EMA-HTA Parallel Consultation

New Process for Early Scientific Advice from the EMA and HTA Bodies

The European Medicines Agency (EMA) has replaced the EMA-HTA Parallel Scientific Advice procedure with a new process that they are calling "Parallel Consultation with Regulators and Health Technology Assessment Bodies" (EMA-HTA Parallel Consultation).[1] There are some useful changes from the EMA-HTA Parallel Scientific Advice process, although the purpose and most of the procedure remains the same.

What is EMA-HTA Parallel Consultation?

EMA-HTA Parallel Consultation[2] provides feedback from regulators and health technology assessment (HTA) bodies on evidence-generation plans to support decision-making on marketing authorisation and reimbursement of new medicines at the same time. Early engagement in the product development phase is encouraged with acceptance of wider and more open discussion agendas compared to later engagement. The objective of the EMA-HTA Parallel Consultation is to help generate optimal and robust evidence that satisfies the needs of both regulators and HTA bodies.

The EMA states that the main benefits of the EMA-HTA Parallel Consultation procedure include:

- streamlined procedure for applicants;
- increased mutual understanding and problem-solving ability between EMA and HTA bodies through a more structured interaction; and,
- improved coordination with, and greater participation of, HTA bodies in parallel consultations through the European Network for Health Technology Assessment's (EUnetHTA)* Early Dialogues Working Party (EDWP) and the EUnetHTA early dialogue (ED) secretariat.

What has changed from EMA-HTA Parallel Scientific Advice?

The major change in the process is that the EMA-HTA Parallel Consultations are now conducted in parallel with the EMA and the EUnetHTA. The procedure is a single gateway for parallel consultations with EMA, EUnetHTA, and HTA bodies on evidence-generation plans. The EUnetHTA ED secretariat facilitates the centralised recruitment of HTA bodies. This is an improvement on the old system which required manufacturers to contact HTA bodies individually.

Although there is one single procedure for EMA-HTA Parallel Consultations, there are two different pathways that the consultation can take on the HTA side – Consolidated Pathway and Individual Pathway.

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*EUnetHTA is a network of government appointed organisations (from EU Member States, EU-accession countries, plus European Economic Area [EEA] and European Free Trade Association [EFTA] countries) and a large number of relevant regional agencies and not-for-profit organisations that produce or contribute to HTA in Europe.

Consolidated Pathway

The Consolidated Pathway guarantees the input of the EUnetHTA EDWP - France (HAS), Germany (GBA), England (NICE), Italy (Italian Medicines Agency: AIFA with alternate Regione Emilia-Romagna: RER), Hungary (National Institute of Pharmacy and Nutrition: NIPN), and a shared seat for The Netherlands/Belgium (Zorginstituut Nederland: ZIN/Rijksinstituut voor Ziekte- en Invaliditeitsverzekering/Institut national d'assurance maladie-invalidité: RIZIV-INAMI) plus up to three additional HTA bodies. Only EDWP members are guaranteed to take part in the consultation but sponsor preferences for other HTAs are taken into account when inviting other HTA bodies to participate.

The advice provided from the HTA bodies includes written answers for shared positions and individual HTA answers to questions for which consensus was not possible.

Individual Pathway

In the Individual Pathway, HTAs are recruited by EUnetHTA. There is no guidance on numbers of HTA bodies that can participate but the previous limit was five. As with the Consolidated Pathway, manufacturers' preferences are taken into account but there are no guarantees that the preferred HTA bodies will accept the invitation.

The advice provided from HTA bodies includes a consolidated list of HTA comments and issues but these are delivered as individual HTA written reports.

Although the Individual Pathway allows individual HTA bodies to be invited, as with the Parallel Scientific Advice, they may decline. Indeed, as the EDWP members are already taking part in all the Consolidated Pathway discussions, these HTA bodies may be less inclined to accept invitations for the Individual Pathway.

Criteria for deciding which pathway is taken

Below are the criteria for agreeing which products will go down the Consolidated Pathway.

The product should aim to bring added benefit to patients 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)

However, the number of slots available are limited and EUnetHTA will decide on the basis of trying to have a "wide array of topics, therapeutic areas, etc.," across the programme, which makes it difficult to predict which pathway the EUnetHTA will decide upon for each product.

What is the process for EMA-HTA Parallel Consultation?

The process for EMA-HTA Parallel Consultation is based around the submission of a detailed Briefing Book followed by a face-to-face meeting between the EMA, HTA assessors, and the manufacturer. There is a standard format for the Briefing Book that consists of background material about the product along with the questions that the manufacturer wants to ask to the EMA, HTA bodies, or both. Each question is supported by the company's rationale for its approach.

The face-to-face meeting is where the EMA and HTA bodies give their verbal feedback to the manufacturer. This is followed by written feedback from both the EMA and EUnetHTA.

The key objectives of the face-to-face meeting include discussing:

- issues of concern or disagreement from regulators and/or HTA bodies with the applicant's proposal regarding the major aspects of trial designs;
- critical divergences between HTA bodies and the regulators on major aspects of trial designs; and,
- potential solutions that could facilitate one trial or one development plan.

6 Weeks

Preparation based on Evidera and PPD experience

1. Align on preferred HTAs; develop questions to ask and align on value
2. Develop hypothesised answers
3. Develop Briefing Book (includes questions and rationale and background material as requested and meeting slides)
4. Validate questions and Briefing Book

1 Month

Letter of Intent (LoI) – Pathway decision

LoI submitted according to fixed dates to EMA and EUnetHTA ED secretariat (include draft Briefing Book if requesting pre-submission teleconference). Fees apply. EDWP decision on eligibility and pathway communicated to applicant within 5 working days.

3 Months

Pre-Submission Phase: Draft Briefing Book

Draft Briefing Book submitted at least 30 days before start of procedure. Comments provided in writing by EMA and EUnetHTA ED secretariat within 15 working days. Additionally, a teleconference may be setup for the pre-submission (draft Briefing Book sent with LoI). Final Briefing Book sent on start of procedure (day 0 - 60 days before meeting).

2-3 Weeks

Meeting

Fixed dates. Focused on list of issues sent to applicant 12 days before meeting. Attendees: EMA, HTA assessors and manufacturer. Slides to be provided. Meeting minutes to be prepared by applicant after meeting (within 5 working days).

Final Advice

Final advice will be issued via letter from the EMA by day 70. EUnetHTA ED secretariat provides final assessments within 15 working days after face-to-face meeting.

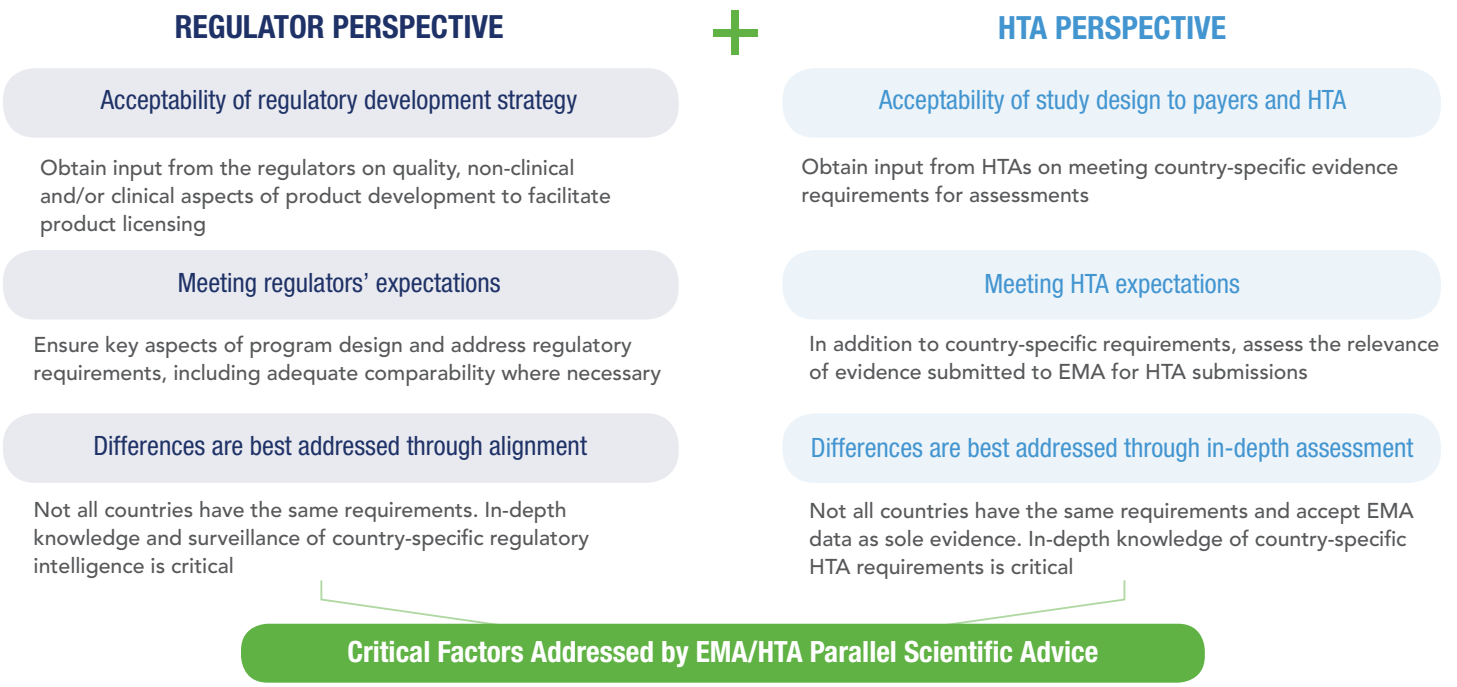
Implementation

1. Alignment of cross-competency teams on Early Scientific Advice result
2. Action plan development and potential amendment of value proposition

Should you undertake an EMA-HTA Parallel Consultation?

There is no doubt that EMA-HTA Parallel Consultation can be a valuable exercise allowing manufacturers to gain the regulator and the HTA perspective in one consultation.

The new EMA-HTA Parallel Consultation process has definite advantages over the old process, such as the coordinating and facilitating role of EUnetHTA. This allows all the contact with HTA bodies to be undertaken centrally by EUnetHTA. The other major improvement is the development of the Consolidated Pathway. This guarantees the input of the EUnetHTA EDWP which includes many of the HTA bodies that manufacturers want to engage with.



However, the main flaw in the system is that it is difficult to predict which drug will be selected for the Consolidated Pathway. If a drug is not selected for the Consolidated Pathway, it will go down the Individual Pathway, which is very similar to the old Parallel Scientific Advice process of inviting selected HTA bodies to participate.

In the past, some HTA bodies limited the number of EMA-HTA Parallel Scientific Advice invitations that they accepted for capacity reasons. There is a risk that the HTA bodies on the EUnetHTA EDWP will be reluctant to participate in Individual Pathway consultations because they are already involved in all the consultations which go down the Consolidated Pathway.

The process of developing a Briefing Book and preparing for EMA-HTA Parallel Consultation is intensive and most companies seek external support to help them through the process. Our advice is to start the preparation early and partner with an organisation that can support the process and the strategic thinking that needs to go into preparing for EMA-HTA Parallel Consultation as well as the action plan coming out of the EMA-HTA Parallel Consultation. Evidera, as a part of PPD, is able to advise on undertaking EMA-HTA Parallel Consultations and on the alternatives that are available to manufacturers who are reluctant to go down this pathway.

References

1. Parallel Consultation with Regulators and Health Technology Assessment Bodies. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001857.jsp&mid=WC0b01ac0580a11c96. Accessed 14 July 2017.
2. Guidance for Parallel Consultation. EMA and EUnetHTA June 2017. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2017/07/WC500230375.pdf. Accessed 14 July 2017.