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

DECISION
PROMULGATING THE ACT ON AMENDMENTS TO
THE MEDICINAL PRODUCTS ACT

I hereby promulgate the Act on Amendments to the Medicinal Products Act, passed by the Croatian Parliament at its session on 3 April 2009.

No: 011-01/09-01/71
Reg: 71-05-03/1-09-2

Zagreb, 6 April 2009

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

THE ACT ON AMENDMENTS TO THE MEDICINAL PRODUCTS ACT

Article 1

In the Medicinal Products Act (Official Gazette 71/07), after Article 2, item 60, item 60 a. is added which reads:

"60.a *Advanced therapy medicinal product* means the medicinal product based on manufacturing processes focused on genes and/or therapeutically modified cells and/or therapeutically modified tissues."

In item 64, the word "Agency" is replaced by the words "competent authority".

Article 2

In Article 7, paragraph 8 is amended to read:

"If the Minister does not give or refuse his pre-approval within the deadline referred to in paragraphs 3, 4 and 5 of this Article, the approval shall be deemed granted."

Article 3

In Article 15, item a) is amended to read:

"a) the medicinal product is essentially similar to the reference medicinal product, provided that the reference product was granted marketing authorisation in the Republic of Croatia or any EU Member State more than six years ago, or the reference medicinal product was granted marketing authorisation in the European Union using the centralised procedure more

than ten years ago, for any strength, pharmaceutical form, method of administration or packaging, or”

Article 4

After Article 15, a new Article 15.a is added which reads:

“Article 15.a

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

a) the medicinal product is of the same kind as the reference medicinal product, provided that the reference product was granted marketing authorisation in the Republic of Croatia or any EU Member State more than eight years ago for any strength, pharmaceutical form, method of administration or packaging.

b) the medical use of active substance or active substances of the drug product has been well-established in the European Union or the Republic of Croatia for at least ten years, with recognised efficacy and safety, as determined on the basis of a detailed scientific bibliography, or that

c) the manufacturer of a reference product and the holder of the marketing authorisation for that reference product authorised in the Republic of Croatia or the European Union have agreed to use from their files the pharmaceutical, pre-clinical and clinical data on the reference product for the purpose of assessment of documentation enclosed to application for obtaining the marketing authorisation for another medicinal product with the same qualitative and quantitative composition in active substances and of the same pharmaceutical form.“

The marketing authorisation holder may not place the medicinal product from paragraph 1, item a) of this item on the market within ten years following the obtaining of the first marketing authorisation for this reference medicinal product.

The ten-year period from paragraph 2 of this item may be prolonged for an additional year if, during the first eight years of the ten-year period, the holder of the marketing authorisation for the reference medicinal product is granted authorisation for one or more new therapeutic indications for the same medicinal product that are considered to be clinically significantly beneficial compared to the existing use of the medicinal product.”

Article 5

In Article 20, paragraph 6 is amended to read:

“In the procedure for issuance of the marketing authorisation, the Agency shall approve the Summary of Product Characteristics, the Patient Information Leaflet and the labelling, and submit them to the marketing authorisation holder.”

Article 6

In Article 22, paragraph 1, item c) after the Croatian word translated as: “proven”, another Croatian word is deleted, with no relevance to the English translation.

Article 7

In Article 24, paragraph 8 is amended to read:

"If the approved amendment requires amendments to data in the decision on the marketing authorisation, the Agency shall issue, along with the approved amendment, a decision on amendments to the marketing authorisation. The Agency's decision may be appealed, though administrative proceedings may be instituted."

After paragraph 8, a new paragraph 9 is added which reads:

"If the approved amendment requires amendments to the Summary of Product Characteristics and/or Patient Information Leaflet and/or labelling, the Agency, along with the approved amendment, shall approve the new amended Summary of Product Characteristics and/or Patient Information Leaflet and/or labelling."

The previous paragraphs 9 and 10 become paragraphs 10 and 11.

Article 8

In Article 47, paragraph 1, item 1 is amended to read:

"1) the name of the medicinal product followed by its strength and pharmaceutical form, and, if appropriate, whether it is intended for nursing infants, children or adults. The international non-proprietary name (INN) or, where unavailable, its common name, shall be included where the medicinal product contains up to three active substances."

Article 9

In Article 63, paragraph 1, the word "licence" is replaced by the word "approval".

Paragraph 2 is amended to read:
"The provision of paragraph 1 of this Article shall not apply to issuing the import approval for:

– medicinal products manufactured from human blood or human plasma,
– substances used for the manufacture of immunological medicinal products and immunological medicinal products,
– radiopharmaceuticals."

After paragraph 2, paragraph 3 is added which reads:

"The Minister shall issue an ordinance establishing detailed conditions for issuing the import approval for drug products from paragraph 2 of this Article."

Article 10

In Article 71, paragraph 2 the words: "and to the Agency", are replaced by the words: "other than those for which this is required neither by the trial protocol nor by the investigator's brochure."

Article 11

In Article 72, paragraph 2, item 1, the words: “to the Agency and the Central Ethics Committee”, are replaced by the words: “at the request of the Agency and/or the Central Ethics Committee.”

Item 3 is amended to read:

“3. immediately, and within no later than 15 days of learning of the information, ensure that all other suspected and serious unexpected adverse reactions are reported to the Agency and the Central Ethics Committee.”

Item 5 is amended to read:

“5. submit on an annual basis the aggregate report about the clinical drug for the period of one year, which contains the list of all suspected serious adverse reactions recorded during the reporting period, and the report on safety of trial subjects, to the Agency and the Central Ethics Committee, and exceptionally also as required by the Agency and/or the Central Ethics Committee.”

Article 12

In Article 110, after paragraph 2, paragraph 3 is added which reads:

“The costs of the procedure for registration, amendments to registration, renewal of registration, and refusal and delisting of the homeopathic medicinal product from the register of homeopathic medicinal products shall be defined by the Agency, subject to approval by the Minister, and borne by the applicant or the registration holder.”

Article 13

In Article 111, after paragraph 8, paragraph 9 is added which reads:

“The provisions of Article 24 of this Act shall appropriately apply to the approval of amendments to authorised homeopathic medicinal products.”

Article 14

In Article 114, paragraph 1, the number “113” is replaced by the number “108”.

In paragraph 1, subparagraph 2, the words: “who is the holder of the marketing authorisation for homeopathic medicinal products” are replaced by the words: “who is the holder of the registration of the homeopathic medicinal product in the register of homeopathic medicinal products”.

Article 15

In Article 115, after paragraph 1, a new paragraph 2 is added which reads:

“The advertising of homeopathic medicinal products referred to in Article 108 of this Act shall be prohibited.”

In former paragraph 2, which becomes paragraph 3, the number “1” is replaced by the number “2”.

Article 16

Article 120 is amended to read:

“The Agency shall engage in the following activities:

– granting marketing authorisations for medicinal products and homeopathic medicinal products;

– keeping the register of homeopathic medicinal products;

– providing expert assessment of the quality, efficacy and safety of medicinal products and homeopathic medicinal products;

– conducting pharmaceutical testing of medicinal products and homeopathic medicinal products;

– performing quality control of medicinal products and homeopathic medicinal products and issuing quality control certificates and marketing authorisations for imported medicinal products;

– analysing and evaluating adverse reactions and safety of subjects in clinical trials;

– drawing up the Croatian pharmacopoeia;

– issuing manufacturing authorisations to manufacturers of medicinal products and homeopathic medicinal products;

– issuing Good Manufacturing Practice (GMP) certificates;

– issuing wholesale distribution authorisations for medicinal products and homeopathic medicinal products;

– issuing retail sale authorisations to stores specialised in the retail sale of medicinal products;

– issuing import and export licences for medicinal products;

– giving approvals for import and export of medicinal products;

– monitoring adverse reactions and non-compliance of medicinal products;

– carrying out urgent recall procedures for medicinal products;

– monitoring the consumption of medicinal products and promoting their rational use;

– proposing measures to the Minister for the supervision of consumption of medicinal products;

– engaging in waste management activities (for its own needs);

– providing information and education about medicinal products;

– offering expert advice from its scope of activities;

– proposing the alignment of medicinal product regulations with those of the European Union and with regulations and guidelines of international institutions;

– establishing international co-operation in the field of medicinal products;

– keeping the register of medical device manufacturers and the register of medical devices;

– analysing and evaluating adverse events and safety of subjects in clinical trials of medical devices;

– issuing wholesale distribution authorisation for medical devices;

- issuing retail sale authorisations to stores specialised in the retail sale of medical devices;

- issuing import and export licences for medical devices;

- giving approvals for the import and export of medical devices;
- performing vigilance of medical devices;
- carrying out urgent recall procedures for medical devices;
- performing classification of medical devices;
- issuing the certificate of registration of medical devices in the register of medical devices;
- providing information and education about medical devices;
- establishing international co-operation in the field of medical devices;
- proposing the alignment of regulations in the field of medical devices with those of the European Union and the regulations and guidelines of international institutions;
– carrying out other tasks from the area of medicinal products and homeopathic medicinal products in accordance with this Act and regulations passed pursuant thereto, and from the area of medical devices in accordance with the Medical Devices Act and the regulations passed pursuant thereto.”

Article 17

In Article 135, item 18, the words: “paragraph 1”, are followed by the words: “and 2”.

Article 18

The Agency is obliged to align its work and operations with the provisions of this Act within three months from the date of its entry into force.

Article 19

Applications for issuance of the marketing authorisation for medicinal products submitted prior to the entry into force of Article 3 of this Act shall be completed pursuant to the provisions of Article 15 of the Medicinal Products Act (Official Gazette 71/07).

Applications for issuance of the marketing authorisation for medicinal products submitted until the entry into force of Article 4 of this Act shall be completed pursuant to the provisions of Article 15 of the Medicinal Products Act (Official Gazette 71/07).

Article 20

The provisions of Article 15 of the Medicinal Products Act (Official Gazette 71/07) shall cease to have effect upon the expiry of three years of the date of accession of the Republic of Croatia to the European Union.

Article 21

This Act shall enter into force on the eighth day after the day of its publication in the Official Gazette, with the exception of Article 3 of this Act which shall enter into force on the date of accession of the Republic of Croatia to the European Union, and Article 4 which shall enter into force following the lapse of three years from the date of accession of the Republic of Croatia to the European Union.

Class: 530-01/09-01/01

Zagreb, 3 April 2009

THE CROATIAN PARLIAMENT
The President of the Croatian Parliament
Luka Bebić, m.p.