ORDER
No. 92/8.02.2006
on change and completion of Order of the Ministry of Health No. 1451/2005 regarding approval of the Guideline on update and change of documentation for the authorization of medicinal products for human use authorized in Romania in view of compliance with European Union requirements

Taking into account Government Emergency Ordinance No. 152/1999 on medicinal products for human use, approved with changes and completions through Law No. 336/2002 with further changes and completions and Government Ordinance No. 125/1998 regarding the setting up, organization and functioning of the National Medicines Agency, approved with changes and completions through Law No. 594/2002, with further changes and completions,

Considering the Approval Report of the General Pharmaceutical Directorate and Medical Devices No. E.N. 6881/2006,

Based on Government Decision No. 168/2005 on organisation and functioning of the Ministry of Health, with further changes and completions,

The **Minister of Health** hereby issues the following order:

ARTICLE 1

Annexes 1 to 8 to Order of the Ministry of Health No. 1451/2005 regarding approval of the Guideline on update and change of documentation for the authorization of medicinal products for human use authorized in Romania in view of compliance with European Union requirements, published in the Official Gazette of Romania, Part 1, no. 66/24.01.2006 shall be replaced with Annexes 1 to 8 to the present order.

ARTICLE 2

The present order shall be published in the Official Gazette of Romania, Part 1.

Minister of Health,
Gheorghe Eugen Nicolaescu

Bucharest, 8 February 2006
No. 92.

ANNEX 1

GUIDELINE
on update and change of documentation for the authorization of medicinal products for human use authorized in Romania, in view of compliance with European Union requirements

CHAPTER 1
Introduction

Article 1

Starting with the date of Romania's Accession to the European Union (EU), documentation of all medicinal products for human use authorized for marketing in Romania shall comply with *Acquis communautaire* provisions in the field of medicinal products for human use.

Article 2

For purposes of conformity of documentation for marketing authorization with *Acquis communautaire* provisions in the field of medicinal products for human use, update or change of documentation of medicinal products for human use already authorized in Romania may be necessary.

Article 3

The present Guideline gives an outline of the procedure and timetable regarding update and change of documentation for the authorization of the medicinal products for human use authorized in Romania, in view of their compliance with EU requirements.

Article 4

Provisions of the present Guideline shall apply to all medicinal products for human use authorized in Romania, except for the following:

a) medicinal products authorized in Romania through CADREAC simplified procedure for medicinal products authorized through centralized procedure in the EU;

b) medicinal products authorized in Romania through CADREAC simplified procedure for medicinal products authorized through mutual recognition procedure in the EU;

c) homeopathic medicinal products;

d) medicinal products for human use classified as traditional herbal medicinal products.

Article 5

Following the date of the present Guideline entry into force, marketing authorization holders shall have the following obligations:

- to specify Legal basis for medicinal product authorization according to provisions of Directive 2001/83/EC of the European Parliament and Council of 6 November 2001 on a Community code relating to medicinal products for human use;
- to identify the status of the respective medicinal products in Member States;
- to specify their intentions regarding respective medicinal product continuation on the Romanian market after Romania's accession to the EU;
- to update and change documentation for authorization to achieve compliance with EU requirements, if necessary.

CHAPTER 2
Specification of legal basis for authorization of medicinal products in accordance with Directive 2001/83/EC provisions

Article 6

Types of marketing authorizations specified in Directive 2001/83/EC are as follows:

1. Authorization for medicinal product provided with full and independent documentation, based on own experimental data, according to Article 8, par. (3) of Directive 2001/83/EC;

2. Authorization for medicinal product provided with full documentation, based on detailed scientific literature data for active substances with well-established medicinal use ("bibliographical authorizations"), according to Article 10, par. (1), letter (a), item (2) of Directive 2001/83/EC;

3. Authorization for medicinal product relating to safety and efficacy data of a reference medicinal product, on consent of marketing authorization holder for the reference medicinal product**,** according to Article 10, par.(1), letter (a), item (i) of Directive 2001/83/EC;

4. Authorization for generic medicinal product, as per Article 10, par. (1), letter a), item 3) of Directive 2001/83/EC;

5. Authorization for medicinal product containing a new combination of known substances ("fixed combination"), according to Article 10, par.(1), letter b) of Directive 2001/83/EC;

6. Authorization for medicinal product provided with "mixed" documentation, based on own experimental data as well as scientific literature data, according to provisions of Part 2, item 7 of the Annex to Directive 2003/63/EC amending Directive 2001/83/EC.

Article 7

(1) The type of marketing authorization specified by the marketing authorization holder in Annex 2 to the present Guideline may not be changed during the process of documentation update and change.

(2) The National Medicines Agency (NMA) shall evaluate documentation according to the type of authorization declared by the applicant.

(3) In case of ambiguous or inadequate data determined during verification of documentation submitted within the process described in the present Guideline, the NMA shall submit the marketing authorization holder questions or requests to complete documentation.

CHAPTER 3
Options provided to marketing authorization holders within the process of update/change of documentation for authorization to ensure compliance with EU requirements

Article 8

(1) In the case of a medicinal product with valid marketing authorization in a particular Member State, the following options are provided to the marketing authorization holder:

- to submit a written statement according to the model presented in Annex 3, to the effect that documentation submitted to the NMA is identical with that submitted to the Member State/States competent authority/authorities; this option may not be used in the case of medicinal products authorized in Germany before 1978, which have not been re-evaluated yet as well as of medicinal products listed for Cyprus, Lithuania, Malta, Poland and Slovenia in Part 4 of the Accession Treaty of 2003, which have not been re-evaluated yet;

- to change documentation submitted to the NMA in order to insure its identity with documentation submitted to Member State/States competent authority/authorities, by submitting completions as well as a written declaration according to the model in Annex 4, to the effect that the documentation thus completed, in the possession of the NMA is identical with that presented to competent Member State/States authority/authorities;

- to ensure conformity of documentation with Directive 2001/83/EC requirements by submission to the NMA of entirely new documentation together with a list of differences from previous documentation submitted as well as a written declaration according to the model in Annex 5, to the effect that documentation submitted to the NMA complies with Directive 2001/83/EC provisions.

Article 9

In the case of medicinal products not authorized for marketing in a Member State, the marketing authorization holder has the following options:

- to submit a written statement according to the model in Annex 6, to the effect that documentation submitted to the NMA for the authorization of the respective medicinal product, meets the terms of with Directive 2001/83/EC provisions;

- to change documentation submitted to the NMA in order to achieve its compliance with Directive 2001/83/EC provisions, by submitting completions, as well as to give a written statement according to the model in Annex 7, to the effect that documentation submitted to the NMA meets the terms of Directive 2001/83/EC provisions;

- to ensure conformity with Directive 2001/83/EC provisions, by submitting entirely new documentation to the NMA, together with a list of differences from previous documentation submitted as well as to give a written statement according to the model in Annex 8, to the effect that documentation submitted to the NMA meets the terms of Directive 2001/83/EC provisions.

Article 10

(1) Completions to documentation for authorization already in possession of the NMA shall be submitted in either former format or in Common Technical Document format, depending on the format of basic documentation already submitted to the NMA.

(2) In the case of entirely new documentation submitted to the NMA, this shall be presented in Common Technical Document format.

CHAPTER 4
Timetable for documentation updating

Article 11

In order to ensure conformity of documentation for authorization with EU requirements, all marketing authorization holders of medicinal products authorized in Romania shall submit their statements to the NMA before 30 June 2006; respective statements shall be drawn up in conformity with models provided in Annexes 2 to 8, as required, in either Romanian or English, accompanied by respective documentation, if necessary.

CHAPTER 5
Marketing authorization renewal

Article 12

(1) In the case of medicinal products requiring renewal within the period extending from 1 July 2006 to 31 December 2006, documentation update shall be achieved on submission of application for renewal of the marketing authorization to the NMA.

(2) In the case of medicinal products for which applications for marketing authorization renewal have been submitted before entry into force of the present guideline, the statements and the documentation mentioned in Article 11 shall be submitted to the NMA before 30 June 2006.

CHAPTER 6
Tariffs

Article 13

(1) In order to update documentation, marketing authorization holders shall pay updating tariffs as provided by Minister of Health Order No. 407/2005.

(2) Provisions of par. (1) of the present Article shall not apply in case the marketing authorization holder only submits the statement related to conformity of authorization documentation with the *Acquis communautaire*.

CHAPTER 7
Final provisions

Article 14

In case statements and documents mentioned in Article 11 of the present guideline are not submitted to the NMA with regard to certain medicinal products before 30 June 2006, marketing authorizations for the respective medicinal products shall be suspended.

Article 15

In case the NMA shall determine inaccuracy of certain statements submitted by marketing authorization holders in conformity with present guideline provisions, marketing authorizations shall be accordingly suspended.

ANNEX 2

STATEMENT
of the marketing authorization holder regarding the legal basis for medicinal product authorization, identification of medicinal product status in Member States and intentions regarding respective medicinal product continuation on the Romanian market after Romania's accession to the EU

Medicinal product authorized in Romania

Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of marketing authorization in Romania	

Legal basis for medicinal product authorization

1. Authorization for medicinal product provided with full and independent documentation, based on own experimental data (according to Article 8, par. (3) of Directive 2001/83/EC) □
The marketing authorization holder considers that the data exclusivity period begins on:
2. Authorization for medicinal product provided with full documentation, based on scientific literature data (according to Article 10, par.(1), letter a), item 2) of Directive 2001/83/EC) □
Reference medicinal product/products: Name of medicinal product/products: Pharmaceutical form: Manufacturer/manufactures/marketing authorization holder/holders:

3. Authorization for medicinal product relating to safety and efficacy data of reference medicinal product, on consent of marketing authorization holder for the reference medicinal product (according to Article 10, par.(1), letter a), item i) of Directive 2001/83/EC) □
Reference medicinal product: Name of medicinal product: Pharmaceutical form: Manufacturer/ marketing authorization holder: Authorization currently valid in Romania: Yes □ No □

4. Authorization for generic medicinal product (according to Article 10, par.(1), letter a), item 3) of Directive 2001/83/EC) □
Reference medicinal product: Name of medicinal product: Pharmaceutical form: Manufacturer/ marketing authorization holder:
SPC in Romania corresponds to SPC of reference medicinal product: Yes □ No □
In case of different SPC, differences at the level of indications, administration route or various doses are supported with sufficient information:
5. Authorization for medicinal product containing a new combination of known substances ("fixed combination") (according to Article 10, par.(1), letter b) of Directive 2001/83/EC) □
6. Authorization for medicinal product provided with "mixed" documentation, based on own experimental data as well as scientific literature data (according to provisions of Part 2, item 7 of the Annex to Directive 2003/63/EC) □
Reference medicinal product/products: Name of medicinal product/products: Pharmaceutical form: Manufacturer/manufacturers/ marketing authorization holder/holders:

Status of medicinal product in Member States

Currently valid authorization of medicinal product in any Member State: Yes □ No □
List of Member States the medicinal product is currently authorized in:
Date of first marketing authorization in the EU:
Marketing authorization holder intends to obtain identity of files submitted in Romania and Member State and submit a statement confirming the similarity of files: Yes □ No □

Intention of marketing authorization holder regarding respective medicinal product continuation on the Romanian market after Romania's accession to the EU

Medicinal product placed on the Romanian market before 30 April 2005 Yes □ No □
Marketing authorization holder intends to end medicinal product sales in Romania and submit an application for authorization withdrawal Yes □ No □

Date:	
Signature of the representative of marketing authorization holder:	
Name and address of the representative of marketing authorization holder:	

ANNEX 3

STATEMENT
of the marketing authorization holder
regarding identity of documentation for medicinal product authorization
as submitted to the National Medicines Agency with documentation for authorization as submitted to the competent authority in a particular Member State

Medicinal product authorized in Romania

Name of medicinal product, pharmaceutical form	
Active substance/substances, content:	
Number of marketing authorization in Romania	

Medicinal product authorized in a certain EU Member State

Member State		
Name of medicinal product, pharmaceutical form		
Active substance/substances, content:		
Number of marketing authorization:		
Marketing authorization granted in:		(year)
Procedure	National	□
	Mutual Recognition	□
Legal basis for medicinal product authorization	Authorization for medicinal product provided with full and independent documentation, based on own experimental data (according to Article 8, par. (3) of Directive 2001/83/EC)	□
	Authorization for medicinal product provided with full documentation, based on scientific literature data (according to Article 10, par.(1), letter a), item 2) of Directive 2001/83/EC) □ Reference medicinal product/products: Name of medicinal product/products: Pharmaceutical form: Manufacturer/manufactures/ marketing authorization holder/holders:	

	Authorization for medicinal product relating to safety and efficacy data of reference medicinal product, on consent of marketing authorization holder for the reference medicinal product (according to Article 10. par.(1), letter a), item i) of Directive 2001/83/EC) □ Reference medicinal product: Name of medicinal product: Pharmaceutical form: Manufacturer/marketing authorization holder:
	Authorization for generic medicinal product (according to Article 10, par.(1), letter a), item 3) of Directive 2001/83/EC) □ Reference medicinal product Name of medicinal product: Pharmaceutical form: Manufacturer/marketing authorization holder:
	Authorization for medicinal product containing a new combination of known substances ("fixed combination") (according to Article 10, par.(1), letter b) of Directive 2001/83/EC) □
	Authorization for medicinal product provided with "mixed" documentation, based on own experimental data as well as scientific literature data (according to provisions of Part 2, item 7 of the Annex to Directive 2003/63/EC) □ Reference medicinal product/products: Name of medicinal product/products: Pharmaceutical form: Manufacturer/manufacturers/ marketing authorization holder/holders:

I hereby state that the above mentioned are true and that the documentation for authorization submitted to the NMA is identical with documentation submitted to the competent authority of the above mentioned Member State.

Date:	
Signature of the representative of the marketing authorization holder:	
Name and address of the representative of marketing authorization holder:	

ANNEX 4

STATEMENT
of the marketing authorization holder
regarding identity of documentation for medicinal product authorization
in the possession of the National Medicines Agency following submission of completions
with documentation for authorization as submitted to the competent authority
in a particular Member State

Medicinal product authorized in Romania

Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of the marketing authorization in Romania	

Medicinal product authorized in a certain EU Member State

Member State:		
Name of medicinal product, pharmaceutical form:		
Active substance/substances, content:		
Number of marketing authorization		
Marketing authorization granted in:		(year)
Procedure	National	□
	Mutual Recognition	□
Legal basis for medicinal product authorization	Authorization for medicinal product provided with full and independent documentation, based on own experimental data (according to Article 8, par. (3) of Directive 2001/83/EC) □	
	Authorization for medicinal product provided with full documentation, based on scientific literature data (according to Article 10, par.(1), letter a), item 2) of Directive 2001/83/EC) □ Reference medicinal product/products: Name of reference medicinal product/products: Pharmaceutical form: Marketing authorization holder/holders:	

	Authorization for medicinal product relating to safety and efficacy data of reference medicinal product on consent of marketing authorization holder for the reference medicinal product (according to Article 10. par.(1), letter a), item i) of Directive 2001/83/EC) □ Reference medicinal product Name of medicinal product: Pharmaceutical form: Marketing authorization holder:
	Authorization for generic medicinal product (according to Article 10, par.(1), letter a), item 3) of Directive 2001/83/EC) □ Reference medicinal product: Name of medicinal product: Pharmaceutical form: Marketing authorization holder:
	Authorization for medicinal product containing a new combination of known substances ("fixed combination") (according to Article 10, par.(1), letter b) of Directive 2001/83/EC) □
	Authorization for medicinal product provided with "mixed" documentation, based on own experimental data as well as scientific literature data (according to provisions of Part 2, item 7 of the Annex to Directive 2003/63/EC) □ Reference medicinal product/products Name of medicinal product/products: Pharmaceutical form: Marketing authorization holder/holders:

List of documentation submitted to achieve identity of documentation in the possession of the NMA with documentation submitted to the competent authority in the Member State

I hereby state that the above mentioned are true and that the documentation for authorization in NMA possession following submission of completions is identical with documentation submitted to the competent authority of the above mentioned Member State.	
Date:	
Signature of the representative of the marketing authorization holder:	
Name and address of the representative of marketing authorization holder:	

ANNEX 5

STATEMENT
of the marketing authorization holder regarding identity of documentation in the possession of the National Medicines Agency following submission of completely new documentation with documentation for authorization submitted to the competent authority in a particular Member State

Medicinal product authorized in Romania

Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of the marketing authorization in Romania:	

Medicinal product authorized in a particular Member State

Member State:		
Name of medicinal product, pharmaceutical form:		
Active substance/substances, content:		
Number of marketing authorization:		
Marketing authorization granted in:		(year)
Procedure:	National	□
	Mutual Recognition	□
Legal basis for medicinal product authorization	Authorization for medicinal product provided with full and independent documentation, based on own experimental data (according to Article 8, par. (3) of Directive 2001/83/EC)	□
	Authorization for medicinal product provided with full documentation, based on scientific literature data (according to Article 10, par.(1), letter a), item 2) of Directive 2001/83/EC)	□
	Reference medicinal product/products: Name of reference medicinal product/products: Pharmaceutical form: Marketing authorization holder/holders:	

	Authorization for medicinal product relating to safety and efficacy data of reference medicinal product on consent of marketing authorization holder for the reference medicinal product (according to Article 10. par.(1), letter a), item i) of Directive 2001/83/EC) □ Reference medicinal product: Name of medicinal product: Pharmaceutical form: Marketing authorization holder:
	Authorization for generic medicinal product (according to Article 10, par.(1), letter a), item 3) of Directive 2001/83/EC) □ Reference medicinal product: Name of medicinal product/products: Pharmaceutical form: Marketing authorization holder:
	Authorization for medicinal product containing a new combination of known substances ("fixed combination") (according to Article 10, par.(1), letter b) of Directive 2001/83/EC) □
	Authorization for medicinal product provided with "mixed" documentation, based on own experimental data as well as scientific literature data (according to provisions of Part 2, item 7 of the Annex to Directive 2003/63/EC) □ Reference medicinal product/products: Name of medicinal product/products: Pharmaceutical form: Marketing authorization holder/holders:

List of differences related to previous documentation submitted to the NMA

I hereby state that the above mentioned are true and that the documentation for authorization in the possession of the NMA following submission of completely new documentation is identical with documentation for authorization submitted to the competent authority of the above mentioned Member State.	
Date:	
Signature of the representative of marketing authorization holder:	
The name and the address of the representative of marketing authorization holder:	

ANNEX 6

STATEMENT
of the marketing authorization holder regarding conformity with Directive 2001/83/EC requirements of documentation for medicinal product authorization submitted to the National Medicines Agency

Medicinal product authorized in Romania

Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of the marketing authorization in Romania	

Medicinal product authorized in marketing authorization holder's country of origin

Marketing authorization holder's country of origin:	
Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of marketing authorization	
Marketing authorization granted in:	(year)

I hereby state that the above mentioned are true and that the documentation for authorization submitted to the NMA complies with Directive 2001/83/EC requirements	
Date:	
Signature of the representative of marketing authorization holder:	
Name and address of the representative of marketing authorization holder:	

ANNEX 7

STATEMENT
of the marketing authorization holder regarding conformity with Directive 2001/83/EC requirements of documentation in the possession of the National Medicines Agency following submission of completions

Medicinal product authorized in Romania

Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of marketing authorization in Romania:	

Medicinal product authorized in marketing authorization holder's country of origin

Marketing authorization holder's country of origin:	
Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of marketing authorization	
Marketing authorization granted in:	(year)

List of differences from previous documentation submitted to the NMA

I hereby state that the above mentioned are true and that documentation for authorization submitted to the NMA following completions complies with Directive 2001/83/EC requirements.	
Date:	
Signature of the representative of marketing authorization holder:	
Name and address of the representative of marketing authorization holder:	

ANNEX 8

STATEMENT

of the marketing authorization holder regarding conformity with Directive 2001/83/EC requirements of documentation in the possession of the National Medicines Agency following submission of completely new documentation

Medicinal product authorized in Romania

Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of marketing authorization in Romania	

Medicinal product authorized in marketing authorization holder's country of origin

Marketing authorization holder's country of origin:	
Name of medicinal product, pharmaceutical form:	
Active substance/substances, content:	
Number of marketing authorization:	
Marketing authorization granted in:	(year)

List of differences from previous documentation submitted to the NMA

I hereby state that the above mentioned are true and that documentation for authorization submitted to the NMA following submission of completely new documentation complies with Directive 2001/83/EC requirements.	
Date:	
Signature of the representative of marketing authorization holder:	
Name and address of the representative of marketing authorization holder:	