A Review of the Differences between the New EMA-EUnetHTA Joint Scientific Consultation Versus the Previous EMA-HTA Parallel Scientific Consultation

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Background

- Pharmaceutical companies face many challenges while designing global clinical development programs for their products as multiple objectives need to be addressed to achieve regulatory approval. Aside from seeking regulatory approval from the European Medicine Agency (EMA), the pharmaceutical companies also face a significant burden to synthesize sufficient evidence to position their products favourably for reimbursement by the Health Technology Assessment bodies (HTAbs). Therefore, early engagement for scientific advice with regulatory agencies and HTA bodies serves as a key driver of patient access and commercial success.
- In 2010, the European Medicines Agency (EMA) established, with individual HTAbs, a pilot on Parallel Scientific Advice where developers could receive simultaneous feedback from both regulators and individual HTAbs on their development plans for new medicines. This process was replaced by the Parallel Consultation (PC) with EMA and EUnetHTA in 2017. The initiative was further replaced by Parallel Joint Scientific Consultation (JSC) between EMA European network for Health Technology Assessment (EUnetHTA) 21 Consortium in 2021. As of September 2023, the Parallel JSC under EUnetHTA21 has ended and in the interim period till January 2025, the G-BA will function as the HTA Coordination Contact and will facilitate a centralised HTAb recruitment for conducting JSC[1,2,6].

Objectives

The objectives of the research were to:

- Compare the two processes: **Parallel consultation** and **Parallel JSC**;
- Assess opportunities and challenges with the two processes;
- Evaluate the impact of the new JSC process on preparation for the JCA.

Methods

- A pragmatic literature search was performed on scientific databases (Pubmed and Embase, Econlit and Medline via PsychInfo–Ovid) from July 2018 up to June 2023 in the English language. Additionally, a grey literature search was also performed to complement information on the new JSC process.

Results

- The pragmatic search retrieved 300 hits on early dialogue frameworks adopted by HTA bodies. The studies were screened for relevance and 10 studies for early dialogue between regulatory bodies and HTA agencies were reviewed in full.
- As suggested, the scientific advice has evolved through the years where Parallel JSC initiative with EUnetHTA 21 replaced parallel consultations of EMA with the former EUnetHTA, that further replaced former Parallel Scientific Advice procedure by EMA and HTA bodies, whereby medicine developers had to contact Member State HTA bodies individually. Figure 1 depicts the evolution process of Parallel Consultation between EMA and HTA bodies and Table 2 entails the key points of comparison between previous EMA-EUnetHTA PC and EMA-EUnetHTA21 JSC.

Figure 1. Depiction of the evolution process of Parallel Consultation between EMA (regulator) and HTA bodies[1,2]

EMA: European Medicines agency; EUnetHTA: European network for Health Technology Assessment Joint Action

Table 2. Comparison between Parallel EMA/ EUnetHTA Consultation and Parallel EMA/ EUnetHTA 21 Joint Scientific Consultation[3,4]

Comparison parameters	Parallel EMA/ EUnetHTA Consultation	Parallel EMA/ EUnetHTA 21 Joint Scientific Consultation
Overall procedure	The Parallel Consultation involves 2 pathways: i) the consolidated Parallel Consultation – which involved input of the EUnetHTA Early Dialogues Working Party (EDWP) including HTA representatives from France (HAS), Germany (GBA), England (NICE), Italy (AIFA with alternate RER), Hungary (NIPN), and a shared seat for the Netherlands/Belgium (ZIN/RIZIV-INAMI), plus up to three additional HTA bodies, and the ii) individual Parallel Consultation involved recruitment of HTA bodies by the EUnetHTA	JSC involves providing a non-binding scientific advice involves input of the Committee for Scientific Consistency and Quality for Joint Scientific Consultation (CSCQ JSC). The CSCQ includes representatives from AEMPS (Spain), AIFA (Italy), G-BA, (Germany), HAS (France), INFARMED (Portugal), KCE/KCE-NIHDI (Belgium), NCPE (Ireland), NIPN (Hungary), NOMA (Norway), TLV (Sweden) and ZIN (Netherlands)
Timelines	These consultations could take place before or after the product was made available on the market	These consultations can take place only **before the start of pivotal clinical** trials on initial evidence generation for Marketing Authorisation Application/ Reimbursement, and Post Licensing Evidence Generation (PLEG)
Format	There was one single procedure for Parallel Consultation; however, there were two different formats the consultation can take, following selection of a product: written only format and F2F meeting format.	There is one single procedure for Parallel EMA/EUnetHTA 21 JSCs within the two Open Calls in EUnetHTA 21; the consultations take place in a F2F meeting format
Selection criteria	Basically, three criteria for selection: 1. A new mode of action for the indication and 2. Targeting a life-threatening or chronically debilitating disease and 3. Responding to unmet need (no treatment or only unsatisfactory treatment available).	Six criteria for selection 1. Unmet medical needs (no treatment or only unsatisfactory treatment available) 2. First in class 3. Potential impact on patients, public health, or healthcare systems 4. Significant cross-border dimension 5. 5. Major Union-wide added value; or 6. Union clinical research priorities. There is no prioritization or ranking of selection criteria in the regulation, nor do all criteria have to be met

AIFA: Agenzia italiana del farmaco; AEMPS: Agencia Española de Medicamentos y Productos Sanitarios; CSCQ JSC: Committee for Scientific Consistency and Quality for Joint Scientific Consultation; EDWP: Early Dialogues Working Party; EMA: European Medicines agency; EUnetHTA: European network for Health Technology Assessment Joint Action; F2F: Face-to-face; G-BA: Gemeinsamer Bundesausschuss; HAS: Haute Autorité de santé; INFARMED: Autoridade Nacional do Medicamento e Produtos de Saúde; KCE: Belgian Health Care Knowledge Centre; NCPE: National Commission for the Promotion of Equality; NICE: The National Institute for Health and Care Excellence; NIPN: National Institute of Pharmacy and Nutrition; NoMA: Norwegian Medicines Agency; PLEG: Post Licensing Evidence Generation; RER: Regione Emilia-Romagna; TLV: Tandvårds- och läkemedelsförmånsverket; ZIN: Dutch 'Zorginstituut'

Opportunities and challenges with the two processes

Challenges with Parallel Consultation:

- The initial Parallel Consultation offered flexibility in terms of advice timings i.e., the advice could be sought before and after the product was available on the market. However, it carried the risk of advice implementation if the product was already on the market. The research highlighted that from 2017 to 2020 (during the era of Parallel Consultations between EMA and EUnetHTA), HTA submission to various EU countries led to delayed market access owing to the lack of alignment with payer requirements. E.g., Delays up to ~48 months in Italy and France; up to 50 months in the UK and Spain and up to 55 months in the Netherlands[5].
- The individual Parallel Consultation involved the recruitment of HTA bodies by the EUnetHTA. However, there was no guidance on the number of HTA bodies that can participate and there was no guarantee that the preferred HTA bodies would accept the invitation.

Opportunities with JSC

- The JSC aims to support the health technology developers by providing inputs on pivotal trial design before the initiation of clinical trials, ensuring the evidence meets the needs of the different decision-makers in terms of quality and appropriateness of the data produced.
- Partnership between EMA and EUnetHTA 21 also allows for streamlined logistics, improved HTA coordination through EUnetHTA 21 JSC Secretariat, and greater participation via the involvement of EUnetHTA 21 CSCQ JSC.
- Joint Scientific Consultations may improve the predictability of JCA and support HTDs in preparing for submission. The Joint Advice from the EMA and EU HTA bodies enables HTDs to adjust their clinical development plans and provides an opportunity for Population, Intervention, comparator and outcome (PICO) alignment.

Discussion

- The Parallel Consultation between EMA and HTA bodies has evolved since 2010 with each change bringing in more efficiency. The current and latest procedure with joint scientific consultation offers a chance to anticipate the PICO scoping, which represents the first step of JCA within the new regulation.
- Manufacturers seeking simultaneous feedback from both the regulators and HTA bodies to bridge the gap in evidence requirements should assess Joint Scientific Consultation as one of the potential options. The pharmaceutical organizations (with JSC experience) and HTA bodies publish the case studies that can further support to assess the value proposition of a new product aiming for JSC.
- The JSC process provides a streamlined flow of stakeholder involvement and improves the predictability of the JCA process. However, there are challenges to be overcome with the process such as limited consultation slots (only 3 slots in the first open call and 5 slots in the second open call) available with strict eligibility requirements, restricting JSC to a very limited number of health technologies.
- From our client engagements, we also found that tight turnaround timelines in the JSC process put enormous pressure on the resource use within the pharmaceutical companies owing to the alignment of cross-functions in a short span of time.

Conclusions

- While pursuing Integrated Scientific Advice with the EMA and HTA bodies remains crucial, the value of JSC process is probably greater to optimise the evidence around clinical data. Therefore, more studies from real cases are needed to provide evidence of JSC value.

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