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SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

## European Medicines Agency recommendation on the procedural aspects and dossier requirements for the consultation of the European Medicines Agency by a notified body on an ancillary medicinal substance or an ancillary human blood derivative incorporated in a medical device or active implantable medical device

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This revision 2 takes into account the changes introduced by Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 93/42/EEC and 90/385/EEC, and introduces updates to references to other EMA guidance documents.

Keywords	<i>Consultation, notified body, ancillary medicinal substance, ancillary human blood derivative, medical device</i>
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<sup>1</sup> Update of section 4.5 related to new fee regulation (EC) No 2024/568 (from 1 January 2025)

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## Executive summary

This recommendation aims to provide interested parties with appropriate guidance on procedural aspects as well as format and data requirements to facilitate the consultation procedure to the European Medicines Agency (EMA) by notified bodies on:

- Medicinal products within the meaning of Article 1(2) of Directive 2001/83/EC incorporated, as an integral part in a medical device and which are liable to act upon the body with action ancillary to that of the device.
- Medicinal product constituents or medicinal products derived from human blood or human plasma within the meaning of Article 1(10) of Directive 2001/83/EC incorporated, as an integral part in a medical device and which are liable to act upon the human body with action ancillary to that of the device.

These substances are referred to hereinafter respectively as ancillary medicinal substances and as ancillary human blood derivatives.

This recommendation applies to any application for consultation submitted to the European Medicines Agency by notified bodies.

## 1. Introduction (background)

This recommendation is intended to provide the relevant interested parties with information about procedural aspects of the application for consultation procedure to the European Medicines Agency by notified bodies on an ancillary medicinal substance or an ancillary human blood derivative incorporated as an integral part in a medical device, as well as guidance on data requirements and format of such applications for consultation.

In all cases, the notified body shall seek an opinion from either one of the competent authorities of medicinal products designated by the Member States or from the European Medicines Agency.

Depending on the type of ancillary medicinal substances concerned, it will either be mandatory or optional to consult the European Medicines Agency.

- In the case of ancillary human blood derivative or medicinal products that fall within the scope of the Annex to Reg. (EC) No 726/2004, it is mandatory for the notified body to consult the European Medicines Agency as the competent authority for the consultation.<sup>2</sup>
- For other ancillary medicinal substances, it is at the discretion of the notified body in consultation with the medical device manufacturer to choose the competent authority designated by the Member States or the European Medicines Agency.

The EMA may be consulted, e.g. where the substance involved was introduced in a medicinal product which has been evaluated by the EMA.<sup>1</sup>

The notified body will give due consideration to the opinion of the European Medicines Agency when making its decision and will not deliver the certificate if the Agency's scientific opinion is unfavourable. In any case, the notified body will convey its final decision to the Agency.

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<sup>2</sup> MEDDEV guidance 2.1/3 rev.3, Dec. 2009, p. 16

## 2. Scope

The scope of this paper is to describe the format and content of the applications for consultation that notified body should submit to the European Medicines Agency, as well as procedural aspects for consultation of the European Medicines Agency on an ancillary medicinal substance or an ancillary human blood derivative incorporated in a medical device.

## 3. Legal basis

### ▪ Article 1(8) of Regulation (EU) 2017/745:

*"Any device which, when placed on the market or put into service, incorporates, as an integral part, a substance which, if used separately, would be considered to be a medicinal product as defined in point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma as defined in point 10 of Article 1 of that Directive, and that has an action ancillary to that of the device, shall be assessed and authorized in accordance with this Regulation."*

For these specific medical devices, in accordance with **Annex IX (Conformity Assessment), section 5.2, of Regulation (EU) 2017/745:**

*"(a) Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product within the meaning of point 2 of Article 1 of Directive 2001/83/EC, including a medicinal product derived from human blood or human plasma and that has an action ancillary to that of the device, the quality, safety, and usefulness of the substance shall be verified, by analogy with the methods specified in Annex I to Directive 2001/83/EC.*

*(b) Before issuing an EU technical documentation assessment certificate, the notified body shall, having verified the usefulness of the substance as part of the device and taking account of the intended purpose of the device, seek a scientific opinion from one of the competent authorities designated by the Member States in accordance with Directive 2001/83/EC or from the EMA, either of which to be referred to in this Section as 'the medicinal products authority consulted' depending on which has been consulted under this point, on the quality and safety of the substance including the clinical benefit or risk of the incorporation of the substance into the device. Where the device incorporates a human blood or plasma derivative or a substance that, if used separately, may be considered to be a medicinal product falling exclusively within the scope of the Annex to Regulation (EC) No 726/2004, the notified body shall seek the opinion of the EMA.*

*(c) When issuing its opinion, the medicinal products authority consulted shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body."*

*(d) The medicinal products authority consulted shall provide its opinion to the notified body within 210 days of receipt of all the necessary documentation.*

*(e) The scientific opinion of the medicinal products authority consulted, and any possible update of that opinion shall be included in the documentation of the notified body concerning the device. The notified body, shall give due consideration to the views expressed in the scientific opinion when making its decision. The notified body shall not deliver the certificate if the scientific opinion is unfavourable and shall convey its final decision to the medicinal products authority consulted.*

*(f) Before any change is made with respect to an ancillary substance incorporated in a medical device, in particular related to its manufacturing process, the manufacturer shall inform the notified body of the changes. That notified body shall seek the opinion of the medicinal products authority consulted, in*

*order to confirm that the quality and safety of the ancillary remain unchanged. The medicinal product authority consulted shall take into account the data relating to the usefulness of incorporation of the substance into the device as determined by the notified body, in order to ensure that the changes have no negative impact on the risk or benefit previously established concerning the incorporation of the substance into the device. The medicinal products authority consulted shall provide its opinion within 60 days after receipt of all the necessary documentation regarding the changes. The notified body shall not deliver the supplement to the EU technical documentation assessment certificate if the scientific opinion provided by the medicinal product authority consulted is unfavourable. The notified body shall convey its final decision to the medicinal products authority consulted.*

*(g) Where the medicinal authority consulted obtains information on the ancillary substance, which could have an impact on the risk or benefit previously established concerning the incorporation of the substance in the device, it shall advise the notified body as to whether this information has an impact on the risk or benefit previously established concerning the incorporation of the substance into the device. The notified body shall take the advice into account in reconsidering its assessment of the conformity assessment procedure.*

## **4. Practical recommendations**

### **4.1. Pre-submission activities**

The European Medicines Agency strongly recommends a pre-submission meeting with the relevant notified body and device manufacturer preferably at least 6 months before the expected date of submission in order to assist them in preparing their application.

The section on ancillary medicinal substances or ancillary human blood derivatives incorporated in medical devices (<http://www.ema.europa.eu – Human regulatory/ Research and development/ Non-pharmaceutical products/ Ancillary medicinal substances>) and the pre-submission guidance for medicinal products on the European Medicines Agency website (<http://www.ema.europa.eu – Human regulatory/Marketing authorisations/pre-authorisation guidance>) may be helpful for applicants when preparing the submission for a consultation procedure to the Agency.

Prior to the submission, the Committee for Medicinal Products for Human Use (CHMP) will appoint one or, if necessary, two of its members to act as rapporteur(s).<sup>3</sup> The notified body will need to provide an “intention to submit letter” preferably at least 6 months before the expected date of submission. This letter should include the date of expected submission and the scientific explanation that the action of the medicinal substance incorporated in the medical device is only ancillary to that of the device (see format in Appendix 2). The classifications of the device and components should be in line with the definitions and examples of MEDDEV guidance 2.1/3 rev 3, December 2009.

### **4.2. Data requirements and format of the application dossier**

Each application for consultation shall be submitted to the European Medicines Agency using the relevant application form, that can be found on the [European Medicines Agency website](#) and containing the information described in this document.

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<sup>3</sup> Procedural Advice on the CHMP/CAT Rapporteur/Co-rapporteur Appointment Principles, Objective Criteria and Methodology (EMA/151751/2010).

Guidance on data requirements and format of the application dossier can be found in Appendix 1. For its preparation the European Medicines Agency has taken as basis the MEDDEV guidance 2.1/3 rev 3, December 2009 and supplemented this with guidance of EudraLex notice to applicants Volume 2B (Presentation and content of the dossier – CTD). In addition, references to specific guidance available for plasma-derived medicinal products, biological/biotechnological products and new chemical entities are given.

For medicinal substances/blood derivatives, with ancillary action that are incorporated in a medical device, the quality, safety and usefulness will be verified, taking account of the intended purpose of the device, by analogy with the appropriate methods specified in Annex I to Directive 2001/83/EC as amended.

The notified body has to provide a report<sup>4</sup> to the European Medicines Agency verifying the usefulness of the ancillary medicinal substance or ancillary human blood derivative as part of the medical device taking into account the intended purpose of the device, in order to ensure that the European Medicines Agency can give an opinion on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the substance into the device.

According to MEDDEV guidance 2.1/3 rev 3, December 2009, the aspect of "usefulness" relates to the rationale for using the medicinal substance in relation to the specific intended purpose of the device. It refers to the suitability of the medicinal substance to achieve its intended action, and whether the potential inherent risks (aspects of "safety") due to the medicinal substance are justified in relation to the benefit to be obtained within the intended purpose of the device.

A clarification was published in the [CHMP Monthly Report for November 2005](#) on the Active Substance Master File (ASMF) and Plasma Master File (PMF) concepts in relation to medical devices incorporating biological medicinal products as ancillary substance.

This clarification states the following:

*"Notified bodies, medical device manufacturers and manufacturers of the ancillary biological substances are advised that the non-applicability of the Active Substance Master File (ASMF) concept to biological active substances and the non-applicability of the concept of open and closed parts to Plasma Master File (PMF) as per the CHMP Monthly report for October 2004 as stated below, are applicable to medical devices incorporating biological medicinal products, including blood derivatives with action ancillary to that of the devices.*

*Therefore, ASMF are not allowed for these types of substances and the PMF should be made available to the medical device manufacturer, as for any other part of the dossier of an ancillary blood derivative."*

Extract from [CHMP monthly report for October 2004](#).

***Non-applicability of the Active Substance Master File (ASMF) concept to biological active substances***

*"Marketing Authorisation Holders (MAH's) and applicants are advised that the concept of Active Substance Master Files, as laid down in Directive 2001/83/EC, as amended, cannot be applied in the context of biological medicinal products.*

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<sup>4</sup> In section 1 of the dossier (see Appendix 1)

*The characterisation and determination of biological active substances' quality requires not only a combination of physico-chemical and biological testing, but also extensive knowledge of the production process and its control.*

*The MAH/applicant for a biological medicinal product could therefore not comply with the requirement to 'take responsibility for the medicinal product' without having full and transparent access to these quality-related data. The use of an ASMF would prevent such access, and should therefore not be allowed for biological active substances.*

*In addition, active substances, which are present in certain medicinal products such as vaccines or cell therapy medicinal products, do not fit with the concept of a 'well-defined' active substance."*

**Non-applicability of the ASMF concept of open and closed parts to Vaccine Antigen Master File (VAMF) and Plasma Master File (PMF)**

*"The legislation does not provide for the use of open/closed parts in the Vaccine Antigen Master file (VAMF) and Plasma Master File (PMF). The concept of open (non-confidential) and closed (confidential) parts is specific to the Active Substance Master File.*

*Regarding the VAMF the legislation specifies that the VAMF holder cannot differ from the MAH/applicant for the concerned medicinal product: there is hence no rationale for an 'open/closed' parts system.*

*For the PMF the legislation specifies that where the MAH/applicant differs from the holder of the PMF, the PMF shall be made available to the MAH/applicant for submission to the competent authority."*

It should be noted that it is not possible to cross-refer to the dossier of nationally authorised medicinal products in support of a notified body consultation procedure. This is because data held in national systems is not available to the European Medicines Agency for evaluation. The Committee for Medicinal Products for Human Use (CHMP) will give an opinion and therefore it should be provided with the relevant data for evaluation.

### **4.3. Consultation procedure to the European Medicines Agency**

The Committee for Medicinal Products for Human Use (CHMP), will appoint one or, if necessary, two of its members to act as rapporteur(s). These CHMP members will each lead a team of experts in the evaluation of the submitted dossier. Input from other CHMP members is provided during the procedure.

The applicant for the consultation procedure is the notified body in accordance with the legal provisions of Regulation (EU) 2017/745. The consultation dossier for submission will be prepared in close collaboration between the medical device manufacturer and the notified body.

The CHMP will follow the same assessment timetable as used for a new application to the European Medicines Agency according to the Centralised Procedure as described in [EudraLex notice to applicants Volume 2A, Chapter 4](#) i.e. a maximum 210 day timetable with the opportunity for clock stops for the applicant to reply to questions or communicated deficiencies.

The CHMP can be asked to shorten the procedure in the following cases:

- the device is for use in serious diseases (life threatening or heavily disabling diseases);
- a known medicinal substance or human blood derivative from a known source is used and when CHMP considers that the evaluation needed is less extensive.

Applicants requesting an accelerated assessment procedure should provide a justification supporting their claim at least two to three months before submitting the initial consultation procedure. The application form can be found at the European Medicines Agency website.

After the evaluation period the CHMP/European Medicines Agency will issue an opinion on the quality and safety of the substance(s) including the clinical benefit/risk profile of the incorporation of the substance(s) into the medical device. The CHMP opinion is sent to the Notified body and to the national competent authority on medical devices of the member state in which the notified body is based.

A public assessment report on the consultation procedure (CPAR) to the European Medicines Agency by a notified body on ancillary medicinal substances incorporated in medical devices will be published on the European Medicines Agency website at the time the notified body has reached a decision on the granting of the CE mark. The relevant medical device manufacturer and ancillary medicinal substance manufacturer will be consulted through the notified body on the CPAR before publication. The general principles for the deletion of commercially confidential information as described in the European Medicines Agency document 'Guide to information on human medicines evaluated by EMA' ([EMA/515416/2015](http://www.ema.europa.eu/515416/2015)) will apply.

#### **4.4. Post-consultation phase**

Where changes are made to an ancillary medicinal substance or ancillary blood derivative incorporated in the device (in particular related to the source, the manufacturing process, the amount and method of incorporation), the notified body shall be informed of the changes and shall consult the Agency in order to confirm that the quality and safety of the ancillary substance is maintained. The Agency will take into account the data related to the usefulness of the incorporation of the substance into the device as determined by the notified body, in order to ensure that the changes have no negative impact on the established benefit/risk profile of the addition of the substance in the device.

These major or minor amendments to the documentation on an ancillary medicinal substance or ancillary human blood derivative incorporated in the medical device provided in the consultation procedure dossier will be classified and evaluated by analogy to the variations regulation (Commission Regulation (EC) 1234/2008).

The section on post-authorisation guidance for medicinal products on the European Medicines Agency website (<http://www.ema.europa.eu – Human regulatory/Post-authorisation/Post-authorisation Q&A>) may be helpful for applicants when preparing the submission for a consultation procedure to the Agency.

Where EMA obtains information on the ancillary substance, that could have an impact on the established benefit/risk profile of the addition of the substance in the medical device, it shall provide the notified body with advice, whether this information has an impact on the established benefit/risk profile of the addition of the substance in the medical device or not. The notified body shall take the updated scientific opinion into account in reconsidering its assessment of the conformity assessment procedure.

#### **4.5. Fees *Rev. Dec 2024***

The fees payable to the European Medicines Agency are established by Council Regulation (EC) No 2024/568. For more information on fees to be paid, applicable fee reductions and payment process,



please refer to the Fee Q&A in Annex IV, Section 7.1, on the Fees payable to the European Medicines Agency [page](#).

## References

Directive 2001/83/EC as amended of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.

REGULATION (EU) 2017/745 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

MEDDEV Guidance 2.1/3 rev 3, December 2009 relating to Borderline products, drug-delivery products and medical devices incorporating, as integral part, an ancillary medicinal substance or an ancillary human blood derivative.

EudraLex, Notice to Applicants Volume 2B (Presentation and content of the dossier – CTD).

EudraLex, Notice to Applicants Volume 2A, Chapter 4 (Centralised procedure).

Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products.

- [New Fee Regulation \(from 1 January 2025\) | European Medicines Agency \(EMA\)](#)

# Appendix 1

## Data requirements and format of the application dossier

### Section 1 comprises

- Application form
- General information of the medical device
  - General description of the medical device
  - Appendix 2 (Scientific explanation that the action of the medicinal substance or human blood derivative incorporated in the medical device is only ancillary to that of the device in line with the MEDDEV guidance 2.1/3 rev 3, December 2009)
- Signed declaration and CV from a qualified expert(s)<sup>5</sup>
- Report from the notified body verifying the usefulness of the incorporation of the ancillary medicinal substance / ancillary blood derivative in the medical device
- Labelling

### Section 2 comprises

- Module 2.3: quality overall summary (relevant parts) for the ancillary medicinal substance or ancillary human blood derivative itself in accordance with the format of Volume 2B, CTD of the notice to applicants (EudraLex, The rules governing medicinal products in the European Union).
- Critical summaries (or expert reports) of the quality, non-clinical and clinical data provided in line with MEDDEV guidance 2.1/3 rev 3, December 2009 for the ancillary medicinal substance or the ancillary human blood derivative incorporated in the medical device. (i.e. critical summaries (or expert reports) of points 2b), 3) and 4) as detailed in Section C.3 of the MEDDEV guidance 2.1/3 rev 3, December 2009)

### Section 3 comprises

- CTD Module 3: relevant parts, for ancillary medicinal substance or ancillary human blood derivative itself, in accordance with the format of Volume 2B, CTD of the notice to applicants (EudraLex, The rules governing medicinal products in the European Union).

**Note:** For non biological ancillary medicinal substances for which an Active Substance Master File (ASMF) or a Certificate of Suitability to the monographs of the European Pharmacopoeia (CEP) is used, refer to the European Medicines Agency guideline on ASMF (EMA/CVMP/134/02 Rev 3/Corr; CPMP/QWP/227/02 Rev 3/Corr).

**Note:** For ancillary human blood derivatives for which a PMF already exists, the relevant information in module 3 already submitted as part of the PMF does not need to be provided with the application dossier for the consultation procedure. In this case, a notification letter should accompany module 3 from the medical device manufacturer including the following:

1. Reference to the PMF number and date of the certification

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<sup>5</sup> When expert reports are used in Section 2 as critical summaries of the documentation, we request a signed declaration of ownership of the report. The expert shall have suitable technical or professional qualifications. A CV of the expert including brief information on their educational background, training and occupational experience shall be included. The professional relationship of the expert to the medical device manufacturer/notified body shall be declared.

2. Declaration that the PMF certificate, evaluation report and PMF dossier are fully applicable for the ancillary human blood derivative
3. Declaration that the PMF holder has submitted the PMF certificate, evaluation report and PMF dossier to the medical device manufacturer

State that the PMF certificate, evaluation report and PMF dossier are available at the European Medicines Agency, and therefore not attached to this notification letter. However, on request, the PMF dossier will be sent to the European Medicines Agency within 48 hours

- Quality documentation following the headings and data requirements of Section C.3 point 2b) of the MEDDEV guidance 2.1/3 rev 3, December 2009 for the ancillary medicinal substance or the ancillary human blood derivative incorporated in the medical device.

## **Section 4 comprises**

- Non-clinical documentation following the headings and data requirements of Section C.3 point 3 of the MEDDEV guidance 2.1/3 rev 3, December 2009 for the ancillary medicinal substance or the ancillary human blood derivative incorporated in the medical device.

## **Section 5 comprises**

- Clinical documentation following the headings and data requirements of Section C.3 point 4 of the MEDDEV guidance 2.1/3 rev 3, December 2009 for the ancillary medicinal substance or the ancillary human blood derivative incorporated in the medical device.

## **Useful guidelines to fulfil the data requirements**

The following [list of guidelines](#) is not exhaustive and there may be other guidelines applicable.

### **1. General guidance**

- [MEDDEV guidance 2.1/3 rev 3, December 2009](#) relating to the application of the Council Directive 90/385/EEC on active implantable medical devices and the Council Directive 93/42/EEC on medical devices.
- EudraLex [Notice to Applicants Volume 2B](#) (Presentation and content of the dossier – CTD).
- Guideline on Active Substance Master File procedure ([EMEA/CVMP/134/02 Rev 3/Corr; CPMP/QWP/227/02 Rev 3/Corr](#)). Please note this guideline is not applicable for biological active substances.

### **2. Guidance for blood derivatives**

#### **Quality**

- Note for guidance on Plasma-derived medicinal products ([EMA/CHMP/BWP/706271/2010](#)).
- Guideline on the scientific data requirements for a Plasma Master File (PMF) ([EMA/CPMP/BWP/3794/03 Rev 1](#)).
- Note for guidance on virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses ([CPMP/BWP/268/95](#)).
- Relevant European Pharmacopoeia monographs.

- Guideline on the investigation of manufacturing processes for Plasma-derived medicinal products with regard to vCJD Risk ([CPMP/BWP/5136/03](#)).
- CHMP position statement on Creutzfeldt-Jacob disease and Plasma-derived and Urine-derived medicinal products. ([CHMP/BWP/303353/2010](#))

#### **Good manufacturing practice**

- Manufacture of medicinal products derived from human blood or plasma, [Annex 14 to the EU Guide to good manufacturing practice](#).

#### **Non-clinical and clinical safety**

- CPMP/CHMP<sup>6</sup> guidance on medicinal blood products from the Blood Products Working Party (BPWP) (<http://www.ema.europa.eu - Regulatory/human medicines/scientific guidelines/clinical efficacy and safety/ blood products>).

### **3. Guidance for biological/biotechnology products**

#### **Quality**

- Relevant CPMP/CHMP<sup>6</sup> Guidelines published on the European Medicines Agency website (<http://www.ema.europa.eu - Regulatory/human medicines/scientific guidelines/biologicals>).
- Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products ([EMEA/410/01 Rev 3](#)).

#### **Good manufacturing practice**

- Manufacture of biological medicinal products for human use, Annex 2 to the EU Guide to good manufacturing practice.

#### **Non-clinical and clinical safety**

- Relevant CPMP/CHMP<sup>6</sup> guidance on biological/biotechnological products from the Safety Working Party (SWP) and other CHMP working parties (<http://www.ema.europa.eu - Regulatory/human medicines/scientific guidelines/non-clinical>) & (<http://www.ema.europa.eu - Regulatory/human medicines/scientific guidelines/clinical efficacy and safety>).

### **4. Guidance for new chemical entities**

#### **Quality**

- Relevant CPMP/CHMP<sup>6</sup> Guidelines published on the European Medicines Agency website (<http://www.ema.europa.eu - Regulatory/human medicines/scientific guidelines/clinical efficacy and safety/quality>).

#### **Good manufacturing practice:**

- Relevant Annexes to the EU Guide to good manufacturing practice.

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<sup>6</sup> The Committee on Proprietary Medicinal Products (CPMP) changed its name to Committee for Medicinal Products for Human Use (CHMP) on 1 May 2004.

## **Non-clinical and clinical safety**

- Relevant CPMP/CHMP<sup>6</sup> guidance on new chemical entities from the Safety Working Party (SWP) and Efficacy Working Party (EWP) and CHMP temporary working parties (<http://www.ema.europa.eu - Regulatory/human medicines/scientific guidelines/non-clinical>) & (<http://www.ema.europa.eu - Regulatory/human medicines/scientific guidelines/clinical efficacy and safety>).
- Guideline on the clinical and non-clinical evaluation during the consultation procedure on medicinal substances contained in drug-eluting (medicinal substance-eluting) coronary stents ([EMEA/CHMP/EWP/110540/2007](http://www.ema.europa.eu - Regulatory/human medicines/scientific guidelines/clinical efficacy and safety)).

1 **Appendix 2**  
2 **Scientific explanation for qualification**

3 **A. Scientific explanation that the action of the medicinal substance or human blood derivative incorporated in the medical device is only**  
4 **ancillary to that of the device in line with the MEDDEV guidance 2.1/3 rev 3, December 2009**

5  
Date: <DD Month YYYY>

Notified body (applicant): <Name>

Medical device manufacturer: <Name>

Medical device: <Name>

Ancillary medicinal substance: <INN> <Common name>

Ancillary human blood derivative <INN> <Common name>

6 **1. Description of medical device**

7 **Type of product, ancillary medicinal substance/ancillary human blood derivative, brief description, principal intended action:**

8 <Text.>

9 *Make reference to medical device / medicinal product definitions*

10 **Intended use:**

11 **Product presentation / composition:**

12 <Text.>

13 *Description of the product (e.g. Quantitative and qualitative composition, route of administration and/or*  
 14 *mode of action, pharmaceutical form (where relevant)).*

15 **2. Method by which the principal intended action is achieved**

<b>Combination product (medical device part(s) + ancillary medicinal substance(s) / ancillary human blood derivative(s))</b>	<b>Principal intended action according to applicant*</b>	Reference to MEDDEV guidance 2.1/3 rev 3, December 2009**
<b>Medical device part(s)</b>	<b>Principal action: &lt;title that clearly describes the action&gt;</b>  Scientific explanation (brief):	Refer to relevant section of the Guideline and to respective example, e.g.  A.2.1.2 – Examples for medical devices  -‘ Haemostatic products, for example...’
<b>Ancillary medicinal substance(s) / ancillary human blood derivative(s)</b>	<b>Ancillary action: &lt;title that clearly describes the action&gt;</b>  Scientific explanation (brief):	Refer to relevant section of the Guideline and to respective example, e.g.  B.4 – Medical devices incorporating a medicinal substance with ancillary action  ‘Examples of such medical devices are: ...’
<i>Add more columns as needed</i>		

16 \* Provide cross-reference to supportive scientific information in Section B.

17 \*\* In addition reference to other regulatory texts can be made where relevant.

18 **3. Regulatory status (if existing)**

19 Status in EU member states (including EEA countries) and outside EU if applicable.

20 Provide examples of similar products that have already been marketed in EU or outside EU.



21 **4. Current use**

22 Description of how medical device is used alone or in combination with the ancillary medicinal substance or ancillary human blood derivative (in EU or outside  
23 EU).

24 **5. Other relevant aspects**

25 <Text.>

26 **B. Supportive scientific information**

27 This section is the most important to reach a conclusion on the ancillary action of the medicinal substance or of the ancillary human blood derivative in  
28 the medical device. In particular scientific information demonstrating the ancillary nature of the medicinal substance or of the human blood derivative (in  
29 line with the demarcation guideline, [MEDDEV guidance 2.1/3 rev 3, December 2009](#)) in the combination product has to be provided. Scientific  
30 information should cover:

- 31
- The mode of action of the components (medical device and medicinal product) on their own and in the combination product.
  - 32 • Any reference / summaries of pre-clinical or clinical experience/trials with the combination product / medicinal product alone / device alone / similar  
33 combination product.
  - 34 • Explanation why the medicinal substance is added to the medical device: identification of those patients that would benefit from this combination  
35 product versus medical device alone.
  - 36 • Consideration of the potential risks associated with the addition of the medicinal substance to the medical device (immune reactions,  
37 carcinogenicity...)

38 This list is not exhaustive and is only intended for guidance.