

Marketing authorisations granted in accordance with regulations which were valid before the entry into force of this Act shall remain valid till the expiry of their original term, unless there are other reasons for their withdrawal.

#### Article 153

The Act on Medicinal Products and Medical Devices (Official Gazette, No 124/97 and 53/01), shall cease to be valid on 1 January 2004.

#### Article 154

This Act shall enter into force on the eighth day from its publication in the Official Gazette, with the exclusion of the provisions from Article 16 paragraph 1 and Article 19 paragraphs 2 and 6 which shall apply as of 1 January 2004.

Class: 530-08/03-01/02  
Zagreb, 17 July 2003

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THE CROATIAN PARLIAMENT  
The President of the Croatian Parliament  
**Zlatko Tomčić**, m.p.