Amsterdam, <insert full date>

<insert Doc.Ref.>

<Committee for Medicinal Products for Human Use (CHMP)><Committee for Advanced Therapies Medicinal Products (CAT)>

<Updated><CHMP><CAT> Assessment report

Consultation on companion diagnostic

*This document gives practical assessment guidance on what should be considered for initial consultation procedure to the European Medicines Agency by Notified Bodies (NB) on a companion diagnostic (CDx).*

Companion diagnostic: <Name>

Concerned medicinal product(s): <Product name>

Procedure No.: <EMEA/H/D/XXX>

Applicant: <Name of notified body>

*[Delete this table at the time of adoption of LoQ]*

|  |  |
| --- | --- |
| <CHMP><CAT> Rapporteur:  |  |
| <CHMP coordinator(s)> *to be included only for CAT procedures* |  |
| EMA PL: |  |
| Start of the procedure: |  |
| Date of this report: |  |
| Deadline for comments: |  |

*Note to the Rapporteur: Assessment reports and comments should be circulated VIA EUDRALINK.* *Product Shared Mailbox: product.name-xxxx@ema.europa.eu.*

***Guidance text*** *is in green italics. You may print a copy of this template with the drafting note, then delete them all in one go:*

*Click on Ctrl-Alt-Shift-S to view the “styles” window. Select “Drafting notes (Agency)” and click on the icon on the right, chose “Select all XXX instances”, press the “Delete” key on the keyboard.*

*Do not change or delete the titles and the numbering style. (Add “Not applicable” if necessary)*

*Suggested font: Verdana 9.*

*Paragraph tab: alignment: left, outline level: body text, indentation: 0, spacing before: 0pt and after: 7pt; line spacing: at least, at: 14pt.*

*The template should be used by both CHMP and PRAC Rapporteur for all assessments. In case of CHMP-led consultation procedure with PRAC involvement, the CHMP and PRAC Rapporteur are expected to use the assessment report template jointly. In such case, CHMP Rapporteur’s ARs can be circulated consecutively as per the timetable or at once as a single document (especially in cases when the two Rapporteurs come from the same NCA).*

Administrative information

|  |  |
| --- | --- |
| **Name of companion diagnostic:** |  |
| **Applicant (Notified Body (NB)) for companion diagnostic:** |  |
| **Manufacturer of companion diagnostic:** |  |
| **Applied intended purpose of companion diagnostic:** |  |
| **Concerned medicinal product(s):** | <Invented Product name(s)> |
| **MAH(s)/Applicant(s) for medicinal product(s)** |  |
| **<CHMP ><CAT> Rapporteur’s contact person:****<CHMP ><CAT> Rapporteur:****<PRAC Rapporteur:>****For CAT procedures:****<CHMP Coordinator(s)>****EMA Product Lead:****EMA Product Assistant:** | **Name:**Tel: Email:**Name:**Tel: Email:**<Name:>**<Tel:> <Email:>**<Name:>**<Tel:> <Email:>**Name:**Tel: Email:**Name:**Tel: Email: |
| **Names of the <CHMP ><CAT> Rapporteur’s assessors:** | **Name:**Tel: Email: |

Declarations

[ ]  The assessor confirms that this assessment does **not** include non-public information, including commercially confidential information (e.g. information shared by other competent authorities or organisations, reference to on-going assessments or development plans etc), irrespective from which entity was received\*.

*\*If the entity from which non-public information originates has consented to its further disclosure, the box should be ticked and there* would *be no need to add details below.*

Whenever the above box is un-ticked please indicate section and page where confidential information is located here:

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List of abbreviations

1. Background information on the procedure
	1. Submission of the dossier

In accordance with the conformity assessment procedure for companion diagnostics falling within the scope of Regulation (EU) 2017/746, the notified body <name> submitted to the European Medicines Agency (EMA) on <date> an application for a scientific opinion regarding the suitability of the device <name> in relation to the following medicinal product(s) concerned:

<include medicinal product(s) concerned>

* 1. Steps taken for the assessment of the suitability of the companion diagnostic with the medicinal product

The Rapporteur as appointed by the CHMP for the consultation and the evaluation team was:

Rapporteur :

<CAT Rapporteur:>

Evaluators:

The CHMP/CAT Rapporteurs should complete the ‘actual’ date at each stage of the procedure. This is the date of circulation of the report to CHMP/CAT members.

*Additional steps may need to be added manually, in accordance with SIAMED timetable, e.g. PRAC steps in case of PRAC involvement.*

| **Status of this report and steps taken for the assessment** |
| --- |
| **Current step¹** | **Description** | **Planned date** | **Actual Date** | Need for discussion² |
| [ ]  | Start of procedure |  |  | [ ]  |
| [ ]  | <CHMP><CAT> Rapporteur Assessment Report |  |  | [ ]  |
| [ ]  | <CHMP><CAT> members comments |  |  | [ ]  |
| [ ]  | Updated <CHMP><CAT> Rapporteur Assessment Report  |  |  | [ ]  |
| [ ]  | <CHMP><CAT> List of questions or Opinion |  |  | [ ]  |

¹ Tick the box corresponding to the applicable step – do not delete any of the steps. If not applicable, add n/a instead of the date.

² Criteria for CHMP plenary discussion: substantial disagreement between the Rapporteur and other CHMP members and/or at the request of the Rapporteur or the Chair.

1. Scientific overview and discussion

*Background information about this consultation procedure*

*‘Companion diagnostic’(CDx) means a device which is essential for the safe and effective use of a corresponding medicinal product to:*

*(a) identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or*

*(b) identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product*

*Regulation (EU) 2017/746 (In Vitro Diagnostic Regulation, IVDR) specifies the requirement for the assessment of the conformity of a device by a notified body, as well as for the consultation procedure on CDx by notified bodies to a competent authority designated by the Member States in accordance with Directive 2001/83/EC or the European Medicines Agency.*

*In accordance with Annex IX Chapter II of the IVDR, the notified body should verify that the clinical evidence and the performance evaluation are adequate and should verify the conclusions drawn by the manufacturer on the conformity with the relevant general safety and performance requirements. That verification should include consideration of the adequacy of the benefit-risk determination, the risk management, the instructions for use, the user training and the manufacturer's post-market surveillance plan, and include a review of the need for, and the adequacy of, the post-market performance follow-up (PMPF) plan proposed, where applicable.*

*In accordance with Annex IX, section 5.2, point (c) of Regulation 2017/746, the consultation procedure will be based on the draft summary of safety and performance (SSP) and the draft instructions for use (IFU) of the CDx. According to Article 29 of the IVDR, the SSP includes, among other elements, the summary of the performance evaluation of the device. It is expected that it follows the* [*MDCG guidance 2022-9 - Summary of safety and performance Template*](https://ec.europa.eu/health/system/files/2022-05/mdcg_2022-9_en.pdf)*.* *The content of the IFU is laid down in Section 20.4.1 of Annex I of the IVDR and includes, among other elements, information on a device's intended purpose and information that allows the user to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the device.*

*According to the Biomarkers, EndpointS and other Tools (*[BEST](https://www.ncbi.nlm.nih.gov/books/NBK326791/)*) glossary, a biomarker can be defined as a characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. Molecular, histologic or physiologic characteristics are types of biomarkers. Such biomarker or biomarkers can be present in healthy subjects and/or in patients.*

* 1. Introduction

*Include a brief description of the device and intended use: claimed indication(s) and target population(s), contraindications / limitations of use, brief device description and technological status of the assay/platform (e.g. new/first in-class, established methodology, follow-on assay or co-developed assay).*

*Include a short summary of the scientific rationale for the use of the biomarker.*

* 1. Suitability of the in vitro companion diagnostic medical device

*The consultation procedure by the CHMP/CAT should focus on the suitability of the CDx for use with the concerned medicinal product(s). The aspect of “suitability” relates to the use of a CDx with a particular medicinal product(s), given the performance and use claimed by the manufacturer.*

*The aspects that are considered when assessing the suitability of a CDx for use with the concerned medicinal product(s) include the scientific rationale (scientific validity) ) for biomarker selection (i.e., the association of an analyte with a clinical condition or a physiological state),* *the analytical performance (i.e., the ability of a device to correctly detect or measure a particular analyte) and clinical performance (i.e., the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user). The technical documentation dossier for the CDx, including the adequacy of the analytical method used to measure the concerned biomarker(s), scientific validity, and the analytical and clinical performance, will be assessed by the notified bodies as part of the conformity assessment. Therefore, as part of the consultation procedure, these aspects should only be discussed to the extent relevant for the conclusion on the suitability of the CDx for use with the medicinal product(s).*

*In this section, please include a discussion on the suitability of the CDx for use with the concerned medicinal product(s)based on the information included in the IFU and SSP:*

* *The focus of the discussion should be on the clinical aspects, i.e. clinical efficacy and clinical safety in relation to the suitability of the device for the medicinal product. This comprises aspects related to identification of patients likely to benefit or to be at increased risk of serious adverse effects, as well as of adverse effects related to both in case of false results. The discussion may also include comments on the scientific rationale for biomarker selection, and analytical performance if needed.*
* *Clinical performance (e.g. positive and negative predictive values) are described in the IFU/SSP either by correlation with a clinical endpoint (for novel assays) or –if available- by concordance study with a clinically valid reference assay.*
	+ *Include a short description of the main clinical data presented in support of the use of the CDx.*
	+ *Discuss the presented clinical performance results in this section in relation to the suitability of the device for the medicinal product. As part of the discussion on clinical performance, changes to the device during the development of the medicinal product up to the proposed CDx should be discussed with regards to their potential impact on the robustness of the clinical data generated.*
	+ *Cut-off point selection should also be discussed with reference to the linked analytical performance since it is of particular importance for the benefit /risk assessment of the medicinal product.*
* *Provide recommendations on possible post-market performance follow-up (PMPF) in relation to the suitability of the device for the medicinal product, as relevant.*
* *Provide comments on clinical risks to be addressed as part of PMPF in relation to the suitability of the device for the medicinal product, as relevant.*
* *If applicable, provide specific comments on the instructions for use and Summary of safety and performance that the Notified Bodies may take into consideration.*
* *This section should conclude by addressing the comparison of the favourable effects vs. unfavourable effects (e.g. known/unknown risks) i.e. benefit/risk determination of the use of the CDx with the medicinal product.*
	1. <Recommended measures to the notified body>

As discussed in section 2.2, it would be recommended that the notified body requests the following from the medical device manufacturer prior to device certification:

| **Area¹** | **Description** |
| --- | --- |
|  |  |
|  |  |

¹ Areas: scientific validity, analytical and clinical performance, clinical benefit, including clinical benefit/risk profile.

*[Recommended measures to the Notified body may include any action that the Notified body should consider requesting to the medical device manufacturer, including post-market performance follow-up (PMPF). This information will not be reviewed by the European Medicines Agency]*

* 1. <PRAC advice>
	2. Overall conclusions

*[Note: This section refers to the overall conclusions on the suitability of the CDx in the context of its use with the concerned medicinal product(s).]*

1. Recommendation

*Instructions to assessor: Please update this section as appropriate in every round of assessment.*

[ ]  Based on the CHMP review of data submitted, this application is subject to a list of questions (see Section 4) before a recommendation can be made.

[ ]  Based on the CHMP review of data submitted, the CHMP considered by <consensus> <majority decision> that <name of companion diagnostic> is <not> suitable for use with <concerned medicinal products> and therefore granted a <favourable><unfavourable> opinion in the consultation procedure.

*In case of ATMPs (use CAT steps as relevant)*

<[ ]  Based on the CAT review of data submitted, this application is subject to a list of questions (see Section 4) before a recommendation can be made.>

<[ ]  The CHMP endorsed the CAT conclusion on a list of questions (see Section 4) before a recommendation can be made. >

<[ ]  Based on the CAT review of data submitted, the CAT considered by <consensus> <majority decision> that <name of companion diagnostic> is <not> suitable for use with <concerned medicinal products> and therefore recommends the granting of a <favourable><unfavourable> opinion in the consultation procedure.>

<[ ]  Based on the draft CHMP opinion adopted by the CAT and the review of data submitted, the CHMP considered by <consensus> <majority decision> that <name of companion diagnostic> is <not> suitable for use with <concerned medicinal products> and therefore granted a <favourable><unfavourable> opinion in the consultation procedure.>

*In case additional measures are recommended in section 2.3 of the AR, please include the following statement.*

<The CHMP also recommends the measures as detailed in section 2.3 of this report to be taken into consideration by the notified body.>

Instructions to assessors: The conclusions from the assessment below should be incorporated in the main body of the assessment report.

Instructions to PL: The Annex needs to be removed at the time of CHMP Opinion.

Annex: Rapporteur’s assessment comments on the consultation

1. <CAT/CHMP> List of questions <as proposed by the Rapporteur>

*[If further clarification is needed for the CHMP to conclude on the suitability of a CDx for use with the concerned medicinal product(s), a list of questions may be issued to be addressed by the notified body and the CDx manufacturer as applicable, within a given timeframe]*

**Major objections**

<None>

***<General information>***

***<Quality aspects>***

*[Include major objections regarding quality characteristics and analytical performance]*

***<Clinical aspects>***

*[Include major objections regarding clinical performance, and clinical benefit including benefit/risk profile of the companion diagnostic for its intended use with concerned medicinal product(s)]*

**Other concerns**

<None>

***<General information>***

***<Quality aspects>***

***<Clinical aspects>***

*[Include other concerns regarding clinical performance, and clinical benefit of the companion diagnostic for its intended use with concerned medicinal product(s)]*

1. Assessment of the responses to the <CAT and> CHMP list of questions