APPLICATION FOR MARKETING AUTHORISATION OF HOMEOPATHIC MEDICINAL PRODUCTS FOR HUMAN USE

SUMMARY OF THE DOSSIER

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APPLICATION FOR MARKETING AUTHORISATION:

ADMINISTRATIVE DATA

The application form is to be used for an application for a marketing authorisation of a medicinal product submitted to the National Medicines Agency under national procedure or new CADREAC simplified registration procedures.

Separate application is submitted for each strength and pharmaceutical form of the medicinal product for human use.

DECLARATION AND SIGNATURE:

Invented name:

Pharmaceutical form:

Homeopathic stock(s) and potency(ies):

Applicant:

Person authorised on behalf of the Applicant for communication* with the National Medicines Agency, during authorisation procedure:

It is hereby confirmed that all existing data which are relevant to the quality, safety and efficacy of the medicinal product have been supplied in the dossier, as appropriate.
It is hereby confirmed that fees will be paid according to the National Medicines Agency rules.
On behalf of the Applicant:

_____
Signature

_____
NAME*

_____
Function

_____
Place Date (year-month-day)

** Note: Please attach letter of authorisation for communication with NMA/signing on behalf of the applicant.*

1. TYPE OF APPLICATION

Note: The following sections should be completed where appropriate..

1.1. THIS APPLICATION CONCERNS:

1.1.1. nCADREAC SIMPLIFIED REGISTRATION PROCEDURE FOR MEDICINAL PRODUCTS FOR HUMAN USE AUTHORISED IN THE EU UNDER MUTUAL RECOGNITION PROCEDURE

❍ **YES** ❍ **NO**

- Reference Member State:
- Date of authorisation: (year-month-day):
- Marketing authorisation number:
  (please provide copy of the authorisation – see Section 5.2)

- Member State(s)/Concerned Member State(s):

AT	☐	BE	☐	CY	☐	CZ	☐	DE	☐	DK	☐	EE	☐	EL	☐
ES	☐	FI	☐	FR	☐	HU	☐	IE	☐	IS	☐	IT	☐	LI	☐
LT	☐	LU	☐	LV	☐	MT	☐	NL	☐	NO	☐	PL	☐	PT	☐
SE	☐	SI	☐	SK	☐	UK	☐								

❍ **1.1.2. NAtIONAL PROCEDURE**

❍ YES ❍ NO

- Please specify If a waiver or amendment of PSUR-cycle is applied for, to harmonise with a substance birthdate:

1.2. THIS IS AN APPLICATION FOR VARIATION TO A MARKETING AUTHORISATION IN PLACE WITH REFERENCE TO ANNEX III OF ORDER OF THE MINISTER OF HEALTH NO. 89/02.02.2004, WHERE APPLICABLE

❍ **YES** *(please complete the section below and Section 1.3.)*

❍ **NO** (*please complete Section 1.3 only)*

Please give:

☐ Qualitative change in declared active substance not defined as a new active substance
❍ Replacement by a different salt/ester, complex/derivative (same therapeutic moiety)
❍ Replacement by a different isomer, mixture of isomers, of a mixture by an isolated isomer

❍ Replacement of a biological substance or product of biotechnology
❍ New ligand or coupling mechanism for a radiopharmaceutical
❍ Change to the extraction solvent or the radio of herbal drug to herbal drug

☐ Change of bioavailability
☐ Change of pharmacokinetics
☐ Change or addition of a new strength / potency
☐ Change or addition of a new pharmaceutical form
☐ Change or addition of a new route of administration

Note:
The applicant of the present application must be the same as the marketing authorisation holder of the existing marketing authorisation
This section should be completed without prejudice to the provisions of Articles 702 (1) and (4), 704 (1), 708 (1) and (7) and 726 of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product

● **For existing marketing authorisation in the Community / Member State where the application is made:**
- Name of the marketing authorisation holder:
- Name, strength, pharmaceutical form of the existing product:
- Marketing authorisation number:

1.3. APPLICATION FOR MARKETING AUTHORISATION SUBMITTED UNDER THE FOLLOWING ARTICLES OF LAW NO. 95/2006 ON HEALTHCARE REFORM, TITLE XVII, THE MEDICINAL PRODUCT

Note: Section to be completed for any application, including applications referred to in Section 1.3

❍**1**.3.1 Article 711 of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product (simplified registration procedure)

❍**1**.3.2 Article 713 of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product (marketing authorisation procedure)

1.4 Administrative data/dossier requirements

Article 711 - Simplified registration procedure

Part of the dossier	Submitted in the Application dossier	
Module 1	❍	
Manufacturing license	❍	
Mock ups of outer and immediate packaging and of package leaflet	❍	
Module 2	❍	
Module 3	❍	
Module 4	❍	
Justification of the homeopathic nature	❍	

Article 713 – Marketing authorisation procedure

Part of the dossier	Submitted in the Application dossier	
Module 1	❍	
Manufacturing license	❍	
SPC in National language	❍	
Package leaflet in National language	❍	
Mock ups of outer and immediate packaging and of package leaflet	❍	
Module 2	❍	
Module 3	❍	
Module 4	❍	
Justification of the homeopathic nature	❍	

2. MARKETING AUTHORISATION/REGISTRATION APPLICATION PARTICULARS

2.1. Name (s)

2.1.1 Name of the homeopathic medicinal product

☐ If different (invented) names in different Member States are proposed in a mutual recognition, these are to be listed in Annex 4.18

2.1.2 Name of the Homeopathic stock(s) and potencies[1]

[1] *The following order of priority should be used: Scientific name of the European Pharmacopoeia or National Pharmacopoeia or, in absence of a monograph, a Scientific Latin name (botanical scientific name) followed by the Homeopathic(s) name(s).*

2.2. Pharmaceutical form, route of administration, container and pack size(s)

2.2.1 Pharmaceutical form (please use current list of standard terms according to European Pharmacopoeia)

2.2.2 Route(s) of administration (use current list of standard terms according to European Pharmacopoeia)

2.2.3 Container, closure and administration device(s), including description of material from which it is constructed (use current list of standard terms according to European Pharmacopoeia)

For each type of pack give:

2.2.3.1 Pack size(s):

Note: For mutual recognition and decentralised procedures, all package sizes authorised in the Reference Member should be listed

2.2.3.2 Proposed shelf life:

2.2.3.3 Proposed shelf life (after first opening container):

2.2.3.4 Proposed shelf life (after reconstitution or dilution):

2.2.3.5 Proposed storage conditions:

2.2.3.6 Proposed storage conditions after first opening container:

☐ Please attach list of mock-ups or samples/specimens sent with the application, as appropriate (please refer to Notice to Applicants, Volume 2A, Chapter 7) (4.17)

2.3 Legal status

2.3.1 Proposed dispensing/classification

(Under Article 695 (19) of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product)

❍ Subject to medical prescription

❍ Not subject to medical prescription

2.3.2 For products subject to medical prescription:

☐ Product on prescription which **may be** renewed (if applicable)
☐ Product on prescription which **may not be** renewed (if applicable)
☐ Product on **special** prescription*****
☐ Product on **restricted** prescription*****

Applicants are invited to indicate which categories they are requesting, however, the NMA reserve the right to apply only those categories provided for in Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product

**Note: for further information please refer to Article 781 of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product*

2.3.3 Supply for products not subject to medical prescription:

❍ Supply through pharmacies only

❍ Supply through non-pharmacy outlets and pharmacies(if applicable)

2.3.4 Promotion for products not subject to medical prescription:

❍ Promotion to health care professionals only

❍ Promotion to the general public and health care professionals

2.4. Marketing authorisation holder/Person de contact/Company

2.4.1 Proposed marketing authorisation holder/person legally responsible for placing the product on the market in Romania

(Company) Name:
Address:
Country:
Telephone:
Telefax:
E-Mail:
Contact person at this address
☐ Please attach proof of establishment of the applicant in Romania or The European Economic Area (EEA) (Annex 4.3)

2.4.2 Person/Company authorised for communication with the National Medicines Agency during authorisation procedure in Romania:

Name:
Company name:
Address:
Country:
Telephone:
Telefax:
E-Mail:

☐ If different from 2.4.1 above, please attach letter of authorisation (Annex 4.4)

2.4.3 Person/Company authorised for communication between the marketing authorisation holder and the National Medicines Agency, after authorisation in Romania, if different from Person/Company under 2.4.2

Name:
Company name:
Address:
Country:
Telephone:
Telefax:
E-Mail:

☐ If different from 2.4.1 above, , please attach letter of authorisation (Annex 4.4)

2.4.4 Qualified person in Romania for Pharmacovigilance

Name:
Company name:
Address:
Country:
24 H Telephone:
Telefax:
E-Mail:

☐ Please provide C.V. of qualified person (Annex 4.5)

2.5 Manufacturers

2.5.1 Authorised manufacturer(s) (or importer) responsible for batch release in Romania in accordance with Articles 748 and 760 of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product **(**as shown in the package leaflet and where applicable in the labelling):

Company name:
Address:
Country:
Telephone:
Telefax:
E-Mail:

▪ Manufacturing Authorisation number:

- ☐ Attach copy of manufacturing authorisation(s)(Annex 4.6)
- ☐ Attach justification if more than one manufacturer responsible for batch release is proposed with eliberarea seriilor produsului (Annex 4.7)

2.5.1.1 Batch control/Testing arrangements

Site(s) in EEA or in countries with MRA/another agreement in operation, where batch control/testing takes place (if different from 2.5.1):

Company name:
Address:
Country:
Telephone:
Telefax:
E-Mail:

2.5.2 Manufacturer(s) of the homeopathic medicinal product and Site(s) of manufacture

(Note: Please give including manufacturing sites of any diluent/solvent presented in a separate container but forming part of the Homeopathic medicinal product):

Name:
Company name:
Address:
Country:
Telephone:
Telefax:
E-Mail:
Please provide brief description of functions performed by manufacturer of dosage form/assembler etc.:

☐ Please attach flow-chart indicating the sequence of the different sites involved in the manufacturing process (Annex 4.8)

- <u>If the manufacturing site is in the EEA</u>:
  - Manufacturing Authorisation number

(under Article 748 of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product):
☐ Please attach copy of manufacturing authorisation (s) (Annex 4.6)

- Name of qualified person
  (if not mentioned in manufacturing authorisation)

- <u>If the manufacturing site is outside the EEA</u>:
  - ☐ Where MRA/another community agreement is in operation, attach equivalent of manufacturing authorisation (Annex 4.6)

  - The site has been inspected for GMP Compliance by an EEA authority or by an authority of countries where mutual recognition agreement /another community agreement is in operation

❍ YES ❍ NO

☐ If YES, please provide in Annex 4.9, for each site, a statement from the competent authority which carried out the inspection, including:

- Last GMP inspection date
- Name of competent authority which carried out the inspection
- Type of inspection (pre/post-authorisation/special/re-inspection)
- Category of products and activities inspected
- Outcome: GMP compliant : ❍ NO ❍ YES

2.5.3 Manufacturer (s) of the dilutions and Site(s) of manufacture

(Note: If different from manufacturer of the finished homeopathic medicinal product):

Name:
Company name:
Address:
Country:
Telephone:
Telefax:
E-Mail:

Please provide brief description of functions performed by manufacturer of dosage form/assembler etc.:

☐ Please attach flow-chart indicating the sequence of the different sites involved in the manufacturing process (Annex 4.8)

• If the manufacturing site is in the EEA:

- Manufacturing Authorisation number
(under Article 748 of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product):
☐ Please attach copy of manufacturing authorisation (s) (Annex 4.6)

- Name of qualified person:
(if not mentioned in manufacturing authorisation)

• If the manufacturing site is outside the EEA:

- ☐ Where MRA/another community agreement is in operation, attach equivalent of manufacturing authorisation (Annex 4.6)

- The site has been inspected for GMP Compliance by an EEA authority or by an authority of countries where MRA/another community agreement is in operation

❍ YES ❍ NO

☐ If YES, please provide in Annex 4.9, for each site, a statement from the competent authority which carried out the inspection, including:

- Last GMP inspection date
- name of competent authority which carried out the inspection
- type of inspection (pre/post-authorisation/special/re-inspection)
- category of products and activities inspected
- outcome: GMP compliant: ❍ YES ❍ NO

2.5.4 Manufacturer(s) of the Homeopathic stock(s):
Note: Only the final manufacturer(s) to be mentioned

Substance:
Name:
Address:
Country:
Telephone:
Telefax:
E-Mail:

• A European Phaemacopoea Certificate of suitability has been issued for the active substance(s)
❍ YES ❍ NO

If YES, please specify:
- Substance:
- Name of the manufacturer:
- Reference number:
- Date of last update (*yyyy-mm-dd*):
☐ Please provide copy in Annex 4.10

• There is a European Drug Master File to be used for the active substance(s) reference/original
❍ YES ❍ NO

If YES, please specify:
- Substance:
- Name of the manufacturer:
- Reference number for EMEA/competent authority:
- Date of submission (*yyyy-mm-dd*):
- Date of last update (*yyyy-mm-dd*):
- ☐ Please attach letter of access for Community/Member State authorities where the application is made (please refer to European DMF procedure for active substance) (Annex 4.10)
- ☐ Please attach copy of written confirmation from the manufacturer of the active substance to inform the applicant in case of modification of the manufacturing process or specifications according to Article Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product. (Annex 4.11)

Where an active substance manufacturer has been inspected by an EEA Country

☐ *The following information is provided in Annex 4.9 for each manufacture site*
- *Last inspection date by an EEA country (year-month-day*)
- *Name of competent authority which carried out the inspection*
- *Type of inspection (pre/post-authorisation/special/re-inspection)*
- *Categories of substance and activities inspected*
- *Outcome:* ❍*Positive* ❍*Negative*

2.5.5 Source/manufacturer(s) of the raw material(s):

Raw material:
Name:
Address:
Country:
Telephone:
Telefax:
E-Mail:

- A European Pharmacopoeia Certificate of suitability has been issued for the raw material(s)
  ❍ YES ❍ NO

If YES, please specify:
- Raw material:
- Name of the manufacturer:
- Reference number:
- Date of last update (*yyyy-mm-dd*):

☐ Please provide copy in Annex 4.10

Where an active substance manufacturer has been inspected by an EEA Country

☐ *The following information is provided in Annex 4.9 for each manufacture site*
- *Last inspection date by an EEA country (yyyy-mm-dd)*
- *Name of competent authority which carried out the inspection*
- *Type of inspection (pre/post-authorisation/special/re-inspection)*
- *Categories of substance and activities inspected*
- *Outcome:* ❍*Positive* ❍*Negative*

2.6 Qualitative and quantitative composition

2.6.1 Qualitative and quantitative composition in terms of the homeopathic active substance(s) and the excipient(s):

A note should be given as to which quantity the composition refers (e.g. 1 capsule)
List the homeopathic active substance(s) separately from the excipient(s).

Name of homeopathic active substance(s)*	Quantity	Unit	Reference/ Monograph standard
1.			
2.			
3.			
etc.			

Name of excipient (s)	Quantity	Unit	Reference/Standard Monograph**
1.			
2.			
3.			etc.

*Note: *The following order of priority should be used: Scientific Latin name of the European Pharmacopoeia or of the Romanian Pharmacopoeia or , in absence of a monograph, a scientific Latin name (botanical scientific name...) followed by the Homeopathic name*

*** Only one name for each substance should be given in the following order of priority: INN, European Pharmacopoeia, the Romanian Pharmacopoeia, Common name, scientific name*

2.6.2 List of materials of animal and/or human origin contained or used in the manufacturing process of the homeopathic medicinal product

NONE ☐

Name	Function* HSA	EX	R	Animal origin susceptible to TSE**	Other animal origin	Human origin	Certificate of suitability for EST (state nr.)
1.	❍	❍	❍	❍	❍	❍	❍
2.	❍	❍	❍	❍	❍	❍	❍
3.	❍	❍	❍	❍	❍	❍	❍
4.	❍	❍	❍	❍	❍	❍	❍ etc.

* HAS= homeopathic active substance; EX=excipient (including starting materials used in the manufacture of the active substance/excipient) R=reagent/culture medium (including those used in the preparation of master and working cell banks)

** EST= transmissible spongiform encephalopathy

☐ If a European Pharmacopoeia Certificate of Suitability for TSE is available according to Article Resolution AP/CSP (99)4 of the Council of Europe, please attach in Annex 4.12

3 OTHER MARKETING AUTHORISATION APPLICATIONS

3.1 <u>FOR NATIONAL APPLICATIONS ONLY, PLEASE COMPLETE THE SECTION BELOW, UNDER ARTICLE 702, m)-o) OF LAW NO. 95/2006 ON HEALTHCARE REFORM, TITLE XVII, THE MEDICINAL PRODUCT</u>:

3.1.1 There is/are other Member State(s) where an application for the same* product is pending:

❍YES ❍NO

If YES, please complete Section 3.2.

3.1.2 There is/are other Member State(s) where an authorisation/registration is granted for the same medicinal product*:

❍YES ❍ NO

If YES, please complete Section 3.2 and provide copy.

There are differences which have therapeutic implications between this application and the applications/authorisations for the same product in other Member States (for national applications, under Article 722 and 723 of Law no.95/2006 on healthcare reform, Title XVII, The Medicinal Product).

❍YES ❍NO

If YES, please give:

3.1.3 There is another Member State(s) where an authorisation/registration has been refused/suspended/ revoked by competent authorities for the same* product

❍YES ❍NO

If YES, please complete Section 3.2

**Note: 'same product' means same qualitative and quantitative composition in active substance(s) and having the same pharmaceutical form from applications belonging to the same mother company or group of companies OR which are 'licensees'.*

3.2. Marketing authorisation/registration applications for the same homeopathic medicinal product in the EEA (*('same product' means same qualitative and quantitative composition in active substance(s)and having the same pharmaceutical form from applications belonging to the same mother company or group of companies OR which are 'licensees'.)*

Note: Please refer to Commission Communication 98/C229/03

☐ Countries which have authorised the medicinal product

Country:
Date of authorisation (*yyyy-mm-dd*):
Invented name:
Authorisation number:

☐ Please attach copy of marketing authorisation/registration (Annex 4.15)

☐ Countries in which authorisation of the medicinal product is pending

Country:
Date of submission (*yyyy-mm-dd*):

☐ Countries in which authorisation of the medicinal product has been refused

Country:
Date of refusal (*yyyy-mm-dd*):

☐ Countries in which authorisation of the medicinal product has been withdrawn (by the Applicant before authorisation)

Country:
Date of withdrawal (*yyyy-mm-dd*):
Invented name:
Reason for withdrawal:

☐ Countries in which authorisation of the medicinal product has been withdrawn (by the Applicant after authorisation)

Country:
Date of withdrawal (*yyyy-mm-dd*):
Authorisation number:
Invented name:
Reason for withdrawal:

☐ Countries whose competent authorities have suspended /revoked authorisation of the medicinal product

Country:
Date of suspension/revocation (*yyyy-mm-dd*):
Reason for suspension/revocation:
Invented name:

3.3 For multiple applications of the same homeopathic medicinal product:

Multiple applications for:
Name of the other product(s):
Date of submission (*yyyy-mm-dd*):
Applicant(S):

3.4. Marketing authorisation/registration applications for the same homeopathic medicinal product, outside the EEA (i.e. from applicants belonging to the same mother company or group of companies OR which are "licensees".)

Note: Please refer to Commission Communication 98/C229/03

☐ Countries which have authorised the medicinal product

Country:
Date of authorisation (*yyyy-mm-dd*):
Invented name:
Authorisation number:

☐ Countries in which authorisation of the medicinal product is pending

Country:
Date of submission (*yyyy-mm-dd*):

☐ Countries in which authorisation of the medicinal product has been refused

Country:
Date of refusal (*yyyy-mm-dd*):

☐ Countries in which authorisation of the medicinal product has been withdrawn (by the Applicant before authorisation)

Country:
Date of withdrawal (*yyyy-mm-dd*):
Invented name:
Reason for withdrawal:

☐ Countries in which authorisation of the medicinal product has been withdrawn (by the Applicant after authorisation)

Country:
Date of withdrawal (*yyyy-mm-dd)*
Authorisation number:
Invented name:
Reason for withdrawal:

☐ Countries whose competent authorities have suspended /revoked authorisation of the medicinal product

Country:
Date of suspension/revocation (*yyyy-mm-dd*):
Reason for suspension/revocation:
Invented name:

4. ANNEXED DOCUMENTS (WHERE APPLICABLE)

☐ **4.1** Proof of payment

☐ **4.2** Consent of the Marketing Authorisation Holder for the reference medicinal product who allows an applicant to make use of the pharmaceutical, preclinical and clinical documentation contained in the file on the medicinal product, with a view to examining subsequent applications (for informed consent marketing authorisation applications)

☐ **4.3** Proof of establishment of the applicant in the EEA

☐ **4.4** Letter of authorisation for communication on behalf of the applicant/marketing authorisation holder

☐ **4.5** Curriculum Vitae of the Qualified Person for Pharmacovigilance

☐ **4.6** Manufacturing Authorisation required under Article Article 748 of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product (or equivalent, outside of the EEA where MRA or other Community arrangements apply). A reference to EudraGMP will suffice when available.

☐ **4.7** Justification for more than one manufacturer responsible for batch release in the EEA

☐ **4.8** Flow-chart indicating all sites involved in the manufacturing process of the medicinal product or active substance (including sites involved in sampling and testing for batch release of products manufactured in third countries). ALL manufacturing and control sites mentioned throughout the whole dossier MUST be consistent regarding their names, detailed addresses and activities.

☐ **4.9** Statement (or GMP Certificate issued by an EEA inspectorate, when available) from the competent authority which carried out the inspection of the manufacturing site(s)/(not older than 3 years). References to EudraGMP will suffice when available. Where applicable a summary of other GMP inspections performed in the last 2 years.

☐ **4.10** Letter(s) of access to Active Substance Master File(s) or copy of European Pharmacopoeia Certificate(s) of suitability

☐ **4.11** Copy of written confirmation from the manufacturer of the active substance to inform the applicant in case of modification of the manufacturing process or specifications according to Annex I to order of the ministry of health on approval of ”Analytical, pharmacotoxicological and clinical norms and protocols in respect of the testing of medicinal products” (transposing Annex I of Directive 2001/83)

☐ 4**.12** European Pharmacopoeia Certificate(s) of suitability for TSE

☐ **4.13** Written consent(s) of the competent authorities regarding genetically modified organisms release in the environment

☐ **4.14** Scientific advice given by CHMP.

☐ **4.15** Copy(ies) of Marketing Authorization(s) granted in an EEA country or third country under Article 702, m)-o) of Law no. 95/2006 on healthcare reform, Title XVII, The Medicinal Product and the equivalent in third countries on request (photocopies of the pages which give the Marketing authorisation number, Date of authorisation and pages which have been signed by the competent authorities).

☐ **4.16** Correspondence with European Commission regarding multiple applications.

☐ **4.17** List of Mock-ups or Samples/specimens sent with the application, as appropriate.

☐ **4.18** List of proposed (invented) names and marketing authorisation holders in the concerned member states.

☐ **4.19** Copy of EMEA certificate for a Vaccine Antigen Master File (VAMF)

☐ **4.20** Copy of EMEA certificate for Plasma Master File (PMF)

☐ **4.21** For each active substance, attach a declaration from the Qualified Person of the manufacturing authorisation holder authorisation holder of each of the manufacturing authorisation holders (i.e. located in EEA listed in Section 2.5.2 where the active substance is used as a starting material that the active substance manufacturer(s) referred to in Section 2.5.3 operate in compliance with the detailed guidelines on good manufacturing practice for starting materials. This does not apply to Blood or blood components