

Amended draft procedure for early dialogue pilots to be conducted by EUnetHTA partners

Based on the procedure used for two preparatory pilots conducted in June and July 2012,
this procedure is to be used for the initial pilots of Early Dialogue within EUnetHTA Joint Action 2.

1. Scope of early dialogue pilots

Pilot early dialogues with HTA organizations representatives may be requested for a new technology for questions pertaining to relative effectiveness, economic and other aspects of development of a drug (new chemical entity or new biological product) or a non-drug technology (e.g. medical device, diagnostic, procedure) with supposed added benefit for patients. Co-development (e.g. drug and diagnostic test, medical device and procedure) can also be included. Pilot early dialogues are restricted to only one indication and/or one line of treatment.

Pilot early dialogues are **prospective in nature** (advice on ongoing trials is out of scope).

An early dialogue allows input on developments which can be taken into account by developers after the early dialogue meeting with HTA bodies. It focuses on development strategies and not on pre-evaluation of data. Early dialogue pilots can be requested during the initial clinical development phase of the technology, ideally at the end of the phase II to discuss the content of the planned Phase III i.e. planned confirmatory trial(s) and the economic rationale. The scope of early dialogue might be broadened in the future (JA2) to include considerations on post appraisal studies.

The “pilot” advice given by HTA organisations **is not binding** either for HTA bodies or for the company.

The specific advice on the drug in development will be shared only with the company that requested advice. Confidentiality agreements will be signed between the company and participating HTA organizations if requested by the company. Organisational/governance and procedural issues related to early dialogue pilots may be shared more widely and will be used to develop a future procedure (to be elaborated during EUnetHTA JA2).

2. Structure/content of the request for an early dialogue pilot

▪ Letter of intent

A letter of intent should be sent by email to HAS (m.pavlovic@has-sante.fr and a.gourvil@has-sante.fr) at least **4 months** in advance of the anticipated start of the procedure. It can be sent without any additional documentation attached. The rest of the documents pertinent to the request are to be sent 2 months later.

It should include the following information:

- Applicant and contact person details
 - Name of technology (company code or INN, and proposed trade name)
 - Description of the technology and mechanism of action
 - Type of technology or product (chemical, biotechnological, advance therapy, therapeutic scientific or technical innovation, diagnostic)
 - Intended indication(/line of treatment) for the scope of the early dialogue
 - Therapeutic field (and ATC code if applicable)
 - Development status
 - Area of advice
 - Aimed start of procedure
 - Company's wishes for HTA bodies to participate to the meeting if applicable (HAS will try to meet company's wishes; however, additional HTA bodies belonging to the EUnetHTA network may be invited)
- #### **▪ Application file including the Questions and Company's positions**

The application file should contain the following information (approximately 50 pages)

- Table of contents
- Lists of figures, tables, abbreviations
- I. Summary: section containing background information on the disease/population to be treated with all relevant information (epidemiology, natural history of the disease, treatments and evolution on treatment), on the technology, on the development, on the regulatory status and explaining the rationale for seeking advice

- II. Questions and company's position: the questions should pertain to relative effectiveness, economic and other aspects of the development of the proposed technology. The wording of questions should be clear and concise. Each question should be followed by a corresponding, separate Company's position including a comprehensive justification of the chosen approach. All key information about the topic should be sufficiently discussed, so that the Company position can function **as a 'stand alone' argument**. In general, **an extension of 1 to 3 pages for each Company position is recommended**. Cross-references to the relevant parts of the briefing document or annexes can be included if additional detail is needed to support the argument.
- III. Background documentation: this section should give a comprehensive scientific overview of the product development program (clinical data obtained up to now, as well as rationale and proposal for the confirmatory clinical trial), providing relevant systematic information in sufficient detail, together with a critical discussion.
- List of key references

Key references, i.e. study protocols (final, draft or outline/ synopsis), study reports (final/draft/synopses), previous scientific advice received, relevant therapeutic guidelines and relevant literature references

3. Procedure for the early dialogue pilots

The letter of intent should be sent by email to the HAS which is the coordinator of these pilots (m.pavlovic@has-sante.fr and a.gourvil@has-sante.fr) at least **4 months** in advance of the anticipated start of the procedure. It can be sent without any additional documentation attached. The rest of the documents included in the request are to be sent 2 months later.

The draft application file (table of contents, summary, questions/company's position and background documentation) should be forwarded to HAS at least **2 months and 15 days** before the face-to-face meeting with HTA bodies.

As soon as the content of the application file is validated by HAS and at least 2 months before the face-to-face meeting, the revised complete dossier should be sent to HAS as 1 electronic copy (start of procedure). In addition, one paper copy of the briefing document (without the annexes) may be sent by the company on request. At least the Cover letter, the briefing document including the question(s)/company's position(s) and the table of contents should be submitted in these final sets in MS Word format, the Annexes and References can be either MS Word or searchable PDF documents (scanned PDF's which cannot be searched/annotated are not acceptable). Prompt delivery of the final package will enable HTA organisations to review the information with sufficient time.

DAYS (calendar days)	ACTION
D -60: Start of procedure	<ul style="list-style-type: none"> • Submission by the company of the early dialogue request validated by HAS to all participating HTA bodies
D -45	<ul style="list-style-type: none"> • A teleconference or e-meeting with HTA bodies is organized by HAS to identify possible missing information related to the application file and to the proposed development plan (list of main issues that should be addressed by the company either in writing or at the next face-to-face meeting). • The company is informed of the outcome of the teleconference/e-meeting and additional data or clarifications requested if needed
D -30	The company provides additional information or clarification as needed
D -7:	Short written answers to company's questions are sent by each HTA participant to the coordinator
D -3:	Individual HTA positions are released to participating HTA organisations in the format of a compiled document

DAYS (calendar days)	ACTION
D 0: Early Dialogue Meeting	<ul style="list-style-type: none"> • Preliminary discussion among HTA organizations (without the company) • Face-to-Face meeting with the company and HTA organizations • Conclusions among HTA organizations (without the company)
D +7	The draft detailed minutes of the meeting relating general and individual HTA bodies positions for each question is provided by the company
D +20: End of procedure	The detailed minutes are reviewed and corrected in writing by HAS and participating HTA organisations. In case of remaining uncertainties, a teleconference or e-meeting with HTA bodies may organized by coordinator.

▪ **Early dialogue meeting organisation**

The early dialogue meeting is a one-day meeting (e.g. from 10.30 a.m to 17.30 p.m) dedicated to one early dialogue procedure. It is organised and hosted by HAS (2 avenue du Stade de France – Saint-Denis La Plaine, France).

The meeting is generally organised as follows:

- 10.30 - 12.30: Preliminary discussion among HTA organizations (without the company)
- 13.30 -16.30: Face-to-Face meeting with the company and HTA organizations
- 16.45 -17.30: Conclusions among HTA organizations (without the company)

Three hours is allocated to the company for the Face-to-Face meeting. The company will address each question and the main issues that were identified by the HTA organisations (if applicable). Each question/issue will then be followed by a general opinion and the opinion of each HTA organisation representatives. Official representatives of HTA bodies will essentially express their personal HTA expert opinion on the subjects to be discussed which is not committing the corresponding agencies.

Preliminary conclusions will be drawn at the end of the Face-to-Face meeting. A debriefing by the HTA organisation representatives will follow in order to further discuss issues and to draw conclusions. The company will be asked to provide minutes of the meeting 7 days after the meeting with the coordinator and all HTA participants.