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Guidance on parallel consultation

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no longer valid - will be updated shortly

Abbreviations

AEMPS	Agencia Española de Medicamentos y Productos Sanitarios
AETSA	Área de Evaluación de Tecnologías Sanitarias de Andalucía
AIFA	Agenzia Italiana del Farmaco, Italy
AQuAS CatSalut	Agència de Qualitat i Avaluació Sanitàries de Catalunya Servei Català de la Salut
ATMPs	Advanced Therapy Medicinal Products
CAT	Committee for Advanced Therapies
CHMP	Committee for Medicinal Products for Human Use
COMP	Committee for Orphan Medicinal Products
EC	European Commission
ED	Early Dialogue
EDWP	Early Dialogues Working Party
EDC	Early Dialogues Committee
EU	European Union
EMA	European Medicines Agency
EUnetHTA	European Network for Health Technology Assessment
F2F	Face to Face
G-BA	Gemeinsamer Bundesausschuss, Germany
HAS	Haute Autorité de Santé, France
HCP	Health Care Professional
HTA	Health Technology Assessment
HTAb	Health Technology Assessment bodies
JA	Joint Actions
LoI	Letter of Intent
NCA	National Competent authority
NIPN	National Institute of Pharmacy and Nutrition, Hungary
NOMA	Norwegian Medicines Agency
PC	Parallel Consultation
PSA	Parallel Scientific Advice
PDCO	Paediatric Committee
PLEG	Post Licensing Evidence Generation
PRAC	Pharmacovigilance Risk Assessment Committee

RER	Regione Emilia-Romagna, Italy
SAWP	Scientific Advice Working Party
SEED	Shaping European Early Dialogues
SME	Small or Medium Enterprises
TC	Teleconference

no longer valid - will be updated shortly

1 Introduction

As the first step to market access, a new medicine requires a marketing authorisation from a medicines regulatory agency. Following regulatory approval, Health Technology Assessment (HTA), providing evidence-based information and analysis, takes place at the national level in accordance with national practices and legislative frameworks¹. Health Technology Assessment is then used to inform subsequent decisions on coverage (reimbursement) and price of an authorised drug at the national level.

Interactions between medicines' developers, Regulators and Health Technology Assessment bodies (HTAbs) or other possible stakeholders to discuss the development plan means that evidence can be generated to meet the needs of respective decision-makers as efficiently as possible. Thus, a strong interaction between Regulators and HTAbs/other relevant stakeholders is critical to facilitate patients' access to important new medicines and hence for the overall benefit of public health.

The European Medicines Agency (EMA) is the EU body responsible for coordinating the existing regulatory and scientific resources put at its disposal by EU Member States for the evaluation, supervision and pharmacovigilance of medicinal products, including the provision of Scientific Advice for regulatory purposes.

The European Network for Health technology Assessment (EUnetHTA) was established to create an effective and sustainable network for HTA across Europe – working together to develop reliable, timely, transparent and transferable information to contribute to HTA in European countries, creating a sustainable system of HTA knowledge sharing, and promoting good practice in HTA methods and processes. EUnetHTA Joint Action 3 (JA3) aims to define and implement a sustainable model for the scientific and technical cooperation on HTA in Europe, and is co-funded by the European Commission (EC). Within EUnetHTA JA3, Work Package 5 (WP5) aims at bridging the gaps between patients, caregivers, technology developers, current registry holders, and authorities in the health care sector, HTA producers and HTA users. Its main objective is to help to generate, all along the technology lifecycle, optimal and robust evidence for different stakeholders, bringing benefits for patient access and public health.

EUnetHTA and EMA platform on evidence generation interactions

This platform comprises enhanced collaboration for Parallel regulatory HTA Scientific Advice/Early Dialogues (henceforward referred to as Parallel Consultation) between EMA and EUnetHTA. Parallel Consultation provides a single gateway for requests for parallel discussions before the start of pivotal clinical trials on initial evidence generation for Marketing Authorisation Application/Reimbursement, and Post Licensing Evidence Generation (PLEG) involving EMA, EUnetHTA and HTA bodies. Partnership of EMA and EUnetHTA also allows for: streamlined logistics, improved HTA coordination through EUnetHTA ED Secretariat, greater participation via the involvement of EUnetHTA HTA Early Dialogue Working Party (EDWP)², and maximum gain from the parallel procedure by optimising opportunities for mutual understanding and problem solving between Regulators and HTAs. This facilitates optimal and robust evidence generation for different stakeholders bringing benefits for patient access and public health.

¹ Development of archetypes for non-ranking classification and comparison of European National Health Technology Assessment systems. Allen et al. Health Policy 2013, Volume 113, Issue 3, December 2013, Pages 305–312

² Composition of the Early Dialogue Working Party: France (Haute Autorité de Santé: HAS), Germany (Gemeinsamer Bundesausschuss: G-BA), Hungary (National Institute of Pharmacy and Nutrition: NIPN), Italy (Italian Medicines Agency: AIFA with alternate Regione Emilia-Romagna: RER), Norway (Norwegian Medicines Agency: NOMA), and Spain (Agencia Española de Medicamentos y Productos Sanitarios: AEMPS with the support of regional agencies Área de Evaluación de Tecnologías Sanitarias de Andalucía: AETSA and Agència de Qualitat i Avaluació Sanitàries de Catalunya Servei Català de la Salut: AQUAS-CatSalut)

For all submitted requests, the EUnetHTA ED Secretariat facilitates centralised HTA recruitment, and selection criteria is applied by the EDWP in order to decide if the request is accepted for a Parallel Consultation. The EDWP selection criteria and process are fully explained below in section 3.3. Other products which are not selected for a parallel consultation could pursue a regular Scientific Advice procedure with EMA and may be eligible for national advice from some HTAbs.

All Parallel Scientific Advices will be conducted through this Parallel Consultation Platform.

This guidance replaces the "Guidance for Parallel Consultation" (EMA/410962/2017 Rev.2) as of the date of publication.

Key modifications in this version include:

- All provided recommendations will be consolidated amongst HTA bodies;
- A shortened procedure with 2 different procedural formats (Written-only or with F2F meeting);
- Updated composition of the EDWP

2 Principles

2.1 Roles and remits

This guidance highlights ideal timelines and actions for each party undertaking a Parallel Consultation.

This is a multi-stakeholder procedure with Regulators and HTAbs being equal partners. As a multi-stakeholder procedure, collaboration and communication between all stakeholders are important to ensure agreement and clarity on the ownership of different actions, and to deliver on the objectives of the exercise.

Each participating body should adhere to the roles and responsibilities under their respective remit.

2.2 Confidentiality

By submitting a request for a Parallel Consultation, the Applicant agrees to the exchange of information between EMA and participating EUnetHTA HTAbs.

The Parallel Consultation process is confidential.

EMA and associated regulatory experts are bound by EMA code of conduct, and confidentiality agreements, and operate under the EMA policy on access to documents (Policy/0043).

EUnetHTA prioritises confidentiality and each HTAb participant and associated expert is required to submit a signed EUnetHTA [Confidentiality Agreement](#).

Therefore, commercially confidential information provided to the EMA and EUnetHTA within the context of a Parallel Consultation is not shared with any party preauthorisation outside of the respective Regulator and HTA networks in the absence of a signed confidentiality undertaking or the consent of the sponsor.

2.3 Conflict of interest

EMA: Conflict of interest of regulatory experts, health care professionals (HCP) and patient representatives is handled in line with Policy 44.

EUnetHTA: Conflict of interest of HTAb participants, health care professionals (HCP) and patient representatives is handled through the EUnetHTA [Declaration of Interest \(DOI\) form](#). Further information can be found in the [EUnetHTA Procedure Guidance for handling Declaration of Interest \(DOI\) form](#).

2.4 Status of parallel consultation outputs

The advice provided by each stakeholder is not legally binding.

European Medicines' Regulators take the Committee for Medicinal Products for Human Use (CHMP) Scientific Advice/Protocol Assistance provided into consideration during the Marketing Authorisation Application (MAA). The Applicant needs to justify fully any deviations from the advice given. Please see the EMA Scientific Advice Guidance document for further details.

Advice provided by EUnetHTA partners is based on the documentation provided by the Applicant. The recommendation reflects the state-of-the-art of medical science and national requirements at the time of advice.

3 Actors and scope

The process described herein is only for Parallel Consultation jointly involving EMA and EUnetHTA. For regulatory-only, or HTA-only procedures, please see EMA and EUnetHTA websites.

3.1 Regulators: actors and scope

The Scientific Advice Working Party (SAWP) is an EMA standing working party with the remit of providing Scientific Advice and Protocol Assistance to Applicants, advising on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of medicinal products (See "Mandate, objectives and rules of procedure of the Scientific Advice Working Party (SAWP)" (EMA/CHMP/SAWP/69686/04 Rev 14).

The SAWP Coordinator is a medicines regulator and a member, or alternate member, of SAWP who is responsible for providing reports further to the Scientific Advice or Protocol Assistance requests, addressing comments from the SAWP Working Parties, and EMA Committees, drafting the SAWP List of Issues, acting as one of the 2 co-chairs for the face to face meeting, and drafting the final report for further input and consideration by SAWP and EMA Committees.

The EMA Scientific Officer supports the SAWP Coordinators with scientific and administrative coordination. This is the principal EMA contact person to which the Applicant and EUnetHTA should address all matters related to an individual procedure.

The EMA Scientific advice secretariat informs the Applicant and EUnetHTA ED Secretariat who has been appointed as EMA Scientific Officer after the receiving the Letter of Intent. EMA sends an EMA contact sheet to the Applicant and the EUnetHTA ED Secretariat including all details for regulator participants (i.e. SAWP Coordinators, EMA Scientific Officer, assistant and other contacts, if applicable) close to the start of the procedure (evaluation phase).

For the EMA, through the Parallel Consultation, the Scientific Advice or Protocol Assistance provided to the Applicant is substantive, is prepared pursuant to Article 57 (1.n) of Regulation (EC) No 726/2004 and is adopted by CHMP having been elaborated through the SAWP.

Applicants may request advice on any medicinal products for use in humans, (as defined in Directive 2001/83 (as amended)), irrespective of the medicinal product's eligibility for the centralised procedure,

and at any stage of the product lifecycle. This may include very early strategic advice, advice on novel development plans, broad advice, plans for pivotal phase III studies, post-authorisation safety and efficacy studies, advice on the development of registries, or risk management planning incorporating risk minimisation measures.

3.2 EUnetHTA and HTAb: actors and scope

The Early Dialogues Working Party (EDWP) is a standing committee composed of permanent national and regional HTAb members i.e. AEMPS (with the support of regional agencies AQuAS-CatSalut and AETSA) for Spain; AIFA/RER for Italy (AIFA and RER respectively share their membership in the ED Working Party and must therefore decide, for each ED, which of them is to participate to a relevant ED); G-BA for Germany; HAS for France; NIPN for Hungary and NOMA for Norway.

The ED Working Party is the standing working party of the HTA bodies for the performance of the scientific advice and is responsible for the following tasks:

- i. assess the eligibility of advice requests in view of the Eligibility Criteria, as specified in Section 3.3.2, and report to the ED Secretariat on the eligibility and acceptance of the scientific advice requests;
- ii. participate in the performance of the scientific advice
- iii. engage national experts in the framework of EDs, who cooperate on a voluntary basis.

A EUnetHTA Scientific Coordinator and Rapporteur will be assigned for each ED from among the EDWP members. The Scientific coordinator is responsible for providing EUnetHTA final consolidated recommendations to the applicant addressing comments from the EDWP, drafting the EDWP List of Issues, acting as one of the 2 co-chairs for the face to face meeting for those procedures requiring a face to face meeting, and drafting the final report for further input and consideration by EDWP.

The Rapporteur supports the Scientific Coordinator in the different tasks listed before.

The EUnetHTA ED Secretariat is responsible for all practical coordination of HTAb participation in a Parallel Consultation. Together with the EMA Scientific Officer, on the regulatory side, the EUnetHTA ED Secretariat acts as the sole HTAb contact point for all Parallel Consultations. Additionally, the EUnetHTA ED Secretariat is responsible for insuring the receivability of a request and all project management on the HTAb side. Finally, the EUnetHTA ED Secretariat is responsible to engage patients and patients' representatives (with the exception of German patients, who will be engaged via G-BA) and HCPs to provide expert input related to i.a. the condition, treatment and expectations of patients and the proposed development.

The EUnetHTA Scientific Coordinator undertakes scientific coordination on behalf of HTAs. For all procedures, the EDC Scientific Coordinator facilitates discussion between HTAbs in advance of meetings, interacts with the EMA and acts as a co-chair for the HTAb for those procedures requiring a face to face meeting. Further information on the Parallel Consultation format can be found in the respective section of this guidance document.

The EUnetHTA Rapporteur collects and consolidates responses from the EDWP and presents consolidated HTAb answers during the F2F Meeting. The Rapporteur interacts with the EDC Scientific Coordinator and EMA on scientific matters.

3.3 HTA involvement in parallel consultations

3.3.1 Call for submissions

The EUnetHTA ED Secretariat will publish a call for applications for Parallel Consultations. Upon receipt of the Letter of Intent, the ED Secretariat examines the document for its acceptability (ensuring all necessary information is included). EUnetHTA reserves the right to contact the Applicant in order to discuss their request. After the call has closed, all acceptable requests are passed to the EDWP. The EDWP scrutinises all requests for Parallel Consultation, according to the established EDWP selection criteria (detailed in section 3.3.3) to decide if a request is selected for a Parallel Consultation.

The EUnetHTA ED Secretariat communicates the outcome of the selection to all Applicants. For those requests that are selected, information will also be provided regarding the final participating HTAbs (including any need for direct subsequent unilateral arrangements or contracts between the individual HTAbs and Applicant, and contact points for such arrangements) to the Applicant and EMA according to the Parallel Consultation format and to the process outlined in [Table 2](#) and [Table 3](#).

3.3.2 EDWP selection criteria, scope and coordination

In a context of resource constraints in JA3, there is a limit to the number of products to be selected for Parallel Consultation.

The product should aim to bring added benefit to patients i.e. by:

A new mode of action for the indication

AND targeting a life-threatening or chronically debilitating disease

AND responding to unmet need (no treatment or only unsatisfactory treatment available)

EUnetHTA aims for a diverse selection of Parallel Consultations and therefore selected EDs should represent a wide array of topics, therapeutic areas etc. (e.g. orphan, ATMPs, anti-infectives, oncology). The Applicant's Letter of Intent should provide sufficient information to substantiate the claimed basis of selection and follow the guidance notes provided with the form.

The generation of consolidated HTA outputs through the EDWP involves identifying aspects of development programs for which there is a shared position amongst HTAbs and attempting to reach consensus amongst HTAbs. Where necessary individual positions will be presented in the document annex. There is a single written report including: consolidated EUnetHTA Final Recommendations for shared positions, and individual HTA answers to those questions for which consensus was not possible. Opportunities for closed discussion with Regulators, with mutual understanding/problem solving are maximised, regardless of the format of the procedure. See [Table 2](#) and [Table 3](#).

3.3.3 Parallel consultation formats

There is one single procedure for Parallel Consultation; however, there are two different formats the consultation can take, following selection of a product: written only format and F2F meeting format. All Parallel Consultations are supported by the EUnetHTA ED Secretariat, thereby benefiting from HTA scientific and administrative coordination, consolidated HTA comments and List of Issues, a concerted effort to find agreement among the EDWP regarding specific issues as well as a consolidated document containing EUnetHTA's Final Written Recommendations. Opportunities for closed discussion amongst HTA, and with Regulators, with mutual understanding are maximised.

Regardless of the format of a parallel consultation the HTAb final output remains the EUnetHTA Final Written Recommendation.

Preliminary exchange on procedure format and associated organisational topics will be exchanged with EMA during the Administrative TC.

3.3.3.1 EUnetHTA decision criteria for procedure format

The decision as to which format the procedure will follow will be decided by the EDWP after review of the Applicant's Draft Briefing Book. This decision will be based on:

- PRIME products
- Complexity of development
- Need for an in-depth discussion with the applicant about the development plan, e.g. in case of unclear development plan or unexperienced companies
- Major issues with the development plan that would benefit from discussion with the applicant.

The applicant will be informed of the decision upon reception of the Final Briefing Book.

3.3.3.2 Written-only Parallel Consultation format

The PC format without a F2F meeting allows for more efficiency and provides the applicant with Final Recommendations in a shorter timeframe while maintaining the exchanges between HTAb and EMA and the high-quality output expected of EUnetHTA. This format allows for the EDWP to work directly on their recommendations following reception of the Final Briefing package and does not require the applicant to produce written answers to a EUnetHTA List of Issues as one will not be produced in the written format since the choice of the format suggests no major issues.

Procedures that do not require a F2F meeting will be approximately 2,5 months in duration starting from reception of the Draft Briefing Book. The full procedure is detailed in [Table 2](#).

3.3.3.3 Parallel Consultation format with F2F meeting

The PC format with a F2F meeting allows for a direct exchange between the participating HTAb and the Applicant. The applicant will be provided with Final Recommendations only a certain timeframe after the F2F meeting, the total duration of the procedure therefore lasts longer. Exchanges between HTAb and EMA and the high-quality output expected of EUnetHTA are guaranteed for this procedure as well. The applicant needs to produce written answers to a EUnetHTA List of Issues.

Procedures that do require a F2F meeting will be approximately 3,5 months in duration starting from reception of the Draft Briefing Book. The full procedure is detailed in [Table 3](#).

3.4 Other stakeholders

From an early stage, the EMA along with HTAbs may consider the need for additional clinical experts in a given procedure and F2F meeting. The inclusion of patient representatives is expected on a routine basis.

EMA

Regulators' clinical experts are identified through National Competent Authorities (NCA) and SAWP members. A Health Care Professional (HCP) representative may also be invited by the EMA through the EMA HCP Working Party framework, as well as other stakeholders as appropriate.

Individual patient experts are identified through patient organisations under the framework for interaction between the EMA and patients and consumers, and their organisations (EMA/637573/2014).

Where possible, patient representatives are invited to attend all TCs and the F2F meeting; briefing of chairpersons (on the inclusion of a patient representative) and patients (on the aims and nature of the meeting) by EMA Scientific Officer is essential. Any additional time or facilities required by patients should be considered.

EMA exchanges with EUnetHTA ED Secretariat on the participation of clinical experts and/or patient representatives.

EUnetHTA

EUnetHTA is committed to involving experts (patients and HCP) in its work – including EDs. Hearing directly from patients about the outcomes that matter to them and how their condition impacts their quality of life and hearing directly from HCP about natural disease history and current disease management are areas that are important from an HTA perspective.

EUnetHTA systematically endeavours to involve patients and patients’ representatives in all of its EDs. In order to best capture this input, EUnetHTA employs three approaches which are outlined in **Table 1** below.

Table 1: EUnetHTA’s three approaches to Expert Involvement

Approach	Expert Deliverables
Approach 1: Expert interviewed regarding the disease and their experience.	<ul style="list-style-type: none"> • Minutes of the interview • Expert contribution visible in final EUnetHTA recommendations • Feedback questionnaire and interview
Approach 2: Approach 1 + discussion with local HTAb regarding submission file (without applicant).	<ul style="list-style-type: none"> • Minutes of the interview • Expert contribution visible in final EUnetHTA recommendations • Feedback questionnaire and interview
Approach 3: Approach 2 + discussion with all participating HTAbs regarding the submission file and participation in the F2F meeting with the applicant ³ .	<ul style="list-style-type: none"> • Minutes of the interview • Expert contribution visible in final EUnetHTA recommendations • Share final EUnetHTA recommendations • Feedback questionnaire and interview

The selection of which approach to be used is the responsibility of the EUnetHTA ED Secretariat, who is also responsible for recruitment. This decision is based on multiple factors including: the identification of a patient and/or healthcare professional corresponding to a specific approach, Furthermore, it is possible that multiple approaches may be used in the same ED.

³ In the case of a procedure with a F2F meeting.

The EUnetHTA ED Secretariat exchanges with EMA on the participation of clinical experts and/or patient representatives.

4 Process

4.1 Simultaneous notification

For all Parallel Consultations, the Applicants who received a notification of pre-selection by EUnetHTA after the Open Call (see section 3.3) should simultaneously notify the EMA Scientific Advice secretariat (scientificadvice@ema.europa.eu) and EUnetHTA ED Secretariat (eunetha-has@has-sante.fr) by means of a Letter of Intent using the available [form](#) for Parallel Consultations. The EMA and EUnetHTA should receive the Letter of Intent and draft briefing package prior to the deadline published for the intended procedure start date.

This Letter of Intent deadline is approximately 1 month (day-30) before the formal procedure start date (day 0 or SAWP 1) and 3 months before the intended face to face meeting (day 60 or SAWP 3 meeting).

The EUnetHTA ED Secretariat conducts a check to ensure the submission is consistent with the date for which the product was pre-selected and sends a confirmation to the Applicant.

The final decision on composition of the participating HTA members, Scientific Coordinator, Rapporteur, and presubmission TC request outcome is communicated to the EMA Scientific Officer, the EMA Scientific Advice secretariat and the Applicant within 5 working days.

EMA and EUnetHTA ED Secretariat will then mutually agree the allocation of face to face meeting slots, accommodating any closed HTA meetings, considering the batch of requests for the intended start date. EMA will confirm the date and time of the F2F meeting in writing to EUnetHTA ED Secretariat and the Applicant by approximately day -40.

4.2 Presubmission phase

For all Parallel Consultations, the presubmission phase starts, when the Applicant sends the draft briefing package to the EMA Scientific Officer, the EMA Scientific Advice secretariat (scientificadvice@ema.europa.eu), and to the EUnetHTA ED Secretariat (eunetha-has@has-sante.fr).

Default without presubmission TC

By default, the presubmission phase is based on written comments on the draft briefing document.

The draft briefing package should be sent at least 30 days before the due start date (Day 0 or SAWP1) of the procedure. (See published EMA Scientific Advice [published timetables](#) for a 70 day procedure; SAWP 3 provides the intended face to face meeting date).

In addition to the standard EMA timetables, EMA sets up a timetable in consultation with the EUnetHTA ED Secretariat for each procedure including closed EMA EUnetHTA interactions following receipt of the Letter of Intent from the Applicant and confirmation of EDC selection/participating HTA bodies from EUnetHTA ED Secretariat. EMA sends this timetable to all participants. Calendar meeting requests are sent by EMA to EUnetHTA ED Secretariat and other regulatory participants shortly after a TC or meeting is confirmed.

The Applicant sends Draft Briefing Document to EMA Scientific Advice secretariat (scientificadvice@ema.europa.eu), and the EUnetHTA ED Secretariat (eunetha-has@has-sante.fr) in accordance with the agreed timeline. It is important that the timelines are adhered to so that that

participants have sufficient time with the draft briefing document in order to provide feedback to the Applicant, and also such that there is sufficient time for the Applicant's revision before the agreed formal start of the procedure. Initial written comments from the EMA and EUnetHTA ED Secretariat (collated comments from HTAbs) are provided directly to the Applicant by 15 working days, where necessary for the optimisation of the draft submission prior to the start of the procedure.

Comments are shared between EMA Scientific Officer and EUnetHTA ED Secretariat, and consider: the scope, wording and clarity of the questions, whether the material provided in the briefing package is sufficient to answer the questions posed, whether all the right questions have been asked or if additional questions should be added, and to consider whether the questions are appropriately addressed to HTAbs, Regulators or both.

Finalising the briefing document

The Applicant sends a revised final briefing document with all annexes and references having addressed the EMA comments and EUnetHTA ED Secretariat points of clarification (if any) to the EMA Scientific Officer and EMA Scientific Advice secretariat (scientificadvice@ema.europa.eu) and to EUnetHTA ED Secretariat (eunetha-has@has-sante.fr), at least 2 full working days before the start of the procedure. One version should be in "track changes" mode and the other should be "clean". Both EMA and EUnetHTA ED Secretariat conduct an administrative check to ensure the briefing package is fit for purpose (i.e. that all annexes and references are present and readable, and that any essential changes have been made to the briefing document).

Following confirmation of validation from both EMA and EUnetHTA ED Secretariat, as well as the confirmation of the PC format from the ED Secretariat, the Applicant sends the final briefing document directly to all EMA contacts in the procedure as instructed and to the EUnetHTA ED Secretariat, via Eudralink, before the start of the procedure. The Applicant should ensure that the final briefing document has been received by all participants.

The presubmission phase ends with the circulation of the final briefing document immediately prior to SAWP 1, as in the published Scientific Advice timelines.

4.3 Evaluation phase

Lists of Issues for F2F meeting format

For all Parallel Consultations, Lists of Issues facilitate the discussion during the face to face meeting by indicating the focus of Regulators' and HTAbs' discussion.

In the regulatory process, the SAWP discusses the first reports (preliminary views) at the SAWP 2 meeting and drafts a Regulators' List of Issues by approximately day 32 of the procedure.

In the EUnetHTA process, EDWP members participating in the advice discuss draft positions and major issues (following FICO) pre-listed by the Scientific Coordinator and Rapporteur during an e-meeting around day 30 of the procedure.

Exchange between regulator and HTAb

The purpose of the pre-face to face TCs is to exchange and understand respective (preliminary) positions of the different Regulator and HTAb participants on the major aspects of trial designs such as population, comparator or endpoints should be identified. Potential solutions that could facilitate one trial, or at least one development plan, could be discussed in advance of the face to face meeting. The Regulator's chairperson for the F2F meeting should be agreed in the pre-face to face TC.

The EMA arranges a first closed preparatory TC between EMA, Regulators and EUnetHTA (ED Secretariat, Coordinator and Rapporteur), to take place around day 32 of the procedure, focusing on draft recommendations and issues identified (for F2F meeting format) by Regulators and HTAbs. If the procedure is following the F2F meeting format, final versions of List of Issues are sent to the Applicant by the EMA and EUnetHTA ED Secretariat respectively after the TC. They are also exchanged between EMA and EUnetHTA ED Secretariat.

Preparation for face to face meeting (applies to F2F meeting format only)

The Applicant can contact the EMA Scientific Officer and/or EUnetHTA ED Secretariat regarding the format of the face to face meeting. This is to ensure that the meeting fulfils the needs of involved stakeholders. The Applicant should send any written responses, if requested according to EMA or HTAb respective Lists of Issues, ideally 12 working days before the face to face meeting directly to all EMA contacts and EUnetHTA ED Secretariat. There should be no major changes to the development plan compared to the final briefing document, unless the process in topic "Amended development plans" has been followed.

The Applicant should send the final presentation and list of participants directly to all EMA contacts and to EUnetHTA ED Secretariat, 4 working days before the face to face meeting. Any changes to the presentation after this date will not be accepted. The presentation can include a very brief introduction, rationale and status of the program. An upper limit of 5 slides for this introduction is recommended to maximise the time available for the questions and discussion. Once sent to the meeting participants, according to the agreed timelines, the presentation should not be amended by the Applicant. There should be no major changes to the development plan compared to the final briefing document, unless the process in topic "Amended development plans" has been followed.

The EUnetHTA ED secretariat is asked to send their final list of attendees to the EMA also in advance of the meeting (1 week before the F2F). The EMA circulates a final list of all participants 2 days in advance of the face to face meeting. The meeting is hosted at the EMA premises.

Amended development plans triggered by the lists of issues or external factors.

Amended development plans triggered by the Lists of Issues or external factors can be accommodated to some extent during the evaluation phase. However, to facilitate sufficient time for review of the amended development plan, it is stressed that the Applicant should advise all parties of their intention to submit an amended development plan as early as possible, before the face to face meeting. The amended plan must be received by all parties, at the latest by 12 working days before the face to face meeting, together with a clear comparative table of changes in the plans and justification for the changes. Any substantial changes to the development plan submitted past this date cannot be addressed within the face to face meeting or minutes.

Face to face discussion meeting

The aims of the face to face meeting are:

- To discuss issues of concern or disagreement from regulators and/or HTAbs with the Applicant's proposal regarding major aspects of trial designs
- To get a mutual understanding of each body's constraints as it has to be acknowledged that regulators and HTA bodies are operating in distinct remits (benefit/risk evaluation vs added value evaluation). Possible resulting divergences between HTAbs and regulators positions on major aspects of the trial design will be discussed.

- To share and discuss preliminary positions on major aspects of trial designs from EUnetHTA with all participants
- To discuss potential solutions that could facilitate one trial design or at least one development plan

The face to face meeting has 2 co-chairs: one from the Regulators and one from the HTAbs. The meeting duration will depend on the range of issues to be discussed and advice format, the maximum length of the meeting is 3 hours.

Before the Applicant enters the room, the Regulators and the HTAbs have the opportunity to have a closed session (between 15 to 45 minutes, the time is determined on a case by case basis in a pre face to face TC; Applicants will be informed accordingly) in order to interact on any possible changes of position after the Applicant's responses and presentation. EUnetHTA will share the outcome of the closed HTAb meeting with EMA with a summary of common positions on major issues and related expert input.

The meeting with the Applicant is interactive, focusing on the issues raised by the Regulator and the HTAbs in the Lists of Issues. It is usual to pause after each question/issue for discussion. During the face to face meeting, the views of each stakeholder should be clearly represented on each issue. Time should be allowed for summing up at the end of the meeting.

Following the face to face meeting, a closed debriefing between HTAbs and Regulators should be held. This is dedicated to the recap, identification and discussion of any outstanding divergences, where such divergences mean that a single development plan/trial could not be carried out. There might be situations in which the divergences cannot be resolved due to differences in the Regulators' and HTAbs' assessment questions and remit. Possible ways to further address these divergences should be considered (e.g. methods for indirect comparisons, multi-stakeholder workshops, broad advice, and qualification procedure or a follow up Parallel Consultation).

The Applicant is expected to send detailed minutes of the face to face meeting, within 5 working days directly to all EMA contacts and to EUnetHTA ED Secretariat. The minutes should reflect the views for each participating stakeholder in the face to face meeting discussion. Areas of agreement and divergence of opinion between Regulators and HTAbs should be summarised by the Applicant. Minutes are regarded as an Applicant's record of the meeting and will not, in general, be endorsed by the participating bodies.

Table 2 Outline of actions for Applicant, EMA and EUnetHTA in Parallel Consultations following the **Written-only format**

Day ⁴	Applicant	EMA	EUnetHTA
Letter of intent and draft briefing package			
D - 30	Applicant submits the letter of intent and the draft briefing document with annexes and references simultaneously to the EUnetHTA ED Secretariat and to the EMA via Eudralink ⁵ .	<p>EMA confirms reception.</p> <p>Communication of EMA contact point (EMA Scientific Officer) to Applicant and EUnetHTA ED Secretariat. The letter of intent is forwarded by the EMA Scientific Advice secretariat to the SAWP for appointment of 2 SAWP Coordinators and, where appropriate, a SAWP Coordinator for questions relating to significant benefit (only applicable for Protocol Assistance).</p>	<p>EUnetHTA ED Secretariat confirms reception to the applicant and informs EDWP.</p> <p>Appointment of Scientific coordinator and rapporteur, information shared with EMA.</p> <ul style="list-style-type: none"> ➤ EUnetHTA ED Secretariat communicates the Draft Briefing Document, annexes and references to EDWP. ➤ Until the list of issue is shared with the applicant, the Scientific coordinator and rapporteur can request any necessary clarifications to the applicant and copied to EMA SA secretariat. ➤ Preliminary assessment of procedure format (Written-only vs F2F) by EDWP.
D - 15		<p>Feedback on Draft</p> <ul style="list-style-type: none"> ➤ Where applicable, comments on the Draft Briefing Document are forwarded to Applicant in writing by ~D -15 and copied to EUnetHTA ED Secretariat. 	<ul style="list-style-type: none"> ➤ External experts are identified and information shared with EMA SA Secretariat.

⁴ All dates are approximative

⁵ The use of a secure link system (for authorised personnel only) will ensure proper transmission of large files and the confidentiality of sensitive documents

		<ul style="list-style-type: none"> ➤ Additional Experts/patients representative are identified and information shared with EUnetHTA ED Secretariat. 	
D - 10		Administrative TC between EMA and EUnetHTA ED Secretariat with preliminary exchange on procedure format and associated organizational topic.	
Validation of Briefing package			
D - 2	<p>Submission of revised briefing package</p> <p>The Applicant sends two versions of the final briefing package together with annexes and references simultaneously to EUnetHTA ED Secretariat and the EMA via Eudralink. in response to the request for clarification. One version of briefing document should be in "track changes" mode and the other should be "clean".</p>	<p>Validation of final briefing document</p> <p>Positive validation of the final briefing document by EMA Scientific Advice secretariat to the Applicant and EUnetHTA ED Secretariat at D -2 together with final instructions.</p>	<p>Validation of final briefing document:</p> <ul style="list-style-type: none"> ➤ EUnetHTA ED Secretariat confirms validation to the Applicant and EMA.
Submission of final briefing package			
D 0	The Applicant sends final briefing package including annexes and references to EUnetHTA ED Secretariat and the EMA via Eudralink.		<ul style="list-style-type: none"> ➤ EUnetHTA ED Secretariat shares the final briefing document with EDWP. ➤ EUnetHTA decision on procedure format announced to company and EMA.

Evaluation Phase			
D + 30/ SAWP 2		<ul style="list-style-type: none"> ➤ Discussion of the first reports during SAWP meeting focusing on controversial issues. ➤ Production of a draft List of Issues , which outlines the topics of Regulators' interest to be addressed by the Applicant in the F2Fmeeting, if deemed necessary. ➤ EMA decision on the type of procedure. 	<ul style="list-style-type: none"> ➤ E-meeting for HTAb discussions on draft recommendations.
D + 35		<p>EUnetHTA ED Secretariat and EMA exchange their respective draft positions.</p> <ul style="list-style-type: none"> ➤ EMA and SAWP Coordinators take part in a closed e-meeting with EUnetHTA ED Secretariat, EUnetHTA Scientific Coordinator and Rapporteur. 	
		<p>Only in case of a DM with the EMA:</p> <ul style="list-style-type: none"> ➤ Finalisation of List of Issues. ➤ After the pre-F2F TC EMA sends SAWP List of Issues to the Applicant and EUnetHTA ED Secretariat. 	
Advice Phase			
D + 45		<p>EMA sends Final Advice Letter to Applicant, unless a discussion meeting with the EMA is to be held. In such a case, subsequent steps are described in Table 3, but only Applicant and EMA actions are applicable.</p>	
D + 50 - 55			<ul style="list-style-type: none"> ➤ Review final draft recommendation ➤ Final Recommendations sent to Applicant

Table 3 Outline of actions for Applicant, EMA and EUnetHTA in Parallel Consultations following the F2F Meeting Format

Day	Applicant	EMA	EUnetHTA
Letter of Intent and draft briefing package			
D - 30	<ul style="list-style-type: none"> ➤ Applicant submits the Letter of intent and the draft briefing document with annexes and references simultaneously to the EUnetHTA ED Secretariat and to the EMA via Eudralink⁶. 	<p>EMA confirms reception</p> <p>Communication of EMA contact point (EMA Scientific Officer) to Applicant and EUnetHTA ED Secretariat. The letter of intent is forwarded by the EMA Scientific Advice secretariat to the SAWP for appointment of 2 SAWP Coordinators and, where appropriate, a SAWP Coordinator for questions relating to significant benefit (only applicable for protocol assistance).</p>	<p>EUnetHTA ED Secretariat confirms reception to the applicant and informs EDWP.</p> <p>Appointment of Scientific coordinator and rapporteur, information shared with EMA.</p> <ul style="list-style-type: none"> ➤ EUnetHTA ED Secretariat communicates the draft briefing document, annexes and references to EDWP. ➤ Until the list of issue is shared with the applicant, the Scientific coordinator and rapporteur can request any necessary clarifications to the applicant and copied to EMA SA secretariat. ➤ Preliminary assessment of procedure format (Written-only vs F2F) by EDWP.
D - 15	<ul style="list-style-type: none"> ➤ 	<p>Feedback on draft</p> <ul style="list-style-type: none"> ➤ Where applicable, comments on the draft briefing document are sent to Applicant in writing by ~D -15 and copied to EUnetHTA ED Secretariat: ➤ Additional Experts/patients representative are identification shared with EUnetHTA ED Secretariat. 	<ul style="list-style-type: none"> ➤ External experts are identified and information shared with EMA.

⁶ The use of a secure link system (for authorised personnel only) will ensure proper transmission of large files and the confidentiality of sensitive documents

D - 10		Administrative TC between EMA and EUnetHTA ED Secretariat with preliminary exchange on procedure format and associated organizational topic.	
Validation of briefing package			
D -2	<p>Submission</p> <p>The Applicant sends two versions of the final briefing document simultaneously to EUnetHTA ED Secretariat and the EMA via Eudralink in response to the request for clarification. One version should be in "track changes" mode and the other should be "clean".</p>	<p>Validation of Final Briefing Document</p> <p>Positive validation of the final briefing document by EMA Scientific Advice secretariat to the Applicant and EUnetHTA ED Secretariat at D -2 together with final instructions.</p>	<p>Validation of final briefing document:</p> <ul style="list-style-type: none"> ➤ EUnetHTA ED Secretariat confirms validation to the Applicant and EMA.
Submission of final briefing package			
D 0	<p>The Applicant sends final briefing package including annexes and references to EUnetHTA ED Secretariat and the EMA via Eudralink.</p>		<ul style="list-style-type: none"> ➤ EUnetHTA ED Secretariat shares the final briefing document with EDWP. ➤ EUnetHTA decision on procedure format announced to company and EMA.
Evaluation Phase			
		<ul style="list-style-type: none"> ➤ Discussion of the first reports during SAWP meeting focusing on controversial issues followed by production of a draft List of Issues, which outlines the topics of Regulators' interest to be addressed by the Applicant in the F2F meeting. 	<ul style="list-style-type: none"> ➤ Preliminary discussion (e-meeting) on EDWP participants' positions on main topics (PICO) of the development proposed and exchanges on related issues. Followed by production of a draft List of Issues, which outlines the topics of HTAb interest to be addressed by the Applicant in the F2F meeting.

			➤ EDWP participants start to discuss the draft written positions.
~D + 32	EUnetHTA ED Secretariat and EMA exchange their respective draft Lists of Issues.		
	EMA and SAWP Coordinators take part in a closed e-meeting (preF2F TC) with EUnetHTA ED Secretariat, EUnetHTA Scientific Coordinator and Rapporteur.		
	➤ Finalisation of List of Issues		➤ Finalisation of List of Issues
	➤ After the pre-F2F TC EMA sends SAWP List of Issues to the Applicant and EUnetHTA ED Secretariat .		➤ After the pre-F2F TC EUnetHTA ED Secretariat sends the List of Issues to the Applicant and the EMA .
Applicant's Written Response to List of Issues			
D + 45	➤ Applicant sends their written responses (if applicable) to the List of Issues raised by the EMA , if applicable and EUnetHTA to EMA and EUnetHTA ED Secretariat (if applicable: notification of amended development plan with changes and justifications).		➤ EUnetHTA ED Secretariat distributes the Applicant's written response and any notification of amended development plan with changes and justification (if applicable) to EDWP participants .
Preparation for Face to Face Meeting			
D + 55	➤ Applicant sends power point presentation to EMA and EUnetHTA ED Secretariat , 4 full working days before F2F meeting, addressing the Lists of Issues for both		➤ Closed HTAb E-meeting: Review comments on 1st draft of recommendation and prepare F2F discussion on preliminary EUnetHTA consolidated recommendation on main topics (PICO).

	HTAbs and Regulators. The Applicant should group related issues together. Further changes after this date will not be accepted.		
	➤ Applicant send list of participants.		
Face to Face Meeting			
D + 60		➤ The meeting takes place at the EMA premises and will normally have 2 co-chairs: one from the Regulators and one from the HTAbs (the EDC Scientific Coordinator).	
	<p>Tripartite session: F2F meeting between EDC and EMA with the Applicant. The meeting duration will depend on the range of issues to be discussed and advice format (maximum 3 h), with 15 minutes closed pre, and 15 minutes closed post F2F (EMA and EUnetHTA). Pre-meeting could be extended to 45 minutes if necessary (e.g. late changes to the development plan). Pre-meeting with EMA and EUnetHTA sharing draft positions, expert's feedback received by the two parties and discussing last minute changes.</p> <p>The Applicant addresses key issues that were identified by EUnetHTA EDC and EMA. An interactive discussion follows on the key issue.</p>		
D + 70	➤	➤ The Regulators' Final Advice Letter is adopted by the CHMP (and by the COMP in case of questions on significant benefit for Protocol Assistance) and sent to the Applicant and EUnetHTA ED Secretariat .	➤ Finalisation of EUnetHTA Written Recommendations.
D + 75			➤ EUnetHTA Final Recommendations sent to Applicant and EMA.
D + 85	Applicant completes and returns feedback questionnaire to the EUnetHTA ED Secretariat .		➤

5 Practical issues

5.1 Fees

The EMA charges fees for this procedure, which are the same as for standard Scientific Advice/Protocol Assistance including the application of any fee incentives. For more information see [Fees payable to the European Medicines Agency](#).

The participation of HTA bodies in the EDs offering consolidated HTA outputs elaborated through EDWP in the frame of the EUnetHTA Joint Action may be partially covered by EUnetHTA JAS budget. However, some HTAbs may charge fees for participation in a Parallel Consultation. Information on fees is available from EUnetHTA ED Secretariat.

5.2 Contact points

It is preferable to have a principal point of contact (with back-up) for each stakeholder. The points of contact should be confirmed for each procedure.

The EUnetHTA ED Secretariat is the point of EUnetHTA contact in relation to all HTA aspects, unless otherwise indicated.

The EMA Scientific Officer is the principal EMA contact person to which the Applicant and EUnetHTA should address all queries related to an individual procedure. Applicants' are instructed to send their documents to EMA contacts as indicated in the contact sheet.

The Applicant should keep the EMA Scientific Officer and EUnetHTA ED Secretariat up to date with changes in contact details.

5.3 Processing of documents

The Parallel Consultation uses Eudralink - a secure system for sending/receiving documents between all parties.

The Applicant is responsible for sending the briefing documents directly to the EUnetHTA ED Secretariat and EMA contacts. The Applicant must ensure that receipt of documents has been acknowledged by all the participants.

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 discussed and agreed with participants. This is in order to guarantee an appropriate time for the revision and the evaluation by Regulators and HTAbs.

The Applicant provides consent to document exchange in the Letter of Intent between EMA and EUnetHTA.

5.4 Briefing document for parallel consultation

A common briefing document is used; each question can be addressed to the Regulators or the HTAbs alone, or to both. Quality and nonclinical questions are possible during a Parallel Consultation procedure and posed to regulators only. In the same manner questions related to health economics are possible and should be directed to HTAb only. The labelling of questions is a guide but does not prevent interested bodies answering questions deemed also relevant and of interest. In any case,

EUnetHTA recommendations will be organised using the PICO approach (i.e. Population, Intervention, Comparators and Outcomes). Applicants are encouraged to submit detailed information concerning the choice of patient reported outcomes and any post-launch evidence generation plans. Use of the associated briefing document template is required ([See published template for Parallel Consultation](#)).

6 Other

6.1 Advice format

The EMA will send the CHMP final Scientific Advice/Protocol Assistance letter to the Applicant in accordance with the [published timelines](#) (i.e. the subsequent CHMP meeting).

The EUnetHTA ED Secretariat sends out final validated written answers to Applicant at day +50-55 for a procedure in Written-only format and day +75 for a procedure in F2F meeting format.

Final outcome letters are exchanged between EMA and EUnetHTA ED Secretariat.

6.2 Follow up procedures

A follow-up procedure to an earlier Parallel Consultation procedure for the same indication is possible. There is no time window during which this has to be completed. The briefing document should contain a clear table of the changes compared to the previously reviewed development plan with justifications.

However, for conflict of interest reasons, HTAb avoid collaborative development with Applicant through iterative process.

7 Summary of documents and meeting aims

Table 4. Description of documents

Documents	Description
Letter of Intent	Formally requests the EMA and EUnetHTA ED Secretariat of the intent to submit a Parallel Consultation.
Draft briefing document	Draft briefing document comprising the questions and Applicant's positions, as well all the relevant information, annexes and references, important to assess such questions.
Final briefing document	Finalised version of the draft briefing document addressing regulators' comments and HTAb's points of clarification, including all annexes and references.
SAWP List Of Issues EUnetHTA List Of Issues	Documents outlining the concerns or disagreements with the Applicant's proposal. Further justifications, clarification or changes to the Applicant's proposals are requested.
Final CHMP Scientific Advice/ Protocol Assistance letter EUnetHTA Final Recommendations	Documents with written answers to the Applicant's questions.