Comments on EUnetHTA 21's D7.1.1 – Practical Guideline for interaction between Health Technology Developer and HTA bodies

Ecker + Ecker GmbH, a healthcare consultancy based in Germany with strong expertise in the early benefit assessment, welcomes the establishment of a European Health Technology Assessment (HTA) fostering closer cooperation between member states on health technology assessment by introducing a permanent framework for this joint work.

The legal requirements for a European HTA have been determined as a legislative act by the end of 2021 with the EU regulation 2021/2282. From 2025, before placing innovative medicinal products on the market, oncology products and ATMP are subject to a European joint clinical assessment. In the next step, Orphan Medicinal Products (OMPs) will follow, beginning in 2028 and from 2030 all medicinal products will have to go through the European assessment.

While the regulation does not come into force until 2025, the process of implementation is already ongoing to ensure effective application from January 2025 onwards. At present, the development of a methodology for joint HTA work is facilitated by the European Network for Health Technology Assessment (EUnetHTA) 21 consortium. Numerous guidelines are currently under development regulating specific aspects of the HTA process. As an important outcome, a consolidated document on the timelines and requirements for EU-HTA would be highly desirable.

On July 20, the EUnetHTA 21 draft deliverable "D7.1.1 – Practical Guideline for interaction between Health Technology Developer and HTA bodies" was published and is now available for public consultation. Within the European HTA, the vivid exchange between HTA bodies (HTAb) and Health Technology Developers (HTD) is crucial and therefore, this draft deliverable (as of April 2022 in version 0.1), represents an important guideline that provides the opportunity to establish a framework for the interaction between HTA bodies, the respective assessors and HTD.

Page number	Line/ section number	Comment and suggestion for rewording
General	-	While the draft guideline "D7.1.1 – Practical Guideline for interaction between Health Technology Developer and HTA bodies" aims to establish an initial framework for the interaction between HTD and HTA bodies, we are deeply concerned that this draft guideline will not enable efficient communication between HTD and HTA bodies within the EU HTA procedure. While from our point of view exchange between HTD and HTA bodies represents a crucial part of the EU HTA process in order to ensure the best possible quality for the submitted dossiers, this guideline limits the communication between the HTD, HTA bodies and respective assessors to a minimum. However, from our perspective, it is essential to allow for dialogues and appropriate interactions between HTD and HTA bodies to take place in the EU HTA procedure. In summary, our main concern with regard to deliverable "D7.1.1 – Practical Guideline for interaction between Health Technology Developer and HTA bodies" is, that only minor, insufficient involvement of HTD within the EU HTA procedure is planned.

The guideline is available here:

D7.1.1 Practical Guidance for HTA-HTD-Interaction

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		– The proposed insufficient exchange between HTD and European HTA bodies is a major point of concern. Exchange between HTD and EU HTA bodies within the procedure is crucial. – Therefore, exchange between HTD and assessors should be established within the assessment, including early stages such as the scoping process as well as the Joint Clinical Assessment (JCA) itself. Possible ways of interaction might comprise for example a letter of intent submitted by HTD, participation of HTD in the scoping meeting, and a publicly available comment by HTD on final JCA.
7	130–131, 143–145	**Statement in guideline:** "*HTAb Assessor and Co-Assessor should have no direct interaction with the HTD. Should the HTD reach out to them directly with questions on the EUnetHTA 21 JCA or JSC, the Assessor and Co-Assessor should direct them to the Secretariat.*" *"The HTD is not allowed to communicate directly with Assessors and/or Co-Assessors of JCA or JSC, nor interact with other HTAb about the ongoing JCA or JSC on a European level unless it is publicly available information."* **Comment:** While we agree that interactions between the assessors and HTD should be organised in a structed framework, we would like to highlight the importance of direct communication between the assessors and HTD in order to ensure the best possible quality of the assessment. As already successfully established during EUnetHTA Joint Action 3, regular interactions between HTD and the assessors should be continued. Moreover, these interactions do represent a common feature of HTA at national level (such as consultations on study design and on the appropriate comparator, written statements and oral hearings in the German benefit assessment process) providing the opportunity for a valuable exchange between assessors and HTD. To ensure a successful EU HTA procedure, the possibility for exchange between assessors and HTD should be established as regular part in the overall process.
7	Footnote 1	**Comment:** Change „*develoSecretariatent*" to "*development*".
8	172	
8	184–187	**Statement in guideline:** "*If, for JCA in EUnetHTA 21, a PICO information meeting is held, such a meeting only serves the purpose to inform the HTD about the consolidated PICO(s), and there is no provision to alter the PICO(s) at this point and no final decisions will be taken during the PICO information meeting. No minutes will be published or shared with the HTD after the meeting, nor will the meeting be recorded*."

		Comment: A PICO meeting, as established within EUnetHTA Joint Action 3, should be incorporated into JCA. Importantly, these meetings should enable the opportunity to exchange information and discuss unclear aspects with regard to the suggested PICO(s). Additionally, since the consolidated PICO scheme is essential for the HTA, minutes of these meetings should be recorded and shared with the HTD.
10	206–212	**Statement in guideline:** *"Under the HTAR, it is envisaged that the Coordination Group shall publish the dates of request periods and state the planned number of JSCs for each of those request periods on the IT platform referred to in Article 30. At the end of each request period, where the number of eligible requests exceeds the number of planned JSCs, the Coordination Group shall select the health technologies that are to be subject to JSCs, ensuring the equal treatment of requests concerning health technologies with similar intended indications. The criteria for selecting from eligible requests for medicinal products and medical devices are outlined in the HTAR (Art. 17 (3))."* **Comment:** While we appreciate the possibility of JSC, both the limited number of JSC as well as the restriction of JSC to "eligible" requests are considered as problematic from our point of view. It must be ensured that a sufficient number of JSCs are available for HTD in order to enable the best possible quality of submitted dossiers. Moreover, as currently stated, requests will only be possible during specific request periods. However, from our point of view, requests for JSC should always be possible, regardless of the certain request periods.
11	224–225	**Statement in guideline:** "*Where a request for JSC was refused, the HTD will be informed thereof and the reasons explained."* **Comment:** Within the guideline, it should be specified what happens if a medicinal product is not selected for a JSC. Are these medicinal products supposed to undergo numerous consultations on national level instead?
12, 13	258–259 (Figure 4.2), 279–280	**Statement in guideline:** *"Initiation of a JCA/CA scoping phase – HTD may attend PICO information meeting (EUnetHTA 21 only)"* *"In the HTAR there is no [PICO information] meeting envisioned between the HTD and HTAb during or after the scoping process."*

		Comment: While in EUnetHTA Joint Action 3, a direct exchange between assessors and HTD within the PICO information meeting represented a crucial part of finalizing the PICO scheme, no such meeting is foreseen in the current draft guideline. However, from our view, a PICO information meeting enabling the active participation of HTD should be implemented within the EU HTA procedure. The HTD should have the opportunity to clarify open questions regarding the PICO scheme and discuss further outstanding issues.
12	272	**Statement in guideline:** *"A Letter of Intent is not foreseen under the HTA Regulation."* **Comment:** In EUnetHTA Joint Action 3, the HTD was given the opportunity to outline a draft PICO scheme in the letter of intent. This input from the HTD as well as the direct exchange between assessors and HTD within the subsequent scoping meeting represented a crucial part of finalizing the PICO scheme. Therefore, a letter of intent should be implemented in the HTA regulation.
12–13	273–277	**Statement in guideline:** ***"Submission of PICO(s) & Request Submission Dossier*** *Both under the HTAR and EUnetHTA 21, as per Art 10 (1) of the HTAR, the Secretariat informs the HTD about the consolidated PICO(s) for the JCA and requests a completed submission dossier as per the PICO(s) by a specified deadline. The HTD has to submit their JCA dossier, after the consolidated PICO(s) has been submitted to the HTD."* **Comment:** In this draft guideline, no specific timelines are mentioned. At which timepoint is the HTD informed about the consolidated PICO(s)? When exactly has the dossier to be submitted? Due to the fact, that data analyses can be very time-consuming depending on the scope of these analyses, consolidated PICO(s) should be communicated as early as possible within the procedure. Therefore, we suggest that the scoping process starts as soon as the marketing authorisation application (MAA) has been confirmed.
13	288–290	**Statement in guideline:** *"The HTD has to submit a dossier according to the scope of the JCA (i.e. submit data or prove there is no data available for all identified PICO(s)), otherwise the dossier has to be declared incomplete"*

		Comment: It should be clearly outlined, which rules apply in order to demonstrate the lack of data. Moreover, it should be clarified, what the consequences of an "incomplete" dossier are.
13	291–294	**Statement in guideline:** *"The time for providing the amended dossier responding to the LoMI [List of Missing Items] depends on the JCA procedure (i.e. medicinal products or medical devices). The objective of the technical check of completeness is to ensure completeness of the dossier to avoid interaction (via Secretariat) between the HTD and the Assessor and Co-Assessor during the actual assessment."* **Comment:** Please specify the duration of the time for providing the amended dossier responding to the LoMI. How should extensive additional requests be handled? Is an extension of the deadline possible or planned in such cases?
13	301–306	**Statement in guideline:** *"For medicinal products only: Although EUnetHTA 21 does not have clock-stops, a grace period to amend the Submission Dossier is allowed if CHMP opinion differs from what was anticipated and only to those sections impacted by the CHMP opinion. The need for and duration of a grace period has to be approved between the Assessor and Co-Assessor and the Secretariat, but can take a maximum of 10 calendar days (starting once CHMP opinion is available). During the grace period the Assessor and Co-Assessor will update the PICO, which will be published approximately 1 week after CHMP opinion."* **Comment:** If we understand the above correctly, this means that the HTD only has 3 calendar days to adjust the dossier accordingly: As stated in the cited paragraph, the grace period corresponds to 10 calendar days, but the updated PICO will be communicated to HTD after 7 days ("approximately 1 week") of the grace period have already passed resulting in only 3 calendar days left to adapt the dossier to the updated label? Importantly, depending on the extent of required modifications (such as additional data analyses or re-analyses of data), the suggested period of 3 calendar days is not sufficient. Even if the requested analyses are already available, 3 calendar days are not sufficient to modify the dossier accordingly. Therefore, the grace period should rather start *after* the updated PICO scheme has been communicated to the HTD. Moreover, so far, this paragraph only refers to EUnetHTA21. However, it should be specified how grace periods are handled within the EU HTA procedure. Overall, the suggested process is not feasible and in the worst case, might lead to incomplete or discontinued dossiers. This in turn could

		undermine the whole EU-HTA process and lead to clinical assessment on a national level exclusively. At present, it is unclear, how exactly it will be handled if the corresponding adjustments are not finalized within the grace period. Notably, the consequences of such delays or discontinuations on national level are not further specificized: Would this potentially result in a later market access?
13	308–314	**Statement in guideline:** *"As per Art. 11(2), interaction with the HTD should be possible at any time during preparation of the JCA in case the Assessor and Co-Assessor consider that further specifications or clarifications or additional information, data, analyses or other evidence are necessary in order to carry out the assessment. [..] Depending on the type of request, a deadline (with a maximum of 5 calendar days for medicinal products and 14 calendar days for MDs/IVDs) to provide the requested information will be communicated."* **Comment:** A deadline of 5 calendar days to provide additional data, analyses or other information requested by the assessor and/or Co-Assessor is not feasible. In case the request is sent on a Friday, only 2 working days are left for the HTD to address the request. Moreover, in certain cases, it should be possible to extend the deadline upon request of the HTD.
14	Section 4.2.3, line 326–327	**Statement in guideline:** "*The HTD shall signal any purely technical or factual inaccuracies in accordance with the timeframes established pursuant to Article 15."* **Comment:** In addition to the factual accuracy check, the HTD should have the opportunity to provide a statement on the final JCA that will be published together with the factual accuracy check.
15	367–368	**Statement in guideline:** *"Discuss if new evidence can be accepted during an ongoing JCA and if so, define a process for submission of this new evidence during an ongoing JCA."* **Comment:** Submission and assessment of new evidence during an ongoing JCA is highly problematic due to the tight submission and assessment schedule already in place. However, the assessment should always be based on the newest scientific results to ensure the best possible quality of the assessment process. Therefore, a process to submit additional data during an ongoing JCA should be developed for cases where either the HTD or Assessor and Co-Assessor deem it necessary.