THE MINISTRY OF HEALTH AND SOCIAL WELFARE

Pursuant to Article 14, paragraph 4, Article 19, paragraph 7, Article 23, paragraph 8, Article 24, paragraph 10, Article 25, paragraph 2, Article 41, paragraph 5, Article 46, paragraph 2, Article 47, paragraph 3, Article 48, and Article 111, paragraph 6 of the Medicinal Products Act (Official Gazette 71/07), the Minister of Health and Social Welfare hereby issues the

ORDINANCE
ON THE PROCEDURE AND METHOD FOR GRANTING MARKETING AUTHORISATIONS FOR MEDICINAL PRODUCTS

I. GENERAL PROVISIONS

Article 1

This Ordinance lays down the procedure, conditions and documentation required for granting, renewal, revocation, and transfer of authorisations for the marketing of medicinal products in the Republic of Croatia, as well as the procedure, conditions and documentation required for the acceptance and approval of variations to the marketing authorisations and documentation of finished medicinal products, to the contents of the Summary of Product Characteristics, package leaflets, and labelling of medicinal products.

Article 2

The provisions of this Ordinance shall appropriately apply to finished medicinal products for which marketing authorisation applications are submitted in the Republic of Croatia, with certain specifics for the following groups of the finished medicinal products:

- biological medicinal products (medicinal products derived from human blood or human plasma, vaccines, etc.),
- radio-pharmaceuticals,
- homeopathic products,
- traditional herbal medicinal products,
- medicinal products for the treatment of severe and rare diseases (*orphan drugs*),
- advanced therapy medicinal products.

The application form and the content of documentation for the groups of medicinal products referred to in paragraph 1 are provided in Annex II which forms an integral part of this Ordinance.

II. PROCEDURE FOR GRANTING MARKETING AUTHORISATIONS FOR FINISHED MEDICINAL PRODUCTS

Article 3

The procedure for granting marketing authorisations for finished medicinal products shall be initiated by submitting written applications to the Agency for Medicinal Products and Medical Devices (hereinafter: the Agency) in accordance with the provisions of the Medicinal Products Act (hereinafter: the Act).

The application for granting the authorisation to place a finished medicinal product on the market shall be submitted by a legal person seated in the Republic of Croatia, who is:

- a manufacturer responsible for the quality, safety and efficacy or the medicinal product, irrespective of whether the product was manufactured by that manufacturer or by another person on his behalf,
- an authorised representative of the foreign manufacturer responsible for the quality, safety and efficacy of the medicinal product, irrespective of whether the product was manufactured by himself or by another person on his behalf or by an authorised representative of the marketing authorisation holder with a qualified person responsible for the release of the finished medicinal product on the EU market.

Where a marketing authorisation was not granted for a medicinal product in any of the states, the marketing authorisation application may be submitted only by a manufacturer seated in the Republic of Croatia as referred to in paragraph 2, subparagraph 1 of this Article.

Article 4

The marketing authorisation application for finished medicinal products placed on the market of the Republic of Croatia shall be submitted in the Croatian language.

For each name of a medicinal product, its pharmaceutical form, strength, type and size/s of the packaging a separate written application referred to in paragraph 1 shall be submitted.
The application for the marketing authorisation for finished medicinal products shall include:

1. the name of the finished medicinal product, followed by the pharmaceutical form, strength, type and size/s of the packaging,
2. the applicant's particulars (the name and address of the legal person seated in the Republic of Croatia),
3. clear indication of the legal basis of reference for the marketing authorisation application (Article 14, Article 15, item a), Article 15, item b), Article 15, item c), Article 17, paragraph 1, item a), Article 17, paragraph 1, item b), Article 17, paragraph 2, Article 18, Article 19 and Article 107 of the Act),
4. information whether the marketing authorisation has been granted for the finished medicinal product in the European Union, in which case the relevant procedure shall be indicated,
5. the date, signature of the responsible person of the applicant, and the stamp.

An applicant may use the same documentation to apply for multiple marketing authorisations for the same medicinal product with a different name.

Article 5

The application referred to in Article 4 shall be accompanied by the medicinal product documentation in accordance with provisions of this Act and the ensuing regulations, subject to indication of the legal basis referred to in Article 4, paragraph 3, item 3 of this Ordinance.

Costs of the marketing authorisation procedure for a finished medicinal product shall be settled by the applicant prior to the grant or refusal of the marketing authorisation.

Article 6

The marketing authorisation application for a medicinal product shall be accompanied by the medicinal product documentation in the format of a Common Technical Document (hereinafter: CTD) in accordance with Article 5 of this Ordinance.

The CTD is an internationally accepted format of drawing up the medicinal products documentation for the needs of the procedure of granting marketing authorisations for finished medicinal products.

By way of derogation from the provision of paragraph 1 of this Article, the applicants for the product marketing authorisation may submit the documentation in the format of the Standard Technical Documentation (hereinafter: STD) instead of the CTD format, subject to the Agency's approval and with a written justification of their inability to submit the documentation in the CTD format.

The STD format of document preparation was recommended by earlier EU guidelines to applicants for marketing authorisations for finished medicinal products.

The applicants shall supplement the documentation referred to in paragraph 3 of this Article with sections and/or data which do not belong to the STD format but are required for the CTD format.

Article 7

Basic sections of the CTD are:

Module 1: Administrative data and medicinal product information
Module 2: CTD summaries
Module 3: Quality of active substance and finished medicinal product
Module 4: Pre-clinical study reports
Module 5: Clinical study reports

The table of contents of the CTD format as well as principles and requirements for the preparation of documentation are provided in Annex I which forms an integral part of this Ordinance.

The content of the STD format referred to in Article 6, paragraph 3 of this Ordinance is provided in Annex III which forms an integral part of this Ordinance.

Applicants for the marketing authorisation for the finished medicinal product, who submit the relevant documentation in the STD format, must also include Module 1 of the CTD format.

Article 8

Except in cases where the original of the documentation or copies verified by a notary public are required in this Ordinance, copies of the medicinal product documentation shall be submitted. The Agency may require access to the original.

Sections of the medicinal product documentation supplied in the CTD format, i.e. Modules 1, 2, and 3, or the corresponding parts of documentation in the STD format (parts I and II) shall be submitted in writing, while the remaining documentation, i.e. Modules 4 and 5 or corresponding parts of the documentation in the STD format (parts III and IV) may be

submitted in electronic form.

However, the Agency may also require written form of submission of the documentation provided in Modules 4 and 5 or the corresponding documentation parts in the STD format.

The Agency shall specify the required number of copies of individual parts of the documentation.

Applicants may submit the medicinal products documentation in the Croatian or the English language, with the exclusion of the documents whose Croatian version is required in this Ordinance.

Module 1

Article 9

An applicant for marketing authorisation for a finished medicinal product shall prepare Module 1 which contains relevant data and documents in the following order:

1.0. The application referred to in Article 4 of this Ordinance;
1.1. The table of contents of medicinal products documentation in accordance with the legal basis indicated in the application;
1.2. A completed application form for granting the marketing authorisation;
1.3. Medicinal product information;
1.3.1 a draft of the Summary of Product Characteristics, package leaflet, outer and immediate packaging and labelling in the Croatian language;
1.3.2. lay-out (design) of the outer and immediate packaging of the medicinal product, if appropriate;
1.3.3. an example specimen of the outer and immediate packaging and packaging leaflet, if appropriate;
1.3.4. data on comprehensibility testing of the package leaflet, if available;
1.3.5. the Summary of Product Characteristics, package leaflet and labelling of the medicinal product authorised in other states;
1.3.6. introduction of the Braille format, if applicable;
1.4. Data on qualified persons responsible for the assessment of documentation sections;
1.4.1. chemical, pharmaceutical and biological documentation/ quality of active substance and finished medicinal product;
1.4.2. pre-clinical documentation;
1.4.3. clinical documentation;
1.5. justification of the application for marketing authorisation in accordance with the legal basis;
1.6. data on potential environmental risks from the medicinal product;
1.7. particulars relating to medicinal products for treatment of rare and severe diseases (*orphan drugs*);
1.8. pharmacovigilance related particulars;
1.8.1. a description of the pharmacovigilance system in the Republic of Croatia;
1.8.2. the Risk Management Plan– if the applicant intends to implement a project in the Republic of Croatia that requires a Risk Management Plan;
1.9. data on clinical studies (a statement that the clinical studies have been conducted in accordance with good clinical practice);
2.0. Other data and documents,

2.1. For medicinal products for which the marketing authorisation has been granted in the EU Member States (through centralised procedure, mutual recognition procedure, or decentralised marketing authorisation procedure), the documents and statements laid down in the Ordinance on special conditions for placing medicinal products authorised in the Member States of the European Union on the market of the Republic of Croatia (Official Gazette 10/08);
2.2. A list of legal persons included in the compiling of the medicinal product dossier, development and testing of the medicinal product or its manufacture as well as written explanation of their relationship with the applicant (where several legal persons participate in compiling the dossier),
2.3. Amendment to the description of the production stage a part of which was taken on by another manufacturer (not indicated in the medicinal product dossier) and amendment to the Expert Report on the medicinal product quality. Via the Report amendment, potential quality deviations from the Quality Expert Report referred to in, item 2.3. of Module 2 shall be assessed and validity of the amended data shall be confirmed,
2.4. The Manufacturer's Quality Certificate for a finished medicinal product batch; in the case referred to in item 2.3. of this Article, also the quality control certificate of the manufacturer that took over a production stage or a justification where the same cannot be provided.

Article 10

In drawing up Module 1, the names of active substances and excipients of a medicinal product should be used in accordance with the Croatian pharmacopoeia, while standardised names should be used for pharmaceutical forms, method of administration and containers (immediate packaging).

Where a substance is not included in the Croatian pharmacopoeia, its name should be created according to the same rules as those used in creating Croatian names for the Croatian pharmacopoeia.

Where a Croatian standard term is not provided for a pharmaceutical form, method of administration or container either in the Croatian pharmacopoeia or in the publication "Standard terms: Pharmaceutical dosage forms, Routes of administration, Containers", then, in addition to the usual Croatian name for the pharmaceutical form, route of administration or container, a detailed description and, where appropriate, relevant English names shall be submitted.

Application form for the marketing authorisation

Article 11

The application form referred to in Article 9, item 1.2. is provided in Annex 1 and forms an integral part of this Ordinance.

For each pharmaceutical form, strength, type and size/s of the packaging a separate application form referred to in paragraph 1 of this Article shall be submitted.

However, only one application form shall be completed for all packaging sizes where an application refers to several sizes of the same packaging type of a finished medicinal product.

In addition to the application form referred to in paragraph 1 of this Article, the applicant shall also submit the following data and documents:

1. proof of the applicant’s entry into the register of the competent commercial court (original or a copy verified by a notary public, within 6 months after submission of the application);
2. the agency contract with the foreign manufacturer/authorisation holder (original or a copy verified by a notary public; if the agency contract was not drawn up in Croatian, it has to be duly authorised and translated by a certified court interpreter);
3. the statement of the applicant's representative to confirm that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any suspected adverse reaction observed either in the Republic of Croatia or in other states;
4. curriculum vitae of the qualified person responsible for pharmacovigilance in the Republic of Croatia;
5. copies of valid manufacturing licences for all reported manufacturing sites of the medicinal product and/or originals of good manufacturing practice certificates not older than 3 years from the submission of the application;
6. a list of all manufacturers included in the manufacture of the medicinal product and/or active substance with indication of the production stage for which they are responsible;
7. the statement of the manufacturer of the finished medicinal product that the active substance was produced in accordance with the guidelines on good manufacturing practice for starting materials;
8. a written consent of the manufacturer or documentation owner on the right of use of the Active Substance Master File for the purpose of granting the authorisation for marketing of a finished medicinal product (»Letter of access«) or a copy of the Certificate of Suitability of the Monographs of the European Pharmacopoeia for the active substance;
9. the statement of the active substance manufacturer that he shall notify the medicinal product manufacturer about any changes in the production or quality of the active substance;
10. the certificate of the European pharmacopoeia on the safety of the substance with respect to the transmission of animal spongiform encephalopathy (TSE certificate of Ph. Eur), if applicable;
11. the list of the states where the medicinal product was authorised for marketing, where the marketing authorisation procedure is underway, and where the marketing authorisation was denied or revoked, t
12. the finished medicinal product certificate or the free sale certificate,
13. proof that the administrative fee has been paid.

The particulars and documents referred to in paragraph 4 of this Article form an integral part of Module 1.

The Agency shall provide the guidelines for the assembling of Module 1 and for the completion of application forms.

Summary of Product Characteristics

Article 12

Data and the table of contents of the Summary of Product Characteristics are printed in Annex IV which forms an integral part of this Ordinance.

A draft Summary of Product Characteristics may contain information on finished medicinal products with the same active substance in their composition and with the same brand name or common name accompanied by the trade mark or the manufacturer's name, but in different pharmaceutical forms and dosages.

For medicinal products authorised for marketing in other states, the latest Summary of Product Characteristics and package leaflet in its original form and translated into English, with indication of the country and the date of authorisation and the statement that the translation complies with the original, shall be provided.

Package leaflet

Article 13

The package leaflet shall be compatible with the Summary of Product Characteristics. The contents and information given in the user package leaflet are provided in Annex V which forms an integral part of this Ordinance.

The package leaflet shall be written and designed to be clear and comprehensible in order to enable the users to act appropriately, when necessary with the help of health professionals. The particulars on the package leaflet shall be easily legible and indelible.

Excipients and other information that differ for each form/dosage of the medicinal product must be indicated separately for each pharmaceutical form/dosage.

The list of excipients with possible influence on the medicinal product efficacy and safety, which must be indicated in the package leaflet and the outer labelling, has been provided in Annex VI which forms an integral part of this Ordinance.

Labelling

Article 14

The labelling proposal for immediate and outer packaging of the medicinal product shall be enclosed, if applicable, in the form of a lay-out (design) containing particulars specified in provisions of Articles 41, 42, 43 and 49 of the Act and provisions of this Ordinance.

In addition to particulars laid down in Article 41 of the Act on Outer Labelling, the manner of dispensing of the medicinal product shall be provided.

In order to clarify some specific information, the outer packaging may include symbols or pictograms or other information in accordance with the Summary of Product Characteristics which is useful for the patient, to the exclusion of any element of a promotional nature.

Article 15

Provisions of this Ordinance related to the labelling and package leaflet shall not apply to finished medicinal products imported in accordance with provisions of Article 64 of the Act.

Article 16

For particular groups of medicinal products referred to in Article 2, the Agency shall issue labelling instructions taking into consideration specifics of those medicinal products.

Samples of medicinal products, which are not intended for sale, shall bear labels or stamps reading: “Not for sale” or “Sample free of charge”.

Article 17

Names of medicinal products expressed in Braille format shall be provided on the outer packaging, but the requirement does not apply to the immediate packaging (e.g. blisters, ampoules or vials).

However, a manufacturer who has expressed names of medicinal products in Braille format on the outer packaging may use the format on the immediate packaging as well.

In absence of the outer packaging, the manufacturers of medicinal products shall be obliged to express names in Braille format on the immediate packaging.

Braille alphabet dots may be placed anywhere on the outer or immediate packaging as long as the underlying text remains easily legible.

Article 18

In the case of medicinal products that are placed on the market in limited quantities and used to treat severe and rare diseases or small number of patients (*orphan drugs*), the minister of health (hereinafter: Minister) may on the Agency's proposal approve the packaging in one of the languages of the EU Member States, as long as the Latin alphabet is used.

The Agency shall submit the proposal referred to in paragraph 1 to the Minister based on the justified application of the applicant.

A list of states where the medicinal product was authorised for marketing and where the procedure is underway

Article 19

In the case of a medicinal product authorised for marketing in other states, a list of the states in which the marketing authorisation was granted (accompanied by the name of the medicinal product, authorisation date and numbers), and of the states in which the authorisation procedure is underway (accompanied by the name of the medicinal product, authorisation date and numbers) as well as the states in which the application was denied or authorisation revoked, shall be provided.

In addition to the list from paragraph 1 of this Article, the applicant shall submit a copy or copies of authorisation/s granted in the relevant EU Member State/s or in the country of establishment of the manufacturer outside the EU.

Particulars of qualified persons responsible for documentation assessment

Article 20

Particulars of qualified persons responsible for the assessment of the pharmaceutical, pre-clinical and clinical documentation shall include a brief curriculum vitae (name and family name, educational experience, additional training, occupation).

The marketing authorisation applicant shall submit the statement (signed and dated) of the qualified person referred to in paragraph 1 saying that all data on individual dossier sections provided in the enclosed Expert Report have been assessed as valid.

Pharmacovigilance

Article 21

The description of the pharmacovigilance system, the Risk Management Plan and the manner and frequency of submission of the Periodic Safety Update Report (hereinafter: PSUR) shall be prepared in accordance with pharmacovigilance regulations.

The latest available PSUR shall be submitted on Module 5, item 5.3.6. of the Report on post-authorisation experience with marketing of all medicinal products in any of the states over at least nine (9) months before applying for the marketing authorisation in the Republic of Croatia.

Medicinal product documentation

Article 22

In line with the legal basis indicated in the marketing authorisation application, the applicant shall enclose written justification and the medicinal product documentation laid down in the Act and the ensuing regulations.

To the authorisation for marketing of the medicinal product pursuant to Article 14 of the Act, the applicant shall enclose the complete medicinal product documentation (Module 1-5 or Module 1 and all required parts of the STD) as provided in Annexes I and III to this Ordinance.

Article 23

Together with the application for authorisation to market a generic medicinal product in accordance with Article 15, item a) of the Act, the applicant shall provide the evidence that a marketing authorisation was issued for any dosage, pharmaceutical form, method of administration or packaging of the reference medicinal product in the Republic of Croatia or in an EU Member State more than six years before the date of the relevant application. Where the authorisation for marketing of the medicinal product referred to in paragraph 1 was

not issued in the Republic of Croatia the applicant shall, in accordance with Article 16 of the Act, indicate the EU Member State in which the marketing authorisation was granted for the reference medicinal product and the year when the initial authorisation was granted.

The applicant shall enclose the medicinal product documentation laid down in Modules 1, 2, 3 and 5 to the application referred to in paragraph 1 of this Article.

The proposal of the Summary of Product Characteristics and of the package leaflet for the Republic of Croatia shall be compatible with the Summary of Product Characteristics and the package leaflet for the reference medicinal product which has been authorised for marketing in the Republic of Croatia or the EU Member State of reference.

Particulars provided in a part of Module 5 must demonstrate that the relevant medicinal product is essentially similar to the reference medicinal product, in line with the Ordinance on bioavailability and bioequivalence studies of medicinal products.

Enclosed pre-clinical and/or clinical reports/expert summaries in a part of Module 2 shall be particularly taking into consideration:

- the assessment that the statement about essential similarity of a medicinal product is founded,
- the assessment of acceptability of impurities present in active substance/s and in the finished medicinal product (including storage-related degradation products),
- the assessment of conducted bioequivalence studies or explanation why the studies were not conducted in accordance with the regulations on bioavailability and bioequivalence,
- the most recent literature bearing reference to the submitted application; articles from reviewed scientific journals shall be acceptable for the purpose,
- any statement in the Summary of Product Characteristics which does not arise from the characteristics of the medicinal product and/or its therapeutic group should be critically assessed and corroborated with published literature data and/or additional studies.

When invoking essential similarity of the medicinal product, the applicant shall submit supplementary data in order to confirm the same safety and efficacy of different salts, esters or derivatives of the authorised active substance.

Article 24

The applicant shall enclose the documentation for Modules 1, 2, 3, 4 and 5 to the marketing authorisation application for the medicinal product with well-established medicinal use in accordance with Article 15, item b) of the Act.

The following must be taken into consideration in order to demonstrate the well-established medicinal use of an active substance:

- the period of time over which the substance has been used,
- the frequency and extent of its use,
- the degree of scientific interest in the use of the substance (reflected in the published scientific literature), and
- the coherence of scientific assessments.

In order to determine a well-established medicinal use of an active substance, the period of time over which the substance has been used in a medicinal product shall not be less than ten years from its first systematic and documented use as a medicinal product in the Republic of Croatia or in the EU.

Modules 4 and 5 shall contain extensive data from the scientific literature in evidence of safety and recognised efficacy of the medicinal product containing the active substance which has been in medicinal use in the Republic of Croatia or in the EU for at least ten years.

The documentation referred to in paragraph 4 of this Article shall contain all data required to assess the safety and/or efficacy and shall include or refer to a review of the relevant literature, taking into account pre- and post-marketing studies as well as published scientific literature concerning experience in the form of epidemiological studies, in particular comparative epidemiological studies. The documentation shall contain both favourable and unfavourable information on the safety and/or efficacy of the medicinal product.

If any safety and/or efficacy information is missing, justification must be given in support of an acceptable safety and/or efficacy level.

Expert reports on pre-clinical and/or clinical documentation shall contain justification and critical assessment of any information different from the one provided for the authorised medicinal product.

The applicant shall take into consideration available post-marketing experience with other medicinal products containing the same active substance.

Article 25

Alongside with the application for the finished medicinal product authorisation based on the reference product documentation pursuant to Article 15, item c) of the Act, the applicant shall submit an original statement given by the representative of the reference product manufacturer and of the marketing authorisation holder, whose documentation the applicant refers to, saying that they agree with the use of their pharmaceutical, pre-clinical and clinical data on the reference product for the purpose of consideration of the submitted marketing authorisation application.

Article 26

Alongside with the marketing authorisation for the medicinal product referred to in Article 17, paragraph 1, item a) of the Act, the applicant shall provide the documentation laid down in Modules 1, 2, 3, 4 and/or 5.

Module 4 and/or Module 5 contain a combination of reports on conducted limited pre-clinical and/or clinical studies and data from scientific literature.

Where the relevant active substance contains the same therapeutic moiety as the active substance of the reference medicinal product but takes the form of different salts, esters and derivatives, evidence shall be provided that there is no difference in the pharmacokinetics, pharmacodynamics and/or toxicity which could affect the safety and/or efficacy balance, otherwise such form will be considered as a new active substance.

Where a medicinal product is intended for a different therapeutic use or is presented in a different pharmaceutical form or administered by different routes or in different dosages or with a different posology, the results of appropriate toxicological and pharmacological tests and/or clinical studies shall be provided.

Article 27

To the marketing authorisation application for a biological medicinal product which is essentially similar to the reference biological medicinal product referred to in Article 17, paragraph 1, item b) of the Act, the documentation from Modules 1, 2, 3 and Modules 4 and 5 shall be added, containing additional data on pre-clinical and clinical studies conducted in order to demonstrate the similar nature of the two biological medicinal products.

In addition to the documentation referred to in paragraph 1, the Agency shall define the scope and type of required additional data (e.g. toxicological and other nonclinical as well as appropriate clinical studies) on a case-by-case basis in accordance with relevant scientific information.

Due to diversity of biological medicinal products referred to in Modules 4 and 5, the applicant shall submit data on conducted studies taking into account the specific characteristics of each individual biological medicinal product.

If a reference, originally authorised medicinal product has more than one indication for use, the efficacy and safety of the bio-similar medicinal product has to be explained/justified or, if necessary, demonstrated separately for each of the claimed indications.

Article 28

For a medicinal product made of at least two active substances not previously authorised in that combination, the applicant shall enclose the full documentation (Module 1-5) to the marketing authorisation application referred to in Article 17, paragraph 2 of the Act.
In specific cases, the safety assessment data related to manufacturing sites and potential adventitious agents shall be provided.

Article 29

Where a finished medicinal product integrates a medicinal product and a medical device which enables the administration of that medicinal product, the medical device documentation for the relevant class of medical devices shall be attached to the application in accordance with Medical Devices Act and the ensuing regulations.

Article 30

Together with the application for the marketing authorisation for medicinal products from the group of particular medicinal products referred to in Article 2, the applicant shall provide the documentation prepared in accordance with Annexes I and II of this Ordinance.

Article 31

The documentation for medicinal products derived from human blood and human plasma shall also contain information on the source material – the human plasma, in the part II C (of the STD format) or Module 3 (in the CTD format) or in a separate Plasma Master File (PMF).

A separate part of the PMF shall contain necessary data on characteristics of human plasma which is used as a source material or raw material in the production of active substances, excipients or medical devices.

The Plasma Master File shall be submitted to the Agency on a yearly basis for the purpose of post-marketing assessment of the relevant medicinal product.

The documentation for vaccines shall contain data on the vaccine antigen in the part II C (of the STD format) or Module 3 (of the CTD format) or in a separate Vaccine Antigen Master File (VAMF), with the exclusion of vaccine against influenza.

A separate part of the Vaccine Antigen Master File shall contain necessary data on biological, pharmaceutical and chemical nature of the active substance/s, i.e. the vaccine antigen for which the marketing authorisation is required.

The provisions of this Ordinance shall appropriately apply to industrially produced allergens which contain one allergen or a defined mixture of allergens authorised for marketing as a finished medicinal product intended for *in vivo* diagnostics or for the treatment of allergic diseases.

Allergens prepared in accordance with a medical prescription for an individual patient are deemed a special kind of magistral formula and provisions of this Ordinance shall not apply to them.

The Agency shall acknowledge the specific nature of medicinal products referred to in paragraphs 1, 4 and 6 of this Article and shall give instructions for drafting the documentation for these products.

Article 32

The documentation submitted with the marketing authorisation application for a traditional herbal medicinal preparation shall be in accordance with the provisions of Article 19 of the Act and Annexes I and II to this Ordinance, and shall take into consideration the specific nature of herbal medicinal products.

Article 33

Provisions of this Ordinance shall appropriately apply to the procedure for granting, renewal, revocation and transfer of marketing authorisations for homeopathic medicinal products as well as authorisations of amendments to the homeopathic products documentation.

Article 34

The Agency shall establish the validity of submitted applications and shall evaluate the submitted medicinal product documentation in accordance with the provisions of the Act and

this Ordinance.

Where the Agency establishes that an authorisation application is not valid, the applicant shall be requested to supplement the application within the time limit set by the Agency.

The Agency may request the applicant to submit additional documentation or an appropriate justification during a marketing authorisation procedure, and shall set the time limit for the purpose.

Should the applicant fail to supplement the application, i.e. provide required additional documentation or appropriate justification within the time limits referred to in paragraphs 2 and 3, the Agency shall refuse the application by means of the decision which cannot be appealed, but against which administrative proceedings can be instituted.

The applicant shall submit the samples of the medicinal product in accordance with Article 14, paragraph 3 of the Act, as well as the reference standards if requested to do so by the Agency, failing which the time period referred to in Article 20, paragraph 1 of the Act shall be suspended until the delivery date of the same.

Where in the opinion of the Agency the conditions for good manufacturing practice at a manufacturing site require control, the time period referred to in Article 20, paragraph 1 of the Act shall be suspended from the date of notifying the manufacturer until the control date.

Article 35

The Agency shall grant authorisations for marketing of medicinal products on the grounds of the conducted authorisation procedure and assessment of legitimacy of submitted applications in accordance with provisions of the Act and the ensuing regulations.

After obtaining the authorisation for marketing of a finished medicinal product, the authorisation holder may request the Agency to provide him with the Report on the documentation and the medicinal product studies, where applicable.

Article 36

In the course of the procedure of granting the authorisation for placement on the market of the Republic of Croatia a medicinal product which is already authorised for marketing in the EU, either through a centralised, decentralised or mutual recognition procedure, the Agency may use the Report on medicinal product documentation issued by the competent regulatory body.

Article 37

A marketing authorisation decision shall contain the following information:

1. the title and head office of the marketing authorisation holder;
2. the name of the medicinal product, alongside with the international non-proprietary name (INN) in Latin or if the INN does not exist, another common name;
3. pharmaceutical form, dosage, type and size(s) of the medicinal product packaging;
4. declared composition of the medicinal product;
5. the name and address of the manufacturer responsible for market release of the medicinal product;

6. validity term of the marketing authorisation;
7. manner and place of dispensing;
8. prescribing method;
9. the method of advertising to general public.

Article 38

After obtaining the authorisation for marketing of a medicinal product, the authorisation holder shall inform the Agency about any restriction or prohibition imposed in any state in which the medicinal product has been authorised for marketing, or about refusal of his marketing authorisation application.

The authorisation holder shall provide the Agency with any information which may affect the assessment of the risk-benefit balance following due administration of the medicinal product.

Article 39

In accordance with Article 11, paragraph 4 of the Act, the marketing authorisation holder shall be obliged to place the medicinal product on the market within the period of three years after obtaining the relevant marketing authorisation.

The Agency shall deem that a medicinal product has been placed on the market after at least one pharmaceutical form, dosage or package size for which the marketing authorisation was granted appears on the market.

The Agency shall pass the decision on revoking an issued marketing authorisation if the authorisation holder fails to place the medicinal product on the market within the time limit referred to in paragraph 1 of this Article.

In cases referred to in Article 11, paragraph 5 of the Act, the authorisation holder shall send to the Agency a written exposition of reasons for failing to place an authorised medicinal product on the market.

Where based on the exposition from paragraph 4 of this Article the Agency, with the consent of the Minister, decides that justified reasons referred to in Article 11, paragraph 5 of the Act exist, the marketing authorisation shall not be revoked.

III. VARIATIONS TO MEDICINAL PRODUCT DOCUMENTATION

Article 40

The authorisation holder for the marketing of a medicinal product shall report to the Agency any variations to the medicinal product documentation based on which the marketing authorisation was granted.

Variations from paragraph 1 of this Article fall into two groups:

1. minor variations (IA, IB), or
2. major variations (II).

Article 41

A list of variations considered as minor (IA, IB), the conditions of application submission, and corresponding parts of the documentation to be provided in accordance with submitted variations application, are provided in Annex VII which forms an integral part of this Ordinance.

Major variations (II) are those that cannot be considered as minor.

Major variations (II) are those that either:

1. do not require initiation of a new marketing authorisation procedure (II), or
2. require initiation of a new marketing authorisation procedure.

An unavoidable variation ensuing directly from another variation shall be considered as a consequential variation. To an IA variation another IA variation may be consequential, to an IB variation another IB or an IA variation may be consequential, while other consequential variations shall be submitted as a part of the variation II.

Article 42

Variations due to urgent safety measures referred to in Article 27 of the Act are variations introduced on account of new information on the use of a finished medicinal product due to which, in the interest of public health protection, urgent restrictions must be imposed on the use of medicinal product as compared to the authorised use of the medicinal product (e.g. narrower therapeutic range, changes in posology, restriction of use to a limited group of patients, extension of contraindications or precautionary measures, etc.).

An authorisation holder shall forthwith notify the Agency in writing about taken urgent safety measure(s).

Urgent safety measure(s) referred to in paragraph 1 shall be deemed accepted if 24 hours from the receipt of a written notification the Agency does not require any additional safety measures.

In the case referred to in paragraphs 1 and 2, the authorisation holder shall submit the application for approval of variation(s) accompanied by documentation in accordance with provisions of this Ordinance, not later than 15 days from the date of taking the urgent safety measure.

Should the Agency ask the authorisation holder to take urgent safety measure(s) in the case referred to in Article 27, paragraph 5 of the Act, the marketing authorisation holder shall forthwith take those measures and shall submit the application for the variation approval, accompanied by the documentation set out in this Ordinance, within time limit set by the Agency.

Article 43

Any change in periodicity of the PSUR submission shall be considered as a major variation (II).

The periodicity of the PSUR submission may be changed on request of the Agency or the marketing authorisation holder.

Change in periodicity of the PSUR submission may result in more or less frequent submission of PSURs in accordance with pharmacovigilance regulations.

However, PSURs shall not be submitted at a lower frequency than once in every 3 years. Marketing authorisation applicants may also propose change in the PSUR periodicity submission in the course of the marketing authorisation procedure or authorisation renewal, subject to the submission of a reasoned request for the introduction of change to the PSUR periodicity submission.

Article 44

Any change to the information provided in the description of the pharmacovigilance system shall be considered as a major variation (II), with the exclusion of replacement of the qualified person responsible for pharmacovigilance or his substitute or change in their curricula vitae and contact data, which are considered as minor variations (IA).

A variation to the Risk Management Plan must be submitted at the time of PSUR submission, or in the following cases:

1. at the request of the Agency (without delay);
2. if a new safety information affects the Risk Management Plan (without delay);
3. within 60 days from discovery of an important pharmacovigilance-related information or from the moment when the results of the medicinal product safety studies become available.

In the application for approval of variation to the Risk Management Plan, the marketing authorisation holder shall briefly describe changes from the Risk Management Plan accepted earlier.

If there are no variations to the Risk management plan at the time of the PSUR submission, the marketing authorisation holder shall accordingly notify the Agency in writing.

Article 45

Major variations to the medicinal product documentation which call for submission of a new marketing authorisation application shall include:

1. Variations concerning the active substance

- different physico-chemical form of the active substance: salts, esters, ethers, complexes, derivatives etc. (having the same therapeutic moiety), without significant change to the substance properties regarding its safety and efficacy;
- different stereochemical form of the active substance: different isomer, isomer mixture or substitution of isomer mixture with one isomer (i.e. substitution of racemate with isomer), without significant change to the substance properties regarding its safety and efficacy;
- replacement of an active substance of biological origin or biotechnologically-derived active substance with another active substance that has slightly different chemico-physical structure (molecular); modification of the vector used to obtain antigen/source of the substance, including new cell bank from a different source,

without significant change to the substance properties regarding its safety and efficacy;
- new ligand or mechanism of binding to radiopharmaceutical,
- replacement of the extraction solvent or herbal substance proportion in a herbal preparation, without significant change to the substance properties regarding its safety and efficacy.

2. Variations relating to strength/ dosage, pharmaceutical form or method of administration of the medicinal product:
- changed active substance bioavailability in the finished medicinal product,
- changed pharmacokinetic properties, e.g changed rate of active substance release,
- change to or addition of new dosage/strength,
- change to or addition of new pharmaceutical form,
- change to or addition of new method of administration.

Together with the application referred to in paragraph 1, the applicant shall provide appropriate documentation in accordance with provisions of the Act and the ensuing regulations with reference to the parts of previously submitted documentation relevant to the new application.

Article 46

The marketing authorisation holder in the Republic of Croatia shall initiate the variation application process by submitting a written application to the Agency.

The following shall be attached to the written application:
1. the completed variation application form,
2. variation documentation,
3. proof that the variation was authorised in the European Union (for the medicinal product authorised for marketing in the EU Member States),
4. proof that the administrative fee has been paid.

The applicant shall cover the costs of the procedure for the authorisation or refusal of a variation as well as the procedure for the authorisation or refusal of variation to the marketing authorisation, before the completion of the procedures.

The variation application form forms an integral part of this Ordinance and is provided in Annex 2.

The variation application and the completed variation application form shall be submitted in Croatian.

For variations requiring the initiation of a new authorisation procedure, the applicant shall attach the completed application form for granting of the medicinal product marketing authorisation (Annex 1).

The Agency shall issue instructions for the completion of the form and for drafting the documents relative to the documentation variation procedure.

Article 47

For each variation a separate variation application shall be submitted.

Where several variations are reported, the applicant shall submit a separate application for each including cross-reference to all other submitted applications and the order of variations.

By way of derogation from paragraph 1, in the case of several variations (I or II) resulting from one variation, the applicant may submit one application but must list all consequential variations and explain their correlation. The applicant shall indicate whether the variation is minor or major (designating the part of documentation to which the major variation applies) in “Application form for variation to a medicinal product documentation”).

Article 48

The Agency shall establish the validity of the submitted application and documentation in accordance with provisions of the Act and this Ordinance.

The Agency shall ask the applicant to either supplement or correct the application which is established as not valid within 30 days from the receipt of the Agency’s notification.

In the course of the variation authorisation procedure, the Agency may ask the applicant in writing to submit additional documentation or present reasoned justification and shall set the time limit for the purpose.

Should the applicant fail to supplement or correct the application within the time limits indicated in paragraphs 2 and 3, or fail to submit the additional documentation or reasoned justification, the Agency shall refuse the application by means of the decision which cannot be appealed, but against which administrative proceedings can be instituted.

Provisions of paragraphs 2, 3, and 4 shall also appropriately apply to the procedures for renewal, revocation and transfer of marketing authorisations for finished medicinal products.

Article 49

The variation application form shall be completed separately for each pharmaceutical form, strength, type and size(s) of the packaging in accordance with the variation type or the part of the documentation to which the variation applies.

Where the same variation (e.g. active substance particulars) applies to several pharmaceutical forms, strengths and packaging types, alongside with separate forms referred to in Article 46, paragraph 2, item 1 the applicant may submit a copy of the same documentation.

Article 50

Together with the variation application and completed form, the documentation drawn up in the CTD format shall be provided.

The documentation content shall depend upon the proposed variation.

The documentation for application of minor variations is provided in Annex VII which forms an integral part of this Ordinance.

The variation documentation may be submitted in the Croatian or English language, with the exclusion of the documentation sections whose Croatian version is required.

The agency shall specify the number of required copies of the variation documentation.

Article 51

For documentation variations which require change to data provided in the authorised Summary of Product Characteristics, package leaflet, and labelling of the medicinal product, the applicant shall provide the Croatian version of the proposal of the Summary of Product characteristics, package leaflet and labelling, indicating which changes were introduced in comparison to the earlier authorised ones, and shall provide a clean copy of proposed changes.

In the case from paragraph 1, where a medicinal product has been authorised in another country the applicant shall also submit the relevant documents authorised in that country.
The Agency shall specify the number of required copies of documents referred to in paragraphs 1 and 2.

Article 52

The following documentation shall be provided with the application for authorisation of the major variation II consisting of the change from previous dispensing on medical prescription to over-the-counter dispensing:

- the completed application form for variation to the medicinal product documentation,
- clinical opinion with critical assessment of the proposed over-the-counter dispensing of the medicinal product with respect to the proposed dosages and indications, and justification displaying large therapeutic broadness of the medicinal product, absence of direct or indirect risk of use without medical supervision subject to the authorised package leaflet observance, well-known efficacy and adverse reactions, no need for further studies, not intended for parenteral use, and feasibility of over-the-counter dispensation in as far as the package size, pharmaceutical form, the highest single or daily dose, or other conditions of the medicinal product use are concerned,
- opinion on the tolerance of the medicinal product based on literature data or studies demonstrating low toxicity, as well as special comment on medicinal product interactions and potential risks of use, potential consequences of incorrect use in the form of either prolonged use or higher dose than prescribed etc., based on the post-marketing follow up of the medicinal product, clinical studies, and data from scientific literature,
- PSUR,
- data on the medicinal product consumption and in particular the data relating to the experience with over-the counter use of the medicinal product in other countries.

Article 53

The Agency shall inform the marketing authorisation holder about approval of a minor variation (IA, IB) within 30 days, and about approval of a major variation (II) within 90 days from the receipt of a valid application.

The Agency shall approve the variations from paragraph 1 which do not require amendments to the marketing authorisation or its parts, via a written notification (Annex IV).
The Agency shall approve or refuse a minor variation (IA, IB) which requires amendments to the marketing authorisation or its parts within 30 days from the receipt of a valid application, and it shall approve a major variation (II) which requires amendments to the marketing authorisation or its parts within 90 days from receipt of a valid application.

Article 54

If the Agency's notification about approval of a minor variation (IA) which does not require amendments to the marketing authorisation or its parts is not provided within 30 days from receipt of a valid application, the variation shall be deemed accepted.

Article 55

The Agency may require submission of the medicinal product samples during the procedure of variation approval/ acceptance.

Article 56

After authorisation of variations to its documentation, the medicinal product which has been manufactured and placed on the market of the Republic of Croatia in accordance with the previously granted marketing authorisation shall be allowed to remain on the market until the expiry of its shelf life.

IV. RENEWAL OF MARKETING AUTHORISATIONS

Article 57

In accordance with Article 23 of the Act, a marketing authorisation holder for the placement of the medicinal product on the market of the Republic of Croatia may submit the application for renewal of the marketing authorisation to the Agency.

The application for renewal of the marketing authorisation shall comprise the following data:

1. the name of medicinal product, its pharmaceutical form, strength, type and size(s) of packaging,
2. the applicant's particulars (title and head office of the legal person seated in the Republic of Croatia),
3. date, signature of the applicant's responsible person, and seal.

Article 58

With the application for renewal of a marketing authorisation, the marketing authorisation holder shall provide the medicinal product documentation in accordance with provisions of the Act, this Ordinance, and the Ordinance on special conditions for placing medicinal products authorised in the Member States of the European Union on the market of the

Republic of Croatia (Official Gazette 10/08).

The marketing authorisation holder shall cover the costs of the procedure for the marketing authorisation renewal by the completion of the procedure.

Article 59

Alongside with the renewal application, the marketing authorisation holder may also submit application(s) for the authorisation renewal of a different pharmaceutical form, dosage or packaging type and size(s) of the same medicinal product, for the purpose of standardisation of all available medicinal product data and information.

Alongside with the application for renewal of marketing authorisation for medicinal products in accordance with Article 57 of this Ordinance, the marketing authorisation holder may simultaneously apply for the authorisation renewal of a different pharmaceutical form, dosage or packaging type and size(s) regardless of the validity term of their respective authorisations, for the purpose of standardisation of all available data and information about the same medicinal product.

In the case from paragraph 1 of this Article, regardless of the validity term of the authorisation whose renewal has been applied for, the Agency shall process the applications simultaneously and shall renew the authorisations in accordance with Article 23, paragraph 2 of the Act.

Article 60

In the course of renewal procedure, the marketing authorisation holder shall prepare the Module 1 which contains data and documents listed below in the following order:
1.0 The application for the renewal of the marketing authorisation,
1.1 The table of contents of the enclosed documentation,
1.2 The application form for the renewal of the marketing authorisation with the following supplements:

- a list of states in which the medicinal product is distributed,
- a list of states in which the marketing authorisation has been granted or the procedure is underway (names of the medicinal product for which the authorisation was granted, authorisation date and numbers),
- particulars of qualified persons for pharmacovigilance, withdrawal of the medicinal product, and persons responsible for providing expert information about the medicinal product,
- chronological presentation of all applied for and approved amendments and emergency safety precautions in the Republic of Croatia over the period starting with the date of granting the marketing authorisation (or latest renewal) for the medicinal product in the Republic of Croatia until the date of submission of the renewal application to the Agency, accompanied by a brief description of amendments,
- a valid manufacturing licence(s) and/or GMP certificate(s) less than 3 years old; or a valid manufacturing licence for manufacturers from the Republic of Croatia,
- the manufacturer’s statement that the active substance(s) in the medicinal product was manufactured in accordance with the good manufacturing practice. The statement shall contain the name and address (manufacturing site) of the active substance manufacturer,
- proof that the administrative fee was paid.

1.3.1 The Summary of Product Characteristics, package leaflet and labelling authorised in the Republic of Croatia as well as the valid Summary of Product Characteristics, package leaflet and labelling authorised in some other country, in English language;
1.3.2 The proposed Summary of Product Characteristics, package leaflet and labelling with indicated amendments and a clean copy of the same;
1.4. Particulars of the experts;
1.4.1. Particulars of the qualified person responsible for quality (curriculum vitae and a statement of the qualified person referred to in Article 65, paragraph 2 with the date and signature of the qualified person);
1.4.2. Particulars of the qualified person responsible for pre-clinical data (curriculum vitae and the statement of the qualified person referred to in Article 65, paragraph 2 with the date and signature of the qualified person);
1.4.3. Particulars of the qualified person responsible for clinical data (curriculum vitae and a statement of the qualified person referred to in Article 65, paragraph 2 with date and signature of the qualified person).

Article 61

The completed form for the authorisation renewal shall be submitted for each pharmaceutical form, strength, type and size(s) of the packaging.

Where an application is submitted for several sizes of the same packaging type, one form shall be completed for all packaging sizes.

The application and the form for the marketing authorisation renewal shall be submitted in the Croatian language.

Article 62

If in the course of the marketing authorisation procedure the Agency requests the samples of the medicinal product, its raw materials, intermediates (where appropriate), or other constituents, the deadline indicated in Article 23, paragraph 5 of the Act shall be suspended until the samples are provided.

Article 63

By way of exception, variations to the Summary of Product Characteristics, package leaflet and labelling of the medicinal product may be applied for in the course of renewal procedure:

- on the grounds of the conclusion from the enclosed PSUR,
- in order to harmonise the names of pharmaceutical forms and constituents with the names from the Croatian pharmacopoeia,
- in order to harmonise the formats of the Summary of Product Characteristics, package leaflet and medicinal product labelling with the provisions of the Act and this Ordinance, without affecting their content.

Any other variation shall require a separate application for the documentation variation.

Article 64

The Agency may request copies of authorisations granted in other countries and explanation of the decision based on which an application for marketing authorisation was refused or an authorisation withdrawn in a country.

Article 65

Besides the documentation prescribed for Module 1, the marketing authorisation holder shall also submit the documentation prescribed for Module 2 and Module 5 with the application for authorisation renewal.

Module 2 shall contain:

- the expert's quality report or statement that every technical and scientific progress made in the manufacturing process and quality control of the medicinal product has been embraced from the time when the marketing authorisation was granted, that all amendments have been applied for, and that active substances and the medicinal product specifications are valid as well as the qualitative and quantitative composition of the medicinal product,
- the expert's report on pre-clinical data or statement supporting the reassessment of the risk-benefit balance based on pre-clinical data collected after the grant or latest marketing authorisation renewal or based on any new data. In absence of such data, the statement that there are no recent pre-clinical data that could affect the risk-benefit balance,
- the expert's report on clinical data shall reflect current risk-benefit balance based on the safety data from the PSUR and safety and efficacy data collected after the grant or latest renewal of the marketing authorisation or after any newly available information, or the statement saying that the medicinal product authorisation may safely be renewed for the next 5-year period, that the Agency shall be informed about any additional data of significance for the risk-benefit balance, and that there are no available clinical data requiring amendment or re-assessment of the risk-benefit balance.

Module 5 shall contain:

- data on post-marketing experience, if available,
- the bridging PSUR which covers the period of 4 years and 4 months following the date of the medicinal product placement on the market of the Republic of Croatia.

By way of exception and subject to written justification, instead of the bridging PSUR, the marketing authorisation holder may submit an additional PSUR for the period following the conclusion of the previous PSUR. The additional PSUR shall not cover a period longer than 12 months, and the conclusive data shall not be older than 60 days from the date of submission of the renewal application.

Article 66

On the Agency' request, in the course of the renewal procedure the marketing authorisation holder shall submit the product quality file in the form of Module 3 or PART II of the STD, if the file was not provided in the previous authorisation/renewal procedure.

Together with the medicinal product quality file referred to in paragraph 1, the marketing authorisation holder shall provide written justification of any amendment to the file approved

in the previous authorisation or renewal procedure.

The Agency shall require submission of the file and statement referred to in paragraphs 1 and 2 of this Article if established that material quality data are missing.

Article 67

Besides the documents laid down in the Article 65 of this Ordinance, the marketing authorisation holder may also submit a renewed quality file of the medicinal product in the form of Module 3.

The renewed quality file referred to in paragraph 1 of this Article shall be supplemented with all variations introduced and approved since the date when the marketing authorisation was granted.

In the case referred to in paragraph 1, the marketing authorisation holder shall enclose the statement of the manufacturer's responsible person saying that the submitted documentation does not contain any different data from those provided in the previously accepted medicinal product documentation.

V. REVOCATION OF MARKETING AUTHORISATIONS

Article 68

The marketing authorisation holder shall submit an application to the Agency to revoke the marketing authorisation in cases indicated in Article 26 of the Act.

The marketing authorisation holder shall notify the Agency in writing about discontinuation of production or withdrawal of the medicinal product from the market six months ahead, except in the case of an urgent withdrawal procedure.

The written application from paragraph 1 shall be submitted separately for each name, pharmaceutical form, strength, packaging type and size(s) of the medicinal product.

With the application for revocation of the marketing authorisation, the applicant shall submit:

- a copy of the valid marketing authorisation for the medicinal product,
- justification of the application, and
- proof that the administrative fee and costs of procedure have been paid.

Article 69

The Agency shall render a decision in order to either grant or refuse the revocation of the marketing authorisation within 30 days from the receipt of a valid application.

VI. TRANSFER OF MARKETING AUTHORISATIONS

Article 70

The marketing authorisation holder for a medicinal product shall submit the application to the Agency for the transfer of the marketing authorisation to another legal person seated in the

Republic of Croatia.

The written application referred to in paragraph 1 shall be submitted separately for each name of the medicinal product, pharmaceutical form, strength, and packaging type and size(s).

The following documents shall be enclosed to the application for the transfer of the marketing authorisation:

1. particulars of the medicinal product for which the authorisation transfer has been required (the name, pharmaceutical form, strength, and packaging type and size(s) of the medicinal product);
2. a copy of the valid marketing authorisation for the medicinal product for which the transfer has been required, together with the approved Summary of Product Characteristics, package leaflet, and labelling;
3. the original or the statement given by the responsible person of the marketing authorisation holder that he agrees with the transfer of the marketing authorisation to another legal person, as well as with transfer to that person of all rights and obligations of the marketing authorisation holder, transfer of the medicinal product dossier based on which the authorisation was granted and of all post-authorisation amendments approved (indicate the medicinal product concerned, the other legal person, and other data),
4. the proof that the legal person seated in the Republic of Croatia to whom the marketing authorisation is being transferred has been entered into the register of the competent commercial court (the original or a copy verified by a notary public, not older than six months from the application submission),
5. the original or the statement given by the responsible person of the legal person seated in the Republic of Croatia to whom the marketing authorisation for the medicinal product is being transferred, that he accepts the transfer of the marketing authorisation, as well as of rights and obligations, responsibilities for the medicinal product, and the medicinal product dossier based on which the authorisation and all authorised amendments were granted (indicate the medicinal product concerned, the other legal person, and other data required),
6. evidence for the right of representation – the Agency Agreement (the original or a copy verified by a notary public; where the language of the agreement is not Croatian, it shall be duly verified and translated by a certified court interpreter),
7. the statement given by the responsible person of the legal person seated in the Republic of Croatia to which the marketing authorisation is being transferred, that he has uninterrupted services of a qualified person responsible for pharmacovigilance in accordance with Article 72 of the Act (curriculum vitae, address, phone and fax numbers) and the description of the pharmacovigilance system as well as the Risk Management Plan, if required,
8. the proposal of the Summary of Product Characteristics, package leaflet and instructions for medicinal product labelling (with the data on legal person to whom the marketing authorisation is being transferred),
9. the proof that the administrative fee was paid.

Article 71

The Agency shall be obliged to either grant or refuse the marketing authorisation transfer of a medicinal product within 30 days from the receipt of a valid application.

The marketing authorisation transfer shall be granted or refused by the decision which cannot be appealed, but against which an administrative procedure can be instituted.

The decision on the marketing authorisation transfer to a new holder shall be issued before expiry of the validity term of the marketing authorisation whose transfer was applied for.

VII. UPGRADING OF MEDICINAL PRODUCTS DOCUMENTATION AUTHORISED FOR MARKETING IN THE REPUBLIC OF CROATIA

Article 72

Documentation upgrading is a procedure by which a medicinal product documentation covered by formerly granted marketing authorisation in the Republic of Croatia is amended in line with the latest scientific and technical progress in the manufacturing process and quality control of medicinal products, with the goal of harmonising the same with the medicinal product documentation laid down in this Ordinance, including also amendment to the Summary of Product Characteristics with the latest information about the medicinal product.

Article 73

The documentation based on which authorisation for marketing of the relevant medicinal product in the Republic of Croatia was granted needs to be upgraded and harmonised with the provisions of the Act and of this Ordinance.

Not later than 12 months from the date of coming into force of this Ordinance, the marketing authorisation holder shall make a written statement saying that the documentation on authorised medicinal product has been harmonised.

In the statement from paragraph 2, the marketing authorisation holder shall provide the particular(s) specified in Article 4, paragraph 3, items 3 and 4 of this Ordinance, for the purpose of documentation upgrading.

The medicinal product documentation to be submitted by the market authorisation holder for upgrading purposes shall be selected depending on harmonisation of the documentation at the time of the upgrading application, taking into account the documentation based on which the first authorisation was granted, as well as approved variations and the documentation amended in the course of the renewal procedure.

The documentation from paragraph 4 may be submitted in the CTD or STD format.

Article 74

Where unable to fully meet the provisions of the Act and this Ordinance, the marketing authorisation holder shall be obliged to provide written justification of the omission of individual documentation parts.

The marketing authorisation holder shall apply for upgrading of the documentation during the first renewal procedure, but not later than within 4 years from the date of the accession of the Republic of Croatia to the European Union.

The marketing authorisation holder can submit an upgrading application to the Agency even before the first authorisation renewal procedure, based on the provisions of this Ordinance.

Should the marketing authorisation holder fail to act in accordance with the provisions of this Article, i.e. fails to upgrade the medicinal product documentation, the Agency shall revoke the relevant marketing authorisation by means of the decision which cannot be appealed, but against which an administrative procedure can be instituted.

X. TRANSITIONAL AND FINAL PROVISIONS

Article 75

The procedures initiated as a result of an application for granting, renewal or variation of an authorisation for marketing of a medicinal product, and an application for the approval of an variation to the medicinal product documentation submitted to the Agency before the date of coming into force of this Ordinance, shall be finalised in accordance with the provisions of the Ordinance on the procedure and method of granting marketing authorisations for medicinal products (Official Gazette 143/98).

Article 76

The marketing authorisations granted in accordance with regulations that were in force before this Ordinance became effective shall stay in force until the expiry of their original validity.

Article 77

On the date of coming into force of this Ordinance, the Ordinance on the procedure and method of granting marketing authorisations for medicinal products (Official Gazette 143/98) shall cease to apply.

Article 78

This Ordinance shall come into force on the eighth day following its publication in the Official Gazette, with the exclusion of the provision of Article 17 which will come into force on the date of accession of the Republic Croatia to the European Union.

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The Minister
Darko Milinović, m. p.