ORDER
on approval of Norms regarding examination of applications for changes to a marketing authorisation leading to an extension application for medicinal products for human use approved through national procedure in Romania

Having in mind provisions of Title XVII "The medicinal product" of Law No. 95/2006 on healthcare reform, as amended as well as those of Government Ordinance No. 125/1998 related to the set up, organisation and functioning of the National Medicines Agency, approved with amendments and supplementations through Law No. 594/2002, with further amendments and supplementations,

based on Government Decision No. 862/2006 on organisation and functioning of the Ministry of Public Health,

on seeing the Approval Report of the Pharmaceutical Directorate No. E.N. 4712/2006,

the minister of public health hereby issues the following order:

Article 1. - Norms regarding examination of applications for changes to a marketing authorisation leading to an extension application for medicinal products for human use approved through national procedure in Romania, according to Annexes 1 and 2.

Article 2. - Provisions of Article 1 of these Norms concern applications for line extension submitted to the National Medicines Agency after the date of this order coming into force

Article 3. - On the date of these Norms coming into force, Order of the minister of health No. 90/02.02.2004, on approval of examination of applications for changes to a marketing authorisation leading to an extension application for medicinal products for human use approved through national procedure in Romania after 1 January 2001, published in the Official Gazette of Romania, Part I, No. 122 of 11 February 2004, shall be repealed.

Article 4. - Annexes 1 and 2 are integral part of this order.

Article 5. – The present order is to be published in the Official Gazette of Romania, Part I.

Minister of public health,
Gheorghe Eugen Nicoleescu

Bucharest, 2 October 2006
No. 1.204.

ANNEX No. 1

NORMS

Norms regarding examination of applications for changes to a marketing authorisation leading to an extension application for medicinal products for human use approved through national procedure in Romania

CHAPTER I

Introduction

Article 1**. -** These Norms establish examination of applications for changes to a marketing authorisation leading to an extension application for medicinal products for human use approved through national procedure in Romania.

Article 2. – Line extension is a fundamental change to marketing authorisation terms, which cannot be approached through a variation procedure to the marketing authorisation but by means of a separate procedure leading to grant of a new marketing authorisation or change of the marketing authorisation in place.

Article 3. **–** These Norms have been devised following Commission Regulation (EC) No. 1084/2003 of 3 June 2003 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use granted by a competent authority of a Member State, Commission Regulation (EC) No. 1085/2003 of 3 June 2003 concerning the examination of variations to the terms of a marketing authorisation for medicinal products for human use falling within the scope of Council Regulation (EEC) No. 2309/93 and the EMEA/19984/2003 Rev 5 Post-authorisation guideline for medicinal products for human use.

CHAPTER II

Scope

Article 4. - These Norms apply to extension applications for marketing authorisation for medicinal products for human use authorised through national procedure.

Article 5**.** – Types of changes requiring submission of an extension application are described in Annex 2 of this decision.

Article 6. – These Norms do not concern applications for variation to marketing authorisation terms.

CHAPTER III

Administrative procedure for examination of applications for extension of marketing authorisations

Article 7. - The marketing authorisation holder, henceforth referred to as the *holder*, submits to the National Medicines Agency an application for extension in the form provided in Annex 1 to regulations in force on marketing authorisation and surveillance of medicinal products for human use, together with the payment form and the authorisation dossier and material provided for under Chapter II *Submission of marketing authorisation applications* of above mentioned regulations.

Article 8. - (1) The National Medicines Agency examines whether the application and the accompanying dossier are appropriately presented.

(2) In case the application and the accompanying dossier are validated, the procedure starts.

(3) In case of non-validation, the application is rejected and the procedure may be resumed by submission of a new application.

Article 9**.** – Following payment of the authorisation fee and tariff and confirmation by the Economic department of cash-in of the respective amounts, the authorisation dossier and necessary material are distributed to evaluation bureaus.

Article 10**.** – The timeline for examination of extension applications is no longer than 210 days as of confirmation of payment.

Article 11**.** – The Evaluation–authorisation department performs an assessment of the submitted dossier and expresses an opinion on the submitted application.

Article 12**.** - In case of a positive opinion, the National Medicines Agency decides on grant of a new marketing authorisation or change of the marketing authorisation in place, as the case may be.

Article 13**.** – The name of the medicinal product will be the same for the extension as it is for the existing marketing authorisation of the medicinal product

Article 14. (1) During assessment of the line extension application or after authorisation of the line extension, the marketing authorisation holder shall submit an application for variation on change of the trade name for the medicinal products in place, required by the fact that approval of the extension determines existence of several strengths or pharmaceutical forms (as the case may be), which have to be included in the trade name.

(2) The procedure involving assessment of the variation notification starts after authorisation of the line extension.

Article 15. – Should the submitted dossier be incomplete, the procedure shall be stopped until submission of additional information requested by the National Medicines Agency.

CHAPTER IV
General provisions

Article 16**.** – Other aspects pertaining to the procedure for authorisation of a line extension to an existing marketing authorisation (set up of the assessment report, laboratory testing, expression of the decision within the marketing authorisation commission, grant of the marketing authorisation and respective annexes etc.) are in line with provisions of Chapter III *Marketing authorisation procedure* of regulations in force on marketing authorisation and surveillance of medicinal products for human use.

ANNEX No. 2

CHANGES
to a marketing authorisation leading to an extension application

1. Changes to the active substance(s):

a) replacement of the active substance(s) by a different salt/ester complex/derivative (with the same therapeutic moiety) where the efficacy/safety characteristics are not significantly different,

b) replacement by a different isomer, a different mixture of isomers, of a mixture by an isolated isomer (e.g. racemate by a single enantiomer) where the efficacy/safety characteristics are not significantly different,

c) replacement of a biological substance or product of biotechnology with one of a slightly different molecular structure. Modification of the vector used to produce the antigen/source material, including a new master cell bank from a different source where the efficacy/safety characteristics are not significantly different,

d) a new ligand or coupling mechanism for a radio-pharmaceutical,

e) change to the extraction solvent or the ratio of herbal drug to herbal drug preparation where the efficacy/safety characteristics are not significantly different.

2. Changes to strength, pharmaceutical form and route of administration*:*

a) change of bio-availability;

b) change of pharmaco-kinetics e.g. change in rate of release,

c) change or addition of a new strength/potency,

d) change or addition of a new pharmaceutical form,

e) change or addition of a new route of administration [(1).]

[(1).] For parenteral administration, it is necessary to distinguish between intra-arterial, intravenous, intramuscular, subcutaneous and other routes