| **Procedure description for EUnetHTA multi-HTA Early Dialogues**  **For Medical Devices** |
| --- |
| **ACTIONS concern:**   * **ED applicant**: company seeking for advice * **ED Committee (EDC):** Composed of HTA Bodies (HTABs) participating in the specific ED. * **EDC Scientific Coordinator:** One member of EDC undertakes scientific coordination on behalf of HTAs. The EDC Scientific Coordinator coordinates the content (scientific) discussion from the HTABs’ perspectives for the concerned ED, collates the HTAB List of Issues and positions/recommendations from the EDC. He will also serve as **chair** for the specific ED face-to-face (f2f) meeting, and presents consolidated HTAB answers. * **EUnetHTA ED Secretariat**: the central contact point for all EDs, responsible for all communication with the Applicant and EDC and external stakeholders |

Abbreviations

ED: Early Dialogues

MD: Medical Device

EDC: Early Dialogue Committee

F2F: Face to Face

1. **Principles and scope of Early Dialogue**
2. ***Principles***

An Early Dialogue (ED) allows for input from HTA bodies on the clinical development program of a health technology (here medical devices). It focuses on development strategies and is not a pre-assessment of available data. The advice is prospective in nature and requests for advice on on-going trials will not be accepted.

The advice provided is non-binding neither for HTA bodies nor for the Applicant and does not predetermine the outcome of the assessment performed later by the individual HTA agencies on that technology.

The scope of the ED is global evidence generation should always include the clinical development plan for the MD submitted as well as pivotal trials (no discussion about feasibility study). Economic studies and discussion relative to device adoption (issues that may impede product’s adoption in real practice) may be added to clinical development discussion. The Applicant chooses areas to be discussed during the ED.

An ED is requested for one indication. In some cases 2 lines of treatment see two indications could be considered for discussion.

The representatives of HTA bodies give advice in light of planned studies and scientific knowledge, based on the documentation submitted by the Applicant and questions raised.

Modifications to the EDMD briefing book and of questions for discussion during the procedure are generally not accepted. However, if between the start of the procedure and the face-to-face meeting the company makes any changes following main issues raised through ED process that could have a major impact on the MD development and on the related discussion (changes in the trial design or in the intended indication, new safety issues etc.) the company should inform the EUnetHTA ED Secretariat about these changes as soon as possible. The EUnetHTA members reserve the right not to respond to last minutes changes in the MD development.

The applicant can only request one meeting for the same technology.

The ED can occur before or after obtaining the CE mark.

1. ***Confidentiality and conflict of interest***

The specific advice on the technology in development is shared with the company that requested the advice, (and potentially with experts, patients and health care professional); the information otherwise remains confidential.

The process is confidential as follows: EUnetHTA is bound by [EUnetHTA code of conduct](file:///\\jersey\Themes\EUnetHTA\02_EUnetHTA_JA3_2016-2020\00_WP5\0.%20Strand%20A\0b.%20Early%20Dialogues%20-%20Medical%20Devices\procedure_for_doicu_handling_ja3_2016.pdf), and confidentiality agreements, and operates under the EUnetHTA policy on access to documents. A EUnetHTA Declaration of Interest and Confidentiality Undertaking ([DOICU](file:///\\jersey\Themes\EUnetHTA\02_EUnetHTA_JA3_2016-2020\00_WP5\0.%20Strand%20A\AppData\Local\Microsoft\Windows\Temporary%20Internet%20Files\Content.Outlook\059ARNDO\Declaration-of-Interest-and-Confidentiality-Undertaking-DOICU-Form.docx)) Form is used in this procedure by all participants (including potential external participants such as clinicians, patient representatives...).

1. **Practical aspects**
2. ***The application***

The application for an ED is to be addressed by e-mail to the EUnetHTA ED Secretariat *(HAS/France): (*[*EUnetHTA-HAS@has-sante.fr*](mailto:EUnetHTA-HAS@has-sante.fr)*)*.

The EDMD application is composed of:

* The Briefing Book summarizing information as rationale for seeking advice, name of product background information, data currently available on the product, product value proposition, proposed clinical studies, proposed economic evaluation , if appropriate, and the company’s questions
* The protocol of pivotal trial as an appendix of the Briefing Book
* The investigator’s brochure, if available
* A zip file containing all publications and study reports referenced in the briefing book

1. ***Eligibility***

* The EUnetHTA ED Secretariat evaluates the validity of the request (i.e. pivotal trial and not feasibility trial) based on the completeness of the documents provided by the applicant.
* EUnetHTA EDs will be restricted to MDs classified as class IIb and III, in vitro diagnostic and digital MDs with following criteria:
  + Unmet medical needs
  + Potential impact on patients, public health, or healthcare systems,
* The request will be considered as eligible if these criteria are met and if at least 3 HTAb are interested and have available resources to participate in the ED.

An ED can only take place only if the clinical trial subject of the ED has not yet begun.

1. ***Implication of external stakeholders***

When an eligibility decision has been made, the EUnetHTA ED Secretariat will be in charge of recruitment of external stakeholders, with the support of national HTAb and European association networks.

1. ***Participation of the stakeholders***

Depending on the expert’s background and on the willingness of the company to exchange product information, experts will have access to the entire Briefing Book. Accordingly, the expert will contribute punctually through an interview about the burden of the disease and current patient management, or in addition, provide his/her own position regarding the development plan with by participating in the pre-meeting with HTAB and the face-to-face meeting with HTA and the company.

1. ***Preparation of the F2F meeting***

The focus of the F2F meeting is the list of issues identified by the EDC. After receiving the individual lists from the EDC, the Scientific Coordinator compiles the List of Issues and organises an e-meeting, the purpose of which is to:

* Differentiate major issues to be discussed during F2F vs. minor issues that could be addressed in Final Written Recommendations or quickly during the meeting
* Review common and divergent positions on each issue
* identify questions for which a common position exist, allowing to produce one single consolidated answer
* discuss issues for which the answers of the HTABs diverge to understand the reasons for divergence and attempt to reach consensus
* have, when necessary, a discussion on whether the diverging requirements can still be accommodated within one trial or not

Following the e-meeting, the list is transmitted to the Applicant. The applicant in turn will provide their slides for the F2F no later than 4 days prior to the meeting date.

1. ***The face to face meeting***

A 2-3 hour meeting is proposed with the HTABs. One or more experts (patient, health professional, etc.) may be invited to participate by EUnetHTA deemed necessary in light of the questions submitted by the applicant

* Exchanges are about the clinical development program
* Documents not provided prior to the meeting cannot be discussed
* Exchanges take into account the data available at the date of the meeting; advice and assessment given are only valuable as of the date of the meeting.

The meetings are organized upon request by the applicant. A consultant can participate in the meeting but a meeting will not be accepted if the consultant is the only one attending.

1. ***Minutes***

After the F2F meeting, the applicant will provide draft minutes and address them to the EUnetHTA ED Secretariat no later than 10 days following the meeting. The EDC members have 10 days to (optionally) comment on the minutes after which time the ED Secretariat will return the document to the applicant. The minutes will remain confidential between the applicant and EUnetHTA.

1. ***Final recommendations***

Final recommendations will be consolidated as much as possible, and individual positions will be given when there is no consensual position. The scientific coordinator gives the EDC feedback on D+110

1. ***Fees***

The participation of HTA bodies in EUnetHTA EDs may be partially covered by the EUnetHTA budget. Nevertheless, some HTABs may charge fees for their participation. Information regarding fees is available upon request from the EUnetHTA ED Secretariat.

1. ***Contact points***

The EUnetHTA ED Secretariat is the single point of contact for the applicant and other stakeholders involved (patients and other experts), unless otherwise indicated.

1. ***Processing of documents***

The EUnetHTA ED Secretariat uses Sharefile – a secure system for sending/ receiving documents between all parties.

The Applicant is responsible for sending the briefing book directly to the EUnetHTA ED Secretariat. The ED Secretariat will ensure the distribution of documents to HTAb.

Document version control, numbering, and adherence to timelines are essential to ensure all parties have the appropriate document at the correct time. It is strongly advised to avoid making significant changes to the documentation/clinical development close to the face to face meeting except where this has been previously discussed and agreed with the ED participants. This is in order to guarantee appropriate time for the revision and the evaluation by HTABs.

1. **Process and timelines**

|  |  |  |  |
| --- | --- | --- | --- |
| **Applicant submission and eligibility decision** | | | |
| **DAYS**  (Calendar) | **Applicant** | | **HTABs** |
|  | * **Applicant** submits a request including the complete briefing book[[1]](#footnote-1), using the EUnetHTA Briefing Book for Medical Devices template. | | * **EUnetHTA ED Secretariat** confirms reception to the Applicant. * **EUnetHTA ED Secretariat** sees the relevance of demand, asks for clarification and additional data if needed |
| **D0** |  | | * After checking general eligibility, **EUnetHTA ED Secretariat** shares the Briefing Book with HTABs, including any exchanges they had with the company |
| **~D0-D15** |  | | * **HTABs** indicate to the EUnetHTA ED Secretariat if they may participate * **Eligibility Decision among voluntary HTAB** * **EDC members** express their interest in including experts, patients or health professional, and if they know someone additionally interested |
| **D15-D50** |  | | * **Constitution of ED Committee** (at least 3 HTABs interested) * **Designation of ED scientific coordinator** * **EUnetHTA ED Secretariat** sends response to the Applicant, with the HTABs participating to the ED (EDC members) and provides EDC members access to the ED work area. * EUnetHTA ED Secretariat is in charge of recruiting experts (patients, health professionals etc.) * **EDC members** provide, via EUnetHTA intranet, Draft Written Positions (in the template provided) on each question received from the Applicant, indicating which of the questions raise particular concerns (= is a potential issue) deserving specific attention from the Applicant. Issues raised can also be unrelated to the questions. Distinction between major issues to be discussed in priority during F2F vs. minor issues for which a short written response to the Applicant would be sufficient. |
| **Preparation for Face to Face meeting** | | | |
| **DAYS**  (Calendar) | **Applicant** | | **HTABs** |
| **~D +50-70** | |  | * **EDC Scientific Coordinator** compiles List of Issues and organises an e-meeting: * Scientific coordinator prepares a presentation with a draft list of issues * Scientific Coordinator organises and leads an e-meeting (1.5 – 2 hours) with the EDC (and if applicable: external experts, patient(s)/patient representative(s))   The purpose of this e-meeting is to:   * Differentiate major issues to be discussed during F2F vs. minor issues that could be addressed in Final Written Recommendations or quickly during the meeting * Review common and divergent positions on each issue * identify questions for which a common position exists, allowing to produce one single consolidated answer * discuss issues for which the answers of the HTABs diverge to understand the reasons for divergence and attempt to reach consensus * have, when necessary, a discussion on whether the diverging requirements can still be accommodated within one trial or not * Following the e-meeting**, the Scientific Coordinator**   -consolidates the List of Issues (Consolidated List of Issues) and posts it on the intranet  -consolidates the Draft Written Recommendations (individual positions and first draft of common position as identified during the e-meeting) using the template available on the intranet and posts it in the ED work area on the intranet   * **EUnetHTA ED Secretariat** alerts EDC when consolidated List of Issues is available. * **EUnetHTA ED Secretariat** sends the compiled List of Issues to the Applicant (+D70) * EDC Scientific Coordinator conducts interview with representative from EU expert organisations and/or EDC members conduct interviews with national expert(s). One identical questionnaire to be used per ED with the English version of the interview minutes will be shared with the EDC. |
| **D+70-85** | | * Applicant reviews EDC list of issues * Applicant submits responses to the key issues (optional) + slides for F2F meeting before D+85. | * **EUnetHTA ED Secretariat** uploads the Applicant’s slides to the ED work area on the intranet. |
| **Face to Face meeting and finalisation** | | | |
| **DAYS**  (Calendar) | | **Applicant** | **HTABs** |
| **~D +90**  **Early Dialogue Meeting** | |  The meeting is organised and hosted by the **EUnetHTA ED Secretariat**. The chair for the HTABs will be the **EDC Scientific Coordinator**.   Preliminary discussion among HTA bodies and external stakeholders on the morning.   **Afternoon session (max. 3 hours): F2F meeting of HTA bodies with the Applicant**   * Conclusions among HTA bodies only | |
| **D90-+100** | |  The Applicant provides detailed **minutes of the meeting** D100 for informational purposes. These may serve in finalizing the HTAB written answers. | * **EDC Scientific Coordinator** updates the common Draft Written Recommendations following discussion at the F2F meeting, uploads them to the work area and alerts EDC members (cc EUnetHTA ED Secretariat). * **EDC members** review and propose changes (in track changes mode) to the common positions and finalise their individual position and posts them in the ED work area, notifying the Scientific Coordinator when finished (D +100). |
| **~D +100-+110** | |  | * **EDC Scientific Coordinator** finalises (in track changes mode) the Common Draft Written Recommendations and posts the document in the ED Work Area for EDC validation (Final Written Recommendations). When done, EDC Scientific Coordinator uploads the Final Written Recommendations and alerts EDC by e-mail (cc EUnetHTA ED Secretariat). 3 working days are allocated for review of the consolidated part and return of comments. ED Scientific coordinator informs the EUnetHTA ED Secretariat when the document is final. * **EUnetHTA ED Secretariat** sends the Final Consolidated HTA ED Written Answers to Applicant. |

1. Including its annexes:

   The protocol of pivotal trial(s)

   The investigator’s brochure, if available

   A zip file containing all publications and study reports referenced in the briefing book [↑](#footnote-ref-1)