January 2006
Final

PROCEDURE
ON THE GRANTING OF MARKETING AUTHORISATIONS BY NEW CADREAC (nCADREAC) DRUG REGULATORY AUTHORITIES FOR MEDICINAL PRODUCTS FOR HUMAN USE ALREADY AUTHORISED IN EU MEMBER STATES FOLLOWING THE CENTRALISED PROCEDURE AND THE VARIATION AND RENEWAL OF SUCH MARKETING AUTHORISATIONS

The purpose of this document is to describe an authorization procedure which can be used by any nCADREAC drug regulatory authority (DRA), Signatory of the New Collaboration Agreement between Drug Regulatory Authorities in Central and Eastern European Countries (nCADREAC) as active member from a candidate country (CC) for granting a marketing authorisation of a medicinal product which has been authorized in European Union (EU) following the Centralised Procedure including the subsequent variations and renewals of such marketing authorisations.

This procedure relates to marketing authorisations which were granted by the European Commission (EC) on the basis of the scientific expertise of the CHMP (Committee for Medicinal Products for Human use), the scientific body of the European Medicines Agency (EMEA) responsible for giving a scientific opinion on medicinal products processed via the centralised procedure), hereafter referred to as „new EMEA expertise", and the recognition of this expertise by nCADREAC DRAs from CC.

The procedure offers the possibility of harmonization of SPC, PIL, labelling and documentation for a product between EU Member States (MSs) and the nCADREAC concerned candidate countries (nC –CCCs).
The procedure described in this document is optional and can only be initiated at the EU Marketing Authorisation Holder (MAH)'s request. The procedure will enter into force on 10 January 2006.

Title I

PRINCIPLES

1. Innovative medicinal products authorised by the centralised procedure could be made available to patients in nCADREAC area without unnecessary delay.

2. The expertise of EMEA represents the best available, consolidated regulatory expertise in the region.

3. It can be assumed that differences in medical practice between the EU MS and nCADREAC area are generally not of major importance for public health, hence the expertise of the EMEA can be assumed to be relevant for nCADREAC area.

4. The medicinal products authorised by the centralised procedure are under continuous supervision of the EMEA and its scientific bodies, which guarantee that reports on serious adverse reactions are evaluated, that periodic safety updates are reviewed at regular periods, that manufacturing facilities are inspected and that appropriate measures are taken, if necessary.
   Marketing authorisations of these products are regularly reassessed and renewed in the EU.

5. Recognition of the expertise of the EMEA by nCADREAC DRAs from CC by adoption of simplified procedures, will be less resource-intensive and provide an enhanced regulatory process.

6. Given that nCADREAC CC have expressed their interest in being EU members in the future, which will involve full participation in the procedure, earlier involvement will have long term benefits. The introduction of common practices and mechanisms for recognition of EMEA expertise and EC decisions are advantageous for nCADREAC DRAs from CC, EU authorities and for applicants because the establishment of common standards and communication interfaces will facilitate mechanisms for integration of nCADREAC CC into EU.

7. According to national legislation nCADREAC DRAs from CC retain their responsibilities for granting of marketing authorisations within their respective territories and may either accept the above principles or impose additional national requirements in accordance with national practices. The procedures of marketing authorisations granted on principles of recognition and granted on principles of national assessment should be clearly distinguished.

8. The acceptance of EMEA expertise is not binding on nCADREAC DRAs from CC. In cases of doubts and questions raised to the EMEA expertise, additional documents to the dossier submitted to EMEA may be required or assessment according to national procedure may be carried out. If recognition is not possible because of serious public health concerns, the EMEA and the applicant should be notified accordingly.

9. The recognition of EMEA expertise implies the acceptance of EU Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL) and labelling. The checking of the appropriateness of translations of the SPC, PIL and labelling is under the responsibility of nCADREAC DRA concerned. The nCADREAC DRA concerned will notify EMEA of any modifications of SPC, PIL and labelling.

10. The recognition of EMEA expertise also implies recognition that "good practices" (GMP, GCP, GLP) have been verified (unless clearly otherwise stated).

11. It is essential that mechanisms for appropriate exchange of information between EU authorities and nCADREAC DRAs concerned on centrally authorised products are established.

12. nCADREAC DRAs concerned will inform EU authorities on all relevant postmarketing experience and all regulatory actions taken with respect to each product authorised according to the described procedure and viceversa.

13. Marketing authorisation in nC-CCCs and in the EU will be based on an identical dossier, even if only selected parts of dossier could be required by individual nCADREAC DRA from CC.

14. Recognition of a EMEA expertise by a nCADREAC DRA from CC is at the request of an applicant and therefore assumes that applicants request this recognition and agree to provide the same dossier and to support full exchange of „confidential" information between nCADREAC DRA concerned and EU authorities.

15. Products, considered to be „harmonised" with EU centrally authorised products, will, as a rule, differ only in defined parameters (MAH, not all package sizes are necessarily authorised in nC-CCCs and in substantiated cases, the name of the medicinal product).

16. Minor deviations from nCADREAC common procedure when recognising EMEA expertise, due to local regulatory practice, legislation and language requirements are possible and should be clearly stated in those nC-CCCs, which accept the common procedure.

17. The simplified common procedure for extensions, variations and renewals of marketing authorisation is acceptable in cases where the simplified procedure had been used for marketing authorisation.

18. Protection of intellectual property rights and confidentiality of submitted documents remain national concerns and local legislation is applicable.

19. Marketing authorisation fee and other fees are charged according to national legislation.

20. There is no link between the described “recognition procedure" and national reimbursement schemes.

21. Re-import of products authorised according to this procedure is outside the scope of this document.

Title II

RESPONSIBILITIES OF CONCERNED PARTIES

• The applicant/MAH in the nC-CCC should ensure that the dossier submitted, or, where appropriate, the parts submitted thereof are identical to the dossier of a product authorised in the EU by the centralised procedure, that all subsequent variations to this dossier, once accepted in the EU, are also submitted and implemented without unnecessary delay in the nC-CCC, and

that all urgent safety measures are implemented simultaneously in the EU and the nC-CCC.

• The MAH in the EU should inform the EMEA that an application will be submitted to one or more nC-CCC, indicate the countries concerned, the name of the product, the Community Marketing Authorisation number, the MAH in the EU as well as the proposed MAH in the nC-CCC. A copy of this information should be provided to the nCADREAC DRA concerned.

• The MAH in the EU should declare that he agrees that the EMEA may make available to the nCADREAC DRA concerned any information on the quality, safety and efficacy of the above product. The extent of this information shall not exceed that which is made available to EU MSs by the EMEA. A copy of this declaration should be provided to the nCADREAC DRA concerned.

• The EMEA should include this information in relevant databases and undertake to notify the nCADREAC DRAs concerned of urgent pharmacovigilance or other safety information once such information is discussed at CHMP level and the CHMP has adopted an opinion on the measures to ensure the safe and effective use of the medicinal product concerned, without prejudice to the outcome of the Commission Decision Making Procedure. Once the Commission Decision is available, the MAH in the nC-CCC will notify the nCADREAC DRA concerned without delay. In case of an Urgent Safety Restriction (USR) procedure, the EMEA will inform the nCADREAC DRAs concerned without delay of the outcome of the USR procedure introducing provisional changes to the product information.

• The nCADREAC DRAs concerned undertake to inform the EMEA at the end of the marketing authorisation or renewal process on its outcome and give the following information: national marketing authorisation number, name, pharmaceutical form/s and strength/s of the product, INN or common name of the active ingredient/s, name of the MAH and authorised package sizes in nC-CCC, information on modifications of SPC, PIL and/or labelling (specifying differences) or, in case of disagreement with the Commission Decision, the scientific conclusions which led to such disagreement. At the end of the variation to marketing authorisation process nCADREAC DRA concerned will inform the EMEA on its outcome only in cases of refusal of the variation or modification of the Commission Decision or the change of data formerly reported to the EMEA. The nCADREAC DRA concerned will send to the EMEA yearly an overview of all finalised variations. A copy of this information should be made available to the applicant. In order to facilitate the processing of this information, a reference to the community marketing authorisation number of the product should be made. The nCADREAC DRAs concerned undertake also to inform the EMEA of any urgent pharmacovigilance or other safety information occurring on their territory. In case of any disagreement with or modification of the Commission Decision the nCADREAC DRA concerned undertakes to also inform all other nCADREAC DRAs concerned.

The nCADREAC DRAs concerned will keep the products authorised following this procedure as much as possible harmonised with the products authorised in EU. The difference between these products and products centrally authorised in the EU, if any, should be in predefined parameters

(MAH, not all package sizes are necessarily authorised in nC-CCC and in substantiated cases the name of the medicinal product). In the case of differences in SPC, these are identified and made known to the EMEA by the nCADREAC DRA concerned. Despite the fact that this voluntary process supports the phasing-in, when a country joins the Community, such Centralised Authorisation Procedure (CAP) Marketing Authorisation (MA) decisions "extend automatically" to the territory of the new Member State. One of the consequences of automatic extension of a CAP MA is the consequent automatic" inapplicability"of the national MA for products, which are as a result considered to be in conflict with the centralized MA. Use of this current type of procedure has been shown to facilitate this phasing in process.

Title III

MARKETING AUTHORIZATION PROCEDURE

Initiation of the procedure

The EU MAH initiates the procedure and notifies the EMEA (see Annex 1) that an application will be submitted in one or more nCADREAC DRAs and indicates:

- the nCADREAC DRA concerned
- the name of the product in the EU, pharmaceutical form(s), strength(s) authorised in the EU
- INN or common name of the active substance(s)
- the Community Marketing Authorisation number(s)
- the EU MAH
- the proposed MAH in the nC-CCC
- the proposed name of the product in the nC-CCC

Furthermore, the EU MAH declares that the EMEA and the European Commission may make available to the nCADREAC DRA concerned any information in relation to the quality, safety and efficacy of the above medicinal product, using the form attached as Annex 1.

The EMEA subsequently includes this information in the relevant database.

Submission of the application

The applicant (i.e. proposed nCADREAC MAH) submits the application to the nCADREAC DRA concerned. The addresses of the nCADREAC DRAs are provided in Annex 3. Furthermore, the proposed nCADREAC MAH certifies that the application is identical with the application accepted in the EU with the exception of the following parameters, where relevant: MAH, pack sizes (not all pack sizes are necessarily authorised in nC-CCC), the name of the medicinal product (in substantiated cases only).

Timing

Applications for simplified procedure may be submitted both before and after the final Commission Decision has been issued depending on the requirements of the nCADREAC DRA concerned. In the case of an earlier application, the fact that a centralised procedure has been started, must be clearly indicated by

submitting the letter from the EMEA informing the applicant of the positive outcome of the validation and of the adopted timetable or the CHMP Opinion. The simplified procedure described in this document can be finished only after the submission of the final Commission Decision by the applicant. The required timing of submission and the period of time expected by the nCADREAC DRA concerned for the issue of a decision is given in the attached table.

Documents to be submitted by the applicant

- application form (the appropriate national application form for the marketing authorisation of a medicinal product)
- modules 1, 2 and 3 of the dossier as accepted by the EMEA and detailed list of contents of modules 4 and 5, providing that these parts are submitted on request
- proposed SPC, PIL in national language and the labelling in national language unless otherwise specified in the attached table; SPC and PIL are translations of the texts approved or in the case of earlier submission of the texts submitted in the EU without changes
- final CHMP Assessment Report including all annexes (see Note below)
- final Commission Decision including all annexes (see Note below)
- declaration by the applicant that
  - => the dossier submitted, or, where appropriate, the parts submitted thereof are identical to the dossier of a product authorised in the EU by the centralised procedure (in the case of an earlier submission, to be identical to the dossier submitted to EMEA), including all information submitted to support any variation which has been applied for and accepted at the time of submission of the application for marketing authorisation at the nCADREAC DRA concerned as well as information concerning post-authorisation commitments, if any
  - => all subsequent variations to this dossier, once accepted in the EU, will also be submitted and implemented without delay by the applicant in the nC-CCC
  - => all urgent safety measures will be immediately notified to the nCADREAC DRA concerned and implemented according to local regulatory requirements simultaneously as in the EU or as soon as possible
  - => in the case where the marketing authorisation will be suspended or withdrawn in the EU (either by the initiative of the MAH or by EC), nCADREAC DRAs concerned will be notified immediately
- copy of the declaration by MAH in the EU (the Declaration is sent to the EMEA) that
  - => an application is being submitted to one or more nCADREAC DRAs, indicating the countries concerned, pertaining to the name of the product, the Community Marketing Authorisation number, the MAH in the EU as well as the proposed MAH in the nC-CCC
  - => he agrees that the EMEA may make available to the nCADREAC DRA concerned any information to the quality, safety and efficacy of the product concerned (the extent of this information shall not exceed

that which is made available to EU MSs by the EMEA)

- list of all resolved/outstanding post-authorisation commitments
- If the application is submitted later than 6 months after the date of the Commission Decision, then the latest available Periodic Safety Update Report (PSUR), which should include any new pharmacovigilance data, shall be submitted.
- Similarly, if any variations to the marketing authorisation in the EU have been applied for and accepted at the time of submission of the application for marketing authorisation in the nCADREAC countries, relevant details should be provided. The information submitted to the EMEA to support these variations should also be submitted in the nCADREAC DRAs concerned and may be annexed to the original dossier (see table of dossier requirements). The following documents should also be provided:
  - => list of all variations to the marketing authorisation that have been approved in the EU, safety, transfer or renewal approved procedures at the time of the date of submission of the application in the nCADREAC DRAs concerned
  - => Commission Decisions granting marketing authorization for the medicinal product for human use, Commission Decision amending the marketing authorisation as a consequence of an approved type II variation, Annex II application, Renewal, Annual Reassessment, transfer of the marketing authorisation or safety procedure, if issued by European Commision, as well as for an approved type IA, IB variation (every six months)
  - => Notifications on a type IB variation to the terms of the marketing authorisation, issued by the EMEA;
  - => Notifications of the minor changes in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)
  - => Acknowledgement of receipt of a valid notification for type IA variation to the terms of the marketing authorization
  - => Variation assessment reports, if issued
- samples as specified in attached table.

Outcome of the procedure

The nCADREAC DRA concerned informs the EMEA (the Head of Unit EMEA Post-Authorisation Evaluation of Medicines for Human Use), with copy to the applicant, at the end of the procedure on its outcome using the form provided in Annex 2.

In case of a favourable outcome (i.e. recognition of the Commission Decision granting the EU marketing authorisation), the following information will be provided:

- name of the medicinal product in the nC-CCC
- national Marketing Authorisation Number(s)
- name of the MAH in the nC-CCC
- date of issue of national Marketing Authorisation
- authorised pharmaceutical form(s), strength(s), pack size(s)
- any differences between SPC, PL, and labelling approved in the

nC-CCC and the EU where relevant

In case of disagreement with the Commission Decision granting the EU marketing authorisation, the scientific conclusions which led to such disagreement are communicated.

The nCADREAC DRA concerned will also inform the other nCADREAC DRAs concerned in case of any disagreement with or modification of the Commission Decision.

Follow-up to the procedure

Upon receipt of information regarding the outcome of the procedure, the EMEA will include such information in the relevant database.

The EMEA will keep its scientific committee, the CHMP informed about the finalisation of any procedure which resulted in a disagreement with or modification of the Commission Decision initiated in accordance with the above described framework. Where necessary, the EMEA will inform the nCADREAC DRAs concerned of the CHMP's consideration of the issue (especially in case of disagreement with the Commission Decision).

Note:

In the case of an application submitted before the final Commission Decision has been issued, the documentation available at this time should be submitted with the application. The final Commission Decision including all annexes, shall be submitted later, when available. The marketing authorisation in the nC-CCC is granted only after the final Commission Decision including all annexes is submitted.

Title IV

VARIATIONS TO THE MARKETING AUTHORISATION

Similar procedure as for marketing authorization will be used for processing such applications.

Timing

An application is submitted within two months of the acceptance of a change in the EU, i.e. type IA, type IB variation, type II variation or Notification of the minor changes in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification), was approved. The appropriate national application form for variation to marketing authorisation is to be used. The period of time expected by the nCADREAC DRA concerned for issue a decision on variation is given in the attached table.

Documents to be submitted by the MAH to the nCADREAC DRA concerned

- application form (the appropriate national application form for the variation to marketing authorisation of a medicinal product)
- the supporting documentation for the variation as accepted by the EMEA

(submitted, if regards module 1, 2 or 3 of the dossier, otherwise only a list of supporting documentation; details of language requirements, electronic application possibilities, number of copies, samples/substances, fees etc. are comparable to the application for authorization, see attached table)

- Commission Decision on type II variation amending the terms of marketing authorisation of a medicinal product, including all annexes
- Letter of European Commision (fax) on type II variation not amending the terms of marketing authorisation of a medicinal product
- Opinion on type II variation, issued by EMEA, including all annexes
- Notification on a type IB variation to the terms of the marketing authorisation, including all annexes, issued by the EMEA
- Notification of the minor changes in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)
- Acknowledgement of receipt of a valid notification for type IA variation to the terms of the marketing authorization
- Variation assessment report, if issued

The nCADREAC MAH submits the variation application to the nCADREAC DRA concerned accompanied by the particulars.

At the end of the procedure the nCADREAC DRA concerned will inform the EMEA (attention of the Head of Unit EMEA Post-Authorisation Evaluation of Medicines for Human Use) only:

- in cases of refusal of the variation application, indicating the scientific conclusions which led to such refusal
- in cases of modification of the Commission Decision granting the variation to the terms of the marketing authorisation, indicating the scientific conclusions which led to such modification
- in cases of changes to the data (i.e. change in the name of the medicinal product in the nC-CCC, change in the name of the MAH in the nC-CCC, change in the authorized pack sizes in the nC-CCC, change in formerly specified differences in SPC, PIL and /or labelling).

Where relevant, the EMEA will keep the CHMP informed about the outcome of the variation procedure. Where necessary, the EMEA will inform the nCADREAC DRA concerned of the CHMP's consideration of the issue (especially in case of disagreement with the Commission Decision).

The nCADREAC DRA concerned will also inform the other nCADREAC DRAs concerned in case of any disagreement with or modification of the Commission Decision.

The nCADREAC MAH will be informed on the outcome in all cases.

nCADREAC DRAs will send the EMEA yearly an overview of all finalised Variation application procedures. The EMEA will subsequently include this information in the relevant database.

Title V

HANDLING OF PHARMACOVIGILANCE INFORMATION

Appropriate mechanisms are put in place in order to allow an efficient communication of pharmacovigilance information.

Therefore, in case of urgent pharmacovigilance or other safety information occurring on the territory of nC-CCC, having an impact on the benefit/risk ratio of the medicinal product, the nCADREAC DRAs concerned will inform the EMEA (attention of the Head of Unit EMEA Post-Authorisation Evaluation of Medicines for Human Use).

The EMEA will inform the nCADREAC DRAs concerned of urgent pharmacovigilance or other safety information having an impact on the benefit/risk ratio of the medicinal product and necessitating a change to the marketing authorisation (withdrawal, suspension, amendment of product information) immediately once such information is discussed at CHMP level and the CHMP has adopted an opinion on the measures to ensure the safe and effective use of the medicinal product concerned, without prejudice to the outcome of the Commission Decision procedure. Once the Commission Decision is available, the nCADREAC MAH will notify the nCADREAC DRA concerned without delay.
In case of an USR procedure, the EMEA will inform the nCADREAC DRAs concerned of the outcome of the USR procedure introducing provisional changes to the product information once such procedure is finalised.

Periodic safety update submission

In accordance with Articles 24(3) of Regulation EC 726/2004, Article 104(6) of Directive 2001/83/EC as amended, Periodic Safety Updates Reports (PSURs) shall be submitted to the EMEA and the Member States immediately upon request or at least every six months after authorization until the placing on the market. PSURs shall also be submitted immediately upon request or at least every six months during the first two years following the initial placing on the Community market and once a year for the following two years. Thereafter, the reports shall be submitted at three-yearly intervals, or immediately upon request.

For products approved before 20 November 2005, transitional arrangements will apply with respect to PSURs submissions.

PSURs are assessed by the EMEA/CHMP and if needed, the appropriate action is taken. These actions are notified to nCADREAC DRAs concerned by the MAH in the nC-CCC as a variation, a suspension or withdrawal.

PSURs should be submitted to nCADREAC DRAs concerned after the marketing authorisation has been issued at the same time as in the EU.

Title VI

RENEWALS OF MARKETING AUTHORISATIONS

Renewal of marketing authorisation should be applied for in periods specified by national legislation of nC-CCC.

The nCADREAC MAH submits the renewal application to the nCADREAC DRA concerned accompanied by the following particulars:

- Commission Decision on the renewal of marketing authorisation of the medicinal product including all annexes
- Opinion on renewal of marketing authorisation of the medicinal product, issued by EMEA, including all annexes
- Assessment Report of CHMP or a supplement to the initial assessment report, if issued
- All the documents submitted by the applicant to the EMEA for renewal, including PSURs
- Declaration of the MAH, that at the time of renewal the product is identical with the product marketed in the EU or that it differs only in specified parameters; modifications of SPC, PIL and labelling will be identified
- List of all approved variations in nC-CCC in the period between authorization and the date of renewal submission
- List of all approved variation in this period in EU
- SPC, PIL and Labelling in nC-CCC language
- If there are any specific requirements, they will be publicly announced.

The nCADREAC DRA concerned will inform the EMEA (attention of the Head of Unit EMEA Post-Authorisation Evaluation of Medicines for Human Use) with a copy to the MAH of the outcome of the renewal process as described in Annex 2.

The EMEA will keep the CHMP informed about the outcome of the Renewal application which resulted in a disagreement with or modification of the Commission Decision and, where necessary, will inform the nCADREAC DRA concerned of the CHMP's consideration of the issue (especially in case of disagreement with the Commission Decision).

The nCADREAC DRA concerned will also inform the other nCADREAC DRAs concerned in case of any disagreement or modification of the Commission Decision.

Title VII

RETROSPECTIVE INCLUSION OF EU CENTRALISED MEDICINAL PRODUCTS IN THE COMMON nCADREAC SIMPLIFIED SYSTEM

Initiation of the procedure

The most practical timing of the procedure is at the time of renewal of marketing authorisation of the medicinal product.

The MAH in the nC-CCC evaluates the status of harmonisation of the medicinal product in question and identifies all variations that are necessary to reach harmonisation as described in Title III of the present procedure .
The MAH in the EU notifies the EMEA on the intention to include the product in question in the common nCADREAC simplified system retrospectively and declares that the EMEA and the European Commission may make available to the nCADREAC DRA concerned any information related to the product in question as described in Title III of the present procedure, using the form in Annex 1.

The EMEA sends the overview of all accepted variations related to the product in question to the nCADREAC DRA concerned.

Submission of the application
The MAH in the nC-CCC informs the nCADREAC DRA concerned on the intention to include the product retrospectively in the common nCADREAC simplified system and on the status of harmonisation of the product. He applies for all necessary variations, using the variation procedures described in Title IV of the present procedure and submits all those documents required by the present procedure both for marketing authorisation and for variations and also the final approval documents issued, which have not been already submitted within the national authorisation procedure, however in any case the following will be submitted:

− copy of Approval of Information Sharing beetween the EMEA, the European Commission and the nCADREAC DRA,

− declaration by the MAH in the nC-CCC that he will keep the product in question harmonised in nC-CCC with the EU and, in the case where the marketing authorisation will be suspended or withdrawn in the EU, nCADREAC DRA concerned will be notified immediately as required by the present procedure (chapter Documents to be submitted by the applicant).

Outcome of the procedure
If after processing all of the submitted variations the nCADREAC DRA concerned agrees with the fact, that the product is harmonised with the current EU status, it informs the EMEA using the form in Annex 2, that the product in question can be included in the common nCADREAC simplified system. The copy of this report is sent to the MAH in the nC-CCC and in specific cases mentioned in the present procedure also to other nCADREAC DRAs.
The EMEA includes the product in its database.

Note:

This simplified procedure can be used on a voluntary basis by the nCADREAC DRAs that signed the nCADREAC - as collaborative members.

Annex 1

Text in italics should be replaced by the data specific to individual submissions.

Name of the product:

EU Marketing Authorisation number/s:

Approval of Information Sharing between the EMEA, the European Commission and the *nCADREAC **DRA***

The *Marketing Authorisation Holder in the EU* hereby notifies to the European Medicines Agency - EMEA, 7 Westferry Circus, Canary Wharf, London El4, United Kingdom and the European Commission Directorate-General Enterprise and Industry, Directorate F –Consumer Goods, F2 Pharmaceuticals, Rue de la Loi 200, B-1049 Brussels, Belgium, of the submission of an application for the following medicinal product to the *nCADREAC DRA:*

name of the medicinal product, dosage form, strength, package size/s
(differences in brand name, if any)
proposed marketing authorisation holder
in country of the nCADREAC DRA

The *Marketing Authorisation Holder in the EU* agrees that the EMEA and the European Commission may make available to *the nCADREAC DRA* any information to the quality, safety and efficacy of the above product. The extent of this information shall not exceed that which is made available to EU Member States by the EMEA or European Commission.

The information will be used by *the nCADREAC DRA* in accordance with applicable laws and regulations for the marketing authorisation and safe use of medicinal products in the country of the *nCADREAC DRA.*
This Declaration is made as of the date first written below and remains valid for the period during which the product is authorised in the European Union and the *nCADREAC country* respectively. The copy of this declaration is sent to *DRA of the nCADREAC.*

Date:

Signature of the Marketing Authorisation Holder
First name, family name:
Address:

Annex 2

Text in italics should be replaced by the data specific to individual submissions.

REPORT ON AUTHORISATION GRANTED /VARIATION APPROVAL/RETROSPECTIVE INCLUSION BY THE nCADREAC DRA OF THE MEDICINAL PRODUCT SUBJECTED TO THE CENTRALISED PROCEDURE IN THE EU

Name of the product in the EU, pharmaceutical form/s, strength/s relevant to this report:
INN or common name of the active ingredient/s:
Community MA number/s of the product:
Name of the MA holder in the EU:

☐ **Report on acceptance/renewal of centralised MA***
☐ **Report on disagreement with the Commission Decision on MA****
☐ **Report on refusal of variation, or Commission Decision on variation or the change of data formerly reported to the EMEA****
☐ **Report on retrospective inclusion of the product in the simplified nCADREAC system**
☐ **Report on safety action/defective product****
☐ **Request to the EMEA****

---

*Name of the product in nCADREAC concerned:
National marketing authorisation number/s:
Date of issue of national marketing authorisation decision:
Name of the marketing authorisation holder in nCADREAC country concerned
Authorised dosage forms, strengths, package size in nCADREAC country concerned
Modification of SPC and PIL (specifying differences, except different name of the product, MA holder, national MA number)**:
Modifications of labelling (specifying differences, except different name of the product, MA holder, national MA number)**:

**Explanatory notes:

Enclosures: none

Date: Name and signature of responsible person within the nCADREAC DRA

Annex 3

Table of specific national requirements of nCADREAC DRAs

The information is valid at the time specified in the table. As individual nCADREACs may implement specific changes, it is their responsibility to provide the recent information and to update presented data.

Country	Timing of submission	Expected handling time	Language of dossier	No. of copies to be submitted	Electronic submission	Need of samples and/or substances	Need of local representative	Fees
Bulgaria	After Commission Decision is issued	3 months for MA, 2 months for variation, after receiving the complete documentation	English or Bulgarian languages. Labelling can be in Bulgarian language or English/ Bulgarian languages.	1 copy of the dossier 4 copies of SPC (in Bulgarian language) 4 copies of PIL (in Bulgarian language) 4 copies of labelling (in Bulgarian language)	CD-ROM, together with paper documentation of identical content. Additionally after approval - SPC and PIL (final approved version) in the Bulgarian language on a 3,5 inch floppy diskette using Word for Windows	• 2 samples of the medicinal product presented in the outer packaging • reference substances (if referred to in the testing procedures)	YES	**MA** (original medicinal product): *Bulgarian Drug Agency (BDA) fee*: 402 BGN levs *Ministry of Health (MoH) fee*: 3 800 BGN levs **MA** (original medicinal product – for II, III, IV etc pharmaceutical form): *BDA fee:* 302 BGN levs *MoH fee:* 950 BGN levs **MA** (original medicinal product – for different quantity of active substance (strength)): *BDA fee:* 202 BGN levs *MoH fee:* 420 BGN levs

								(original medicinal product): *Bulgarian Drug Agency (BDA) fee*: 201 BGN levs *Ministry of Health (MoH) fee*: 3040 BGN levs (original medicinal product – for II, III, IV etc pharmaceutical form): *BDA fee:* 151 BGN levs *MoH fee:* 760 BGN levs (original medicinal product – for different quantity of active substance (strength)): *BDA fee:* 101 BGN levs
Croatia	After Commission Decision is issued	5 months for MA, 3 months for variation, after receiving the complete documentation	English, Croatian Labelling in Croatian	English, Croatian Labelling in Croatian	English, Croatian Labelling in Croatian	2 samples + reference substance	yes	MA: - 2.800 € Variations: - type I: 240 € - type II: 900 € Transfer of MA: 240 €

Romania	After Commission Decision is issued	3 months for MA, 2 months for variation, after receiving the complete documentation	English, Romanian Labelling can be in Romanian, English or French	1 copy	Possible submission of the dossier in Word, pdf, rtf, jpg and tiff format, CD-ROM, together with paper documentation of identical content; SPC and PIL (final approved version) in the Romanian language on a 3,5 inch floppy diskette using Word for Windows	• 2 samples of the medicinal product presented in the outer packaging (ready to place on the market)	yes	MA: - new active substance/obtained by biotechnology/biologi-cal products: 2105 € Variations: -type IA: 210 € -type IB: 330 € -type II: 460 € Transfer of MA: 300 €

* In the case of submission before the Commission Decision has been issued, the letter from the EMEA informing the applicant on positive outcome of the validation and on the adopted timetable shall be submitted with the application.
** Pre-submissions before the Commission approval are possible if only the Commission Decision and its annexes are missing. Full application starts when these, together with the details of the possible modifications of the originally submitted documents, are available.

Annex 4

Contact points for regulatory information exchange in nCADREAC DRAs

nCADREAC DRA	NAME AND ADDRESS	CONTACT PERSONS	e-mail/web-site	TELEPHONE NUMBER	FAX NUMBER
Bulgaria	Bulgarian Drug Agency 26, Yanko Sakazov Blvd., 1504 Sofia Bulgaria	Emil Hristov MD Executive director	hristov@bda.bg bda@bda.bg www.bda.bg	(+359 2) 9434046	(+359 2) 9434487
Croatia	**Agencija za lijekove i medicinske proizvode** Ksaverska cesta 4 HR-10000 Zagreb Croatia	Dr. Siniša Tomić Head of Agency	sinisa.tomic@almp.hr almp@almp.hr http://www.almp.hr	++385 1 46 93 830 ext.101	++385 1 46 73 275

Romania	**National Medicines Agency** 48 Aviator Sanatescu Str, 011478 Bucharest, Romania	Magdalena Badulescu –President Rodica Badescu - Vicepresident	m.badulescu@anm.ro rodica.badescu@anm.ro http://www.anm.ro	0040 21 316 10 79	00 40 21 316 34 97