Application form

For consultation by a notified body on an ancillary medicinal substance used in a medical device

Application form

This application form is to be used for an application for a **scientific opinion** on an ancillary medicinal substance used in a medical device submitted to AIFA in accordance with Regulation (EU) 2017/745.

A combined form is acceptable for a range of strengths/concentrations of an ancillary medicinal substance in a medical device/range of medical devices (e.g. different strengths) and for a range of similar devices (e.g. a range of catheters made of the same material) incorporating the same medicinal substance from the same manufacturer (give information successively, where appropriate).

Evaluation for class III MD III according to Annex IX chapters I, II, III to:	
Consultation procedure for certification / renewal of certification	☐
Supplementary Consultation	☐

Name of medical device(s):
Description of the medical device:
Ancillary medicinal substance(s):
Strength/concentration of ancillary medicinal substance(s):
Presentation(s) of ancillary medicinal substance(s) as part of the medical device:
appointed person by ON management
Notified Body Director

This section is reserved to the ON

It is hereby confirmed that the Notified Body (NB) has verified the usefulness of the ancillary medicinal substance(s) as part of the medical device(s) and provided an assessment report on this verification and that all existing data which are relevant to the quality and safety of the ancillary medicinal substance(s) including the clinical/benefit risk profile have been supplied in the dossier.
It is hereby confirmed that fees will be paid according to the AIFA rules.

Medical Device previously classified according to rule 13, annex IX of directive 93/42 / EEC *give a reason in case of negative answer*	Yes	No
	☐	☐
For the medical device previously classified according to the rule 13, annex IX of directive 93/42 / EEC, indicate any changes made to the technical documentation (in line with the MCDG 2020-12 Guideline):		
to the ancillary medicinal substance	Yes	No

in case of positive answer indicate the modification and the section of the reference technical documentation	☐	☐
To the manufacturing process	Yes	No
in case of positive answer indicate the modification and the section of the reference technical documentation	☐	☐i
the way the substance is incorporated into the device	Yes	No
in case of positive answer indicate the modification and the section of the reference technical documentation	☐	☐
to design, manufacturing of the device which could influence the quality, safety or usefulness of the ancillary substance, *in case of positive answer indicate the modification and the section of the reference technical documentation*	Yes ☐	No ☐
changes in the documentation of the device due to the new MDR requirements, for example in clinical evaluation, which have a bearing on the quality, safety usefulness of the ancillary substance. *in case of positive answer indicate the modification and the section of the reference technical documentation*	Yes ☐	No ☐
changes in the assessment of the device	Yes	No
in case of positive answer indicate the modification and the section of the reference technical ocumentation	☐	☐

any administrative changes related to	Yes	No
in case of positive answer indicate the modification and the section of the reference technical documentation	☐	☐
names or addresses	Yes	No
in case of positive answer indicate the modification and the section of the reference technical documentation	☐	☐
documents layout	Yes	No
in case of positive answer indicate the modification and the section of the reference technical documentation	☐	☐
other	Yes	No
please specify	☐	☐

Has the medical device been evaluated by another Competent Authority? *In case of positive answer, specify:*	Yes	No
	☐	☐
Name		
Country		
City		
Also attach:		
1. A declaration from the manufacturer stating that the medical device has been previously evaluated by another competent authority and that no changes have been made		
2. The assessment report of the previous competent authority		
Possible notes		

Declaration and signature

Name of medical device(s):	<Name>
Ancillary medicinal substance(s):	<Ancillary>
Strength/concentration of ancillary medicinal substance(s):	<Strength/concentration>
Presentation(s) of ancillary medicinal substance(s) as part of the medical device:	<Presentation(s)>
Notified body:	<Name>
Person authorised for communication on behalf of the notified body:	<Name>
Medical device manufacturer:	<Medical device manufacturer>

It is hereby confirmed that the notified body (NB) has verified the usefulness of the ancillary medicinal substance(s) as part of the medical device(s) and provided an assessment report on this verification and that all existing data which are relevant to the quality and safety of the ancillary medicinal substance(s) including the clinical/benefit risk profile have been supplied in the dossier.

It is hereby confirmed that the notified body submits this application in the context of an assessment of conformity of the above referred medical device upon request of the medical device manufacturer.

It is hereby confirmed that the notified body shall pay directly to AIFA the fees for this procedure according to the AIFA rules.

On behalf of the notified body:

_____

Signature(s)

Name: <Name>

Function: <Function>

Place and date <Place> <DD-MM-YYYY>

Table of contents

1. Type of application

This application concerns

☐ **Initial consultation** on an ancillary medicinal substance (i.e. in case of a medical device containing the ancillary medicinal substance that has not been yet evaluated by AIFA).

☐ Initial consultation on a known **ancillary medicinal substance** from a **known source** (i.e. where the medicinal substance has been evaluated by the AIFA **in connection with a previous marketing authorisation and/or a previous successful notified body consultation**).

Previous authorisation/consultation

☐ Consultation on a medical device incorporating an ancillary medicinal substance (give details in 3.1).

2. Application particulars

2.1. Description of the ancillary medicinal substance

2.2. Does this application involve more than one ancillary medicinal substance?

☐ Yes ☐ No

If yes, indicate the number of different medicinal products containing the ancillary medicinal substances used in the manufacture of the medical device: <Number>

2.2.1. Name of the medicinal product(s) containing the ancillary medicinal substance(s)

Insert 'not applicable' if this application only concerns an active substance used as ancillary medicinal substance.

<N/A>

<Name of the medicinal product(s)>

2.2.2. Name of the ancillary medicinal substance(s)

<Name>

Note: Only one name should be given for each substance in the following order of priority: INN[*1], Ph.Eur., National Pharmacopoeia, common name, scientific name.

2.2.3. Intended purpose of the ancillary medicinal substance(s) in the medical device

<Text>

2.3. Description of the medical device

Does this application involve more than one medical device?

☐ Yes ☐ No

If yes, indicate the number of different medical devices: <Number>

[1] The active substance should be declared by its recommended INN, accompanied by its salt or hydrate form if relevant.

2.3.1. Proposed (trade) name of the medical device(s)/range of medical device(s) in the Community/Iceland/Liechtenstein/Norway

<Name>

If different (trade) names are proposed, these should be listed below:

Member State	Name	Serial number (if available)

2.3.2. Proposed (trade) name of every medical device

<Text>

2.3.3. Short description of the medical device/range of medical device(s)

<Text>

2.3.4. Intended purpose of the medical device/range of medical devices(s)

<Text>

2.3.5. Route of administration[2]

<Text>

2.3.6. Strength/concentration and presentation(s) of the ancillary medicinal substance

Strength/concentration: <Text>

Presentation(s): <Text>

[2] Use current list of standard terms – European Pharmacopoeia where applicable.

2.3.7. Packaging components of the medical device/range of medical devices, including description of material from which it is constructed[3]

For each medical device and type of pack give:

2.3.7.1. Package size(s)

<Text>

2.3.7.2. Proposed shelf life (unopened)

<Text>

2.3.7.3. Proposed shelf life (in use)

<Text>

2.3.7.4. Proposed storage conditions

<Text>

2.4. Notified body, contact person, medical device manufacturer

2.4.1. Notified body

Name of notified body:	<Name>
Contact person:	<Contact person>
Address:	<Address>
	<Address 2>
Country:	<Country>
Telephone:	<+XX XX XXXX XXXX>
E-mail:	<E-mail address>

2.4.2. Person/company authorised for communication on behalf of the notified body during the AIFA consultation procedure

Name of contact*:	<Contact person>
Address:	<Address>
Address 2:	<Address 2>
Country:	<Country>
Telephone:	<+XX XX XXXX XXXX>
E-mail:	<E-mail address>

*☐ If different to 2.3.1 above, attach letter of authorisation (Annex 4.1)

[3] Use current list of standard terms - European Pharmacopoeia where applicable.

2.4.3. Medical device manufacturer

Name:	<Name>
Address:	<Address>
Address 2:	<Address 2>
Country:	<Country>
Telephone:	<+XX XX XXXX XXXX>
E-mail:	<E-mail address>

2.5. Manufacturers

2.5.1. Manufacturers of the ancillary medicinal substance (s)

For medicinal products used as ancillary medicinal substance complete Section 2.4.1.1 to 2.4.1.3.
For active substances used as ancillary medicinal substance complete ONLY Section 2.4.1.1a) and b) and 2.4.1.3.

2.5.1.1. a) Authorised manufacturer(s) (or importer) responsible for batch release in the EEA in accordance with Article 40 and Article 51 of Directive 2001/83/EC as amended

Section to be copied if more than one manufacturing site applies.

Name:	<Name>
Address:	<Address>
	<Address 2>
Country:	<Country>
Telephone:	<+XX XX XXXX XXXX>
E-mail:	<E-mail address>

Manufacturing Authorisation number: <Number>
☐ Attach copy of manufacturing authorisation(s) (Annex 4.2)
Or
☐ Enter EudraGMP manufacturing authorisation reference: <Ref>

If available:
☐ Attach latest GMP certificate (Annex 4.4)
Or
☐ Enter EudraGMP certificate reference number: <Number>

2.5.1.1.1. Contact person in the European economic area (EEA) for product defects and recalls

For previously centrally authorised medicinal products only.

Name:	<Name>
Address	<Address>
	<Address 2>
Country:	<Country>
24H contact number:	<+XX XX XXXX XXXX>
E-mail:	<E-mail address>

2.5.1.1.2. Batch control/testing arrangements

Site(s) in the EEA or in countries where a mutual recognition agreements (MRA) or other community arrangements apply, where batch control/testing takes place as required by Article 51 of Directive 2001/83/EC

Company name:	<Name>
Address:	<Address>
	<Address 2>
Country:	<Country>
Telephone:	<+XX XX XXXX XXXX>
E-Mail:	<E-mail address>

Brief description of control test carried out by the laboratory(ies) concerned:
<Description>

☐ Attach copy of manufacturing authorisation(s) or other proof of GMP compliance (Annex 4.2)
Or
☐ Enter EudraGMP manufacturing authorisation reference: <Ref>

2.5.1.2. Manufacturer(s) of the ancillary medicinal product and site(s) of manufacture

Include manufacturing sites of any diluent/solvent presented in a separate container but forming part of the ancillary medicinal product, quality control / in-process testing sites, and importer(s).

Company name:	<Name>
Address:	<Address>
	<Address 2>
Country:	<Country>
Telephone:	<+XX XX XXXX XXXX>
E-mail:	<E-mail address>

Brief description of functions performed:
<Description>

☐ Attach flow-chart indicating the sequence and activities of the different sites involved in the manufacturing process, including testing sites (Annex 4.3)

- Site is in the EEA
  - Manufacturing authorisation number: <Number>

  ☐ Attach manufacturing authorisations (Annex 4.2)
  Or
  Enter EudraGMP manufacturing authorisation reference: <Ref>

  If available:
  ☐ Attach latest GMP certificate (Annex 4.4)
  Or
  ☐ Enter EudraGMP certificate reference number: <Number>

  - Name of qualified person: <Name>

  (If not mentioned in manufacturing authorisation)

- Site is outside the EEA

  ☐ Attach equivalent of manufacturing authorisation in accordance with Article 8(k) of Directive 2001/83/EC (Annex 4.2)

  - Has the site been inspected for GMP Compliance by an EEA authority or by an authority of countries where MRA or other Community arrangements apply within the terms of the agreement?
    ❍ No ❍ Yes

  If yes, please provide in Annex 4.4:
  ☐ A statement less than 3 years old from the competent authority which carried out the inspection,
  Or
  If available:
  ☐ Attach latest GMP certificate (Annex 4.4)
  Or
  ☐ Enter EudraGMP certificate reference number: <Number>

  - Has the site been inspected for GMP Compliance by any other authority (including those of countries where MRA or other Community arrangements apply but not within the respective territory)?
    ❍ No ❍ Yes

  ☐ If yes, please provide summary information in Annex 4.4 (and, if available a GMP certificate or a statement from the competent authority which carried out the inspection).

2.5.1.3. Manufacturer(s) of the ancillary active substance(s) and site(s) of manufacture

All manufacturing sites involved in the manufacturing process of each source of active substance, including quality control / in-process testing sites, should be listed. Brokers or supplier details alone are not acceptable. For biotech products include all sites of storage of master and working cell bank and preparation of working cell banks.

Active substance:	<Name active substance>
Company name:	<Name>
Address:	<Address>
	<Address 2>
Country:	<Country>

Telephone: <+XX XX XXXX XXXX>
E-mail: <E-mail address>
Brief description of manufacturing steps performed by manufacturing site:
<Description>

☐ Attach flow-chart indicating the sequence and activities of the different sites involved in the manufacturing process, including batch control sites (Annex 4.3)

☐ For each ancillary active substance, attach a qualified person declaration that the ancillary active substance is manufactured in compliance with the detailed guidelines on good manufacturing practice for starting materials (annex 4.9)

- Has the site been inspected for GMP Compliance by an EEA authority or by an authority of countries where MRA or other Community arrangements apply within the terms of the agreement?
  ❍ No ❍ Yes

If yes, please provide in Annex 4.4:
☐ A statement less than 3 years old from the competent authority which carried out the inspection,
Or
If available:
☐ Attach latest GMP certificate (Annex 4.4)
Or
☐ Enter EudraGMP certificate reference number: <Number>

- Has the site been inspected for GMP compliance by any other authority (including those of countries where MRA or other community arrangements apply but not within the respective territory)?
  ❍ No ❍ Yes

☐ If yes, please provide summary information in Annex 4.4 (and, if available a GMP certificate or a statement from the competent authority which carried out the inspection).

- Has a Ph.Eur. certificate of suitability been issued for the active substance(s):
  ❍ No ❍ Yes ☐ Provide copy in Annex 4.5

If yes:
- substance: <Substance>
- name of the manufacturer: <Name>
- reference number: <Ref. number>
- date of last update: <YYYY-MM-DD>

- Is an Active Substance Master File (European Drug master File) to be used for the active substance(s) reference/original?
  ❍ No ❍ Yes

If yes:
- substance: <Substance>
- name of the manufacturer: <Name>
- reference number for AIFA/ competent authority: <Ref. number> <Competent authority>
- date of submission: <YYYY-MM-DD>
- date of last update: <YYYY-MM-DD>
- ☐ attach letter of access for Community/Member State authorities where the application is made (see "European ASMF procedure for active ingredients") (Annex 4.5)
- ☐ attach copy of written confirmation from the manufacturer of the ancillary active substance to inform the Notified Body in case of modification of the manufacturing process or specifications according to Annex I of Directive 2001/83/EC (Annex 4.6)

2.5.1.4. If applicable, contract companies used for clinical trial(s) bioavailability or bioequivalence or used for the validation of ancillary medicinal substance manufacturing processes

For each contract company, state where analytical tests are performed and where clinical data are collected and give:

Title of the study: <Title>
Protocol code: <Code>
EudraCT number: <Number>
Name of the company: <Name>
Address: <Address>
Address 2: <Address 2>
Country: <Country>
Telephone: <+XX XX XXXX XXXX>
E-mail: <E-mail address>
Duty performed according to contract:

2.5.2. Manufacturer of medical device/range of medical devices*

Name of company: <Name>
Address: <Address>
Address 2: <Address 2>
Country: <Country>
Telephone: <+XX XX XXXX XXXX>
E-mail: <E-mail address>

* Relevant to the incorporation of the ancillary medicinal substance in the medical device.

2.6. Information on the medicinal product(s) containing ancillary medicinal substance(s)

2.6.1. Qualitative and quantitative composition of the medicinal product containing ancillary medicinal substance(s)

The medicinal product contains:

Name of ancillary medicinal substance(s)[4]	**Quality**	**Unit**	**Reference/monograph standard**
<Name>	<Quality>	<Unit>	<Ref>
<Name>	<Quality>	<Unit>	<Ref>

Name of other ingredient(s)[5] of the medicinal product(s)	**Quality**	**Unit**	**Reference/monograph standard**
1. <Name>	<Quality>	<Unit>	<Ref>
2. <Name>	<Quality>	<Unit>	<Ref>
3. <Name>	<Quality>	<Unit>	<Ref>
4. <Name>	<Quality>	<Unit>	<Ref>
5. <Name>	<Quality>	<Unit>	<Ref>

[4] Only one name for each substance should be given in the following order of priority:
INN (accompanied by its salt or hydrate form if relevant), Ph.Eur., National Pharmacopoeia, common name, scientific name.

Details of any overages should not be included in the columns but stated below:

- ancillary medicinal substance(s)
  <Name>
- other ingredient(s) of the ancillary medicinal substance
  <Name>

2.6.2. Packaging components of the medicinal product, including description of material from which it is constructed[5]

For each type of pack give:

2.6.2.1. Package size(s)

<Text>

2.6.2.2. Proposed shelf life (unopened)

<Text>

2.6.2.3. Proposed shelf life (in use)

<Text>

2.6.2.4. Proposed storage conditions

<Text>

2.6.3. List of materials of animal and/or human origin contained or used in the manufacturing process of the ancillary medicinal substance or as other ingredients of the medicinal product

None: ☐

Section to be added if more than three.

Name	**Function[6]**			**Animal origin susceptible to TSE[7]**		**Other animal origin**	**Human origin**
	AS	**OI**	**R**				
1.	☐	☐	☐	☐ yes[8]	☐ no	☐	☐
2.	☐	☐	☐	☐ yes[9]	☐ no	☐	☐
3.	☐	☐	☐	☐ yes[9]	☐ no	☐	☐

[5] Use current list of standard terms - European Pharmacopoeia where applicable.
[6] AS= ancillary medicinal substance OI=other ingredients (incl. starting materials used in the manufacture of the ancillary medicinal substance /other ingredients), R=reagent/culture medium (incl. those used in the preparation of master and working cell banks).
[7] As defined in section 2 (scope) of the CHMP Note for Guidance.
[8] If a Ph. Eur. certificate of suitability for TSE is available according to resolution AP/CSP (99) 4 of the Council of Europe attach it in Annex 4.7.

2.6.4. Does the ancillary medicinal substance contain or consist of Genetically Modified Organisms (GMOs) within the meaning of Directive 2001/18/EC?

❍ no ❍yes

If yes, does the product comply with Directive 2001/18/EC?
❍ no ❍yes

☐ Attach a copy of any written consent(s) of the competent authorities to the deliberate release into the environment of the GMOs for research and development purposes where provided for by Part B of the above-mentioned Directive (Annex 4.8).

3. Other applications for the same ancillary medicinal substance

Note: 'same ancillary medicinal substance' means a marketing authorisation for a medicinal product or a consultation on a medical device incorporating the same ancillary medicinal substance from the same manufacturer.

3.1. Details of applications for the same ancillary medicinal substance in the EEA (including any application to the AIFA)[9]

☐ Authorised*
Country: <Country>
Date of authorisation / consultation: <DD-MM-YYYY>
Invented name: <Name>
Authorisation number/AIFA procedure number: <Number>

☐ Pending
Country: <Country>
Date of submission: <DD-MM-YYYY>

☐ Refused
Country: <Country>
Date of refusal: <DD-MM-YYYY>

☐ Withdrawn (by applicant before authorisation)
Country: <Country>
Date of withdrawal: <DD-MM-YYYY>
Invented name: <Name>
Reason for withdrawal: <Text>

[9] i.e. marketing authorisation for a medicinal product or a consultation on a medical device incorporating the same ancillary medicinal substance from the same manufacturer.

☐ Withdrawn (by applicant after authorisation)
Country: <Country>
Date of withdrawal: <DD-MM-YYYY>
Authorisation number <Number>
Reason for withdrawal: <Text>
Invented name: <Name>

☐ Suspended/revoked (by competent authority)
Country: <Country>
Date of suspension/revocation: <DD-MM-YYYY>
Reason for suspension/revocation: <Text>
Invented name: <Name>

3.2. Details of applications for the same ancillary medicinal substance derivative outside the EEA[10]

☐ Authorised
Country: <Country>
Date of authorisation: <DD-MM-YYYY>
Invented name: <Name>

☐ Pending
Country: <Country>
Date of submission: <DD-MM-YYYY>

☐ Refused
Country: <Country>
Date of refusal: <DD-MM-YYYY>

☐ Withdrawn (by applicant before authorisation)
Country: <Country>
Date of withdrawal: <DD-MM-YYYY>
Trade name: <Name>
Reason for withdrawal: <Text>

☐ Withdrawn (by applicant after authorisation)
Country: <Country>
Date of withdrawal: <DD-MM-YYYY>
Invented name: <Name>
Reason for withdrawal: <Text>

☐ Suspended/revoked (by competent authority)
Country: <Country>
Date of suspension/revocation: <DD-MM-YYYY>
Reason for withdrawal/revocation: <Text>
Invented name: <Name>

[10] i.e. Marketing authorisation for a medicinal product or medical device approval using the same medicinal substance from the same manufacturer.

4. Annexed documents (where appropriate)

4.1 ☐ Letter of authorisation for communication on behalf of the notified body.

4.2 ☐ Manufacturing authorisation required under Article 40 of Directive 2001/83/EC (or equivalent, outside of the EEA where MRA or other community arrangements apply); any proof of authorisation in accordance with Article 8(k) of Directive 2001/83/EC.

4.3 ☐ Flow-chart indicating all manufacturing and control sites involved in the manufacturing process of the ancillary medicinal product and ancillary active substance.

4.4 ☐ GMP certificate(s) or other GMP statement(s); where applicable a summary of other GMP inspections performed.

4.5 ☐ Letter(s) of access to active substance master file(s) or copy of Ph. Eur. certificate(s) of suitability.

4.6 ☐ Copy of written confirmation from the manufacturer of the ancillary active substance to inform the Notified Body in case of modification of the manufacturing process or specifications according to Annex I of Directive 2001/83/EC as amended.

4.7 ☐ Ph. Eur. certificate(s) of suitability for TSE.

4.8 ☐ Written consent(s) of the competent authorities regarding GMO release in the environment.

4.9 ☐ For each active substance, attach a declaration(s) from the qualified person of the manufacturing authorisation holder in Section 2.4.1.1 and from the qualified person of each of the manufacturing authorisation holders (i.e. located in EEA) listed in Section 2.4.1.2 where the ancillary active substance is used as a starting material that the ancillary active substance is manufactured in compliance with the detailed guidelines on good manufacturing practice for starting materials. Alternatively, such declaration may be signed by one qualified person on behalf of all QPs involved (provided this is clearly indicated).