

21 April 2021
EMA/694619/2020

Final Minutes of EMA/EUnetHTA virtual meeting

16 December 2020

Role	Name
Co-chairs:	Hans-Georg Eichler and Niklas Hedberg
Present:	<p><u>EUnetHTA</u>: Iñaki Imaz (AETS-ISCIH), Anna Zaremba (AOTMiT), Tuomas Oravilahti (FIMEA), Regina Skavron (G-BA), Chantal BÉlorgey (HAS), Chantal Guilhaume (HAS), Alex Correia (INFARMED), Alric Ruether (IQWiG), Beate Wieseler (IQWiG), Marit Hystad (NoMA), Bjørn Oddvar Strøm (NoMA), Sari Ormstad (NIPHNO), Niklas Hedberg (TLV), Frederieke Diemer (ZIN), Marcus Guardian (ZIN), Catharina Helmink (ZIN), Lauren Law (ZIN), Chaienna Schreuder-Morel (ZIN), Merle Tenberg (ZIN), Anne Willemsen (ZIN).</p> <p><u>EC</u>: Flora Giorgio, Ioana Raluca-Siska, Julia Schmitz.</p> <p><u>EMA</u>: Peter Arlett, Michael Berntgen, Marco Cavaleri, Emer Cooke, Jayne Crowe, Francois Domergue, Hans-Georg Eichler, Ella Jansen, Bruno Sepodes.</p>

Item	Draft agenda	Name	Time
1.	Welcome by EMA's Executive Director	Emer Cooke	10 min 10.00-10.10
2.	Introduction to the day and adoption of the draft agenda	Hans-Georg Eichler and Niklas Hedberg	10 min 10.10-10.20
3.	Update from DG SANTE on activities related to the EMA/EUnetHTA collaboration	Flora Giorgio	10 min 10.20-10.30
4.	Introduction to DARWIN EU (Data Analytics and Real-World Interrogation Network) and opportunities for collaboration	EMA: Peter Arlett	30 min 10.30-11.00



Item	Draft agenda	Name	Time
5.	Response to COVID-19 as priority area for EMA/EUnetHTA collaboration during the final phase of JA3	EUnetHTA: Anne Willemsen EMA: Marco Cavaleri, Spiros Vamvakas	20 min 11.00-11.20
6.	Optimising the regulatory output as reference for HTA: <ul style="list-style-type: none"> Feedback from recent research Experiences from the webinars 	EUnetHTA: Frederieke Diemer (ZIN), Anne Willemsen EMA: Michael Berntgen, Ella Jansen (Maastricht University)	20 min 11.20-11.40
7.	Concluding activities of EUnetHTA JA3	Marcus Guardian	10 min 11.40-11.50
8.	Closing remarks	Hans-Georg Eichler and Niklas Hedberg	5 min 11.50-11:55

This was the 20th meeting between the European Medicines Agency (EMA) and representatives from the European Network for Health Technology Assessment (EUnetHTA). As usual, the meeting was attended by the European Commission.

Such bilateral meetings are held between EMA and EUnetHTA since 2010. On this occasion, due to the COVID-19 pandemic, it was decided to arrange the bilateral in a virtual format and of shorter duration. The primary focus of the meeting was to review the status of specific items from the [EMA/EUnetHTA workplan 2017-2021](#).

In her welcome address EMA's new Executive Director Emer Cooke noted that over the past decade EMA and EUnetHTA have established a strong partnership based on constructive and fruitful cooperation. Optimising the path from development, evaluation through to access to medicines is the foundation for this work. Prospective planning of evidence, engagement in methodologies as well as mutual understanding of decision making are paramount. The more regulators and HTA bodies ensure that clinical evidence is designed to substantiate the clinical benefit, or its clinical value, the better they deliver in the interest of the ultimate stakeholder, the patient. EMA's Regulatory Science Strategy to 2025 highlights the aim to contribute to HTA's preparedness and downstream decision making for innovative medicines; equally the availability and accessibility of medicines features strongly in the strategy EMA has published together with the Heads of Medicines Agencies. And also the European Commission's Pharma Strategy focuses strongly on initiatives to facilitate access to medicines. It is with this in mind that we should deliver on our EMA/EUnetHTA work plan and demonstrate the value of cooperation.

The draft agenda was adopted without changes.

Update from DG SANTE on activities related to the EMA/EUnetHTA collaboration

The European Commission provided an update on the state of play of the legal proposal on HTA collaboration, HTA-related Commission initiatives as well as EU cooperation on HTA beyond May 2021. The negotiations on the legal proposal had resumed under the German Presidency and are expected to be continued under the Portuguese Presidency. In the Pharmaceutical Strategy for Europe the theme on "Delivering for patients: fulfilling unmet medical needs and ensuring accessibility and affordability of medicines" features strongly. The EC in collaboration with MS is engaged in the preparatory work and development of the European Health Data Space (EHDS). Other relevant initiatives include the

Europe's Beating Cancer Plan and the EU4Health Programme. In terms of EU cooperation on HTA beyond May 2021, a call for tender regarding EU cooperation on HTA is expected to be launched shortly. This is important in view of EUnetHTA Joint Action 3 coming to a close shortly. The joint between EMA/EUnetHTA as documented in the workplan is an important pillar for describing future working arrangements and is expected to also be reflected in EUnetHTA's White paper (see below). The cooperation between HTA bodies and EMA is also expected to be continued and strengthened under the possible future legal framework for EU HTA.

Introduction to DARWIN EU (Data Analytics and Real-World Interrogation Network) and opportunities for collaboration

DARWIN EU (Data Analytics and Real World Interrogation Network) and opportunities for collaboration stem for Big Data Task Force Top-ten data recommendations. The vision is to establish and maintain a secure EU data platform that supports better decision-making throughout the product lifecycle with reliable evidence from real world healthcare (see [business case for DARWIN](#)). DARWIN EU will be a distributed network for fast access and analysis with data that stays local. There will be a third party coordination centre and EMA will have responsibility for managing the network. Data exchanged within the network will be anonymous. DARWIN EU services aim to support regulatory decisions from 2023. Whilst there are a number of regulatory use cases, there are opportunities for collaboration with downstream decision makers such as HTA bodies. DARWIN EU can deliver for better medicines regulation *and* be early deliverable for European Health Data Space. In the discussion it was noted that the quality of real world studies need to be understood in order to allow robust decision making. Examples in the COVID pandemic have shown how the quality of data, methods and reporting can be variability for observational studies and therefore all three steps (data, methods and reporting) need to be taken into account when judging evidentiary value. With this in mind, DARWIN EU as infrastructure could support quick pragmatic RCTs in a pandemic. More generally, DARWIN EU provides an opportunity to build the infrastructure to generate relevant data across the product life-cycle. It was therefore agreed that bringing the HTA perspective into the DARWIN EU governance would be of value

ACTIONS:

- EMA to formally invite through EUnetHTA an HTA representative to take a seat in the DARWIN Advisory Board

Response to COVID-19 as priority area for EMA/EUnetHTA collaboration during the final phase of JA3

EUnetHTA reported about its activities in relation to the COVID-19 pandemic. The development of an European publication database on COVID-19 with relevant publications from all national HTA organisations within the EU was established, covering treatments and diagnostics. Furthermore, for pharmaceuticals two new review frameworks were established: rolling collaborative reviews, which provide continuous monitoring of evidence and are descriptive in nature, and rapid collaborative reviews, which summarise available evidence, describe the strengths/limitations, include EUnetHTA PICO and can focus on evidence gaps. Rapid Collaborative Reviews however, are not living documents like the RCRs and will only be updated on a case-by-case basis. These EUnetHTA Rolling Procedures are not meant to substitute a joint REA adhering to the agreed procedures, aiming at critical appraisal of the clinical evidence submitted for approval. Experience so far is that these are demanding efforts in terms of coordination, such as designing appropriate methods and procedures to have timely publications, hence requiring significant investment. Collaboration with EMA focused on topic prioritisation by mutually reviewing horizon scanning information and also a product-specific webinar for Rapid Collaborative Reviews (on remdesivir), which was considered of value by participating HTAs.

ACTIONS:

- Explore the opportunity to hold webinars also for COVID-19 vaccines, subject to broader interest by EUnetHTA partners

Optimising the regulatory output as reference for HTA

To inform the discussion on optimising the regulatory output as reference for HTA, Ella Janssen from the Maastricht University presented results from her recent research "Information exchange between Regulators and HTABs on evidence needs for benefit-risk and relative effectiveness assessments", with focus on regulatory outputs. On the basis of a systematic literature review, pair-wise comparison of EPARs and REAs, as well as expert interviews, she identified a number of recommendations how to improve the EPAR to make it more useful for HTA bodies. These concern the description of evidence uncertainties, details on assessment design choices and evidence used for benefit-risk assessment, and provision of numerical 'raw' data.

Furthermore, EUnetHTA presented recent experience from a Joint REA (PTJA-010). In terms of usefulness for the REA work it was noted that the CHMP assessment report included relevant supportive analyses but that there was a need to clarify the different ways of analysing the data at different time points. The webinar between HTA authors and CHMP rapporteurs was a useful instrument to allow such clarifications.

During the discussion it was confirmed that the research is consistent with the alignment through early dialogues, e.g. on active comparators and relevant endpoints. From CHMP perspective it was considered important to progress these conversations on the optimisation of the EPAR and whilst progress has been made over time there are still elements to further enhance, such as enhanced reporting on relevant QoL aspects. It will therefore be a joint effort to continue addressing any findings. This should be done on the basis of the research as well as the experience with the webinars.

ACTION:

- Develop a list of elements to be addressed in updated guidance on the CHMP assessment report in order to further optimise its usefulness for down-stream decision making.

Concluding activities of EUnetHTA JA3

EUnetHTA provided an overview of the activities until the closing of Joint Action 3 (JA3) in May 2021. Looking at the deliverables of JA3, by October 2020 the majority of deliverables have been approved or submitted. The EUnetHTA productions (pharma and other technologies) included 18 Joint Assessments on Pharma, 27 Collaborative (25) and Joint (2) Assessments on Other Technologies, 34 Early Dialogues (1 MD) plus 5 ongoing, 5 Post Launch Evidence Generation pilots as well as 18 Covid-19-related assessments. The EUnetHTA White Paper on a Future Model of EU HTA Collaboration is in development. The aim is to compile the outputs of JA3 into a document that describes in a single framework the way we worked, what we have achieved, what we have learnt and what we recommend for the future. Furthermore, reflections on a network post-JA3 were provided.

ACTION:

- EMA to contribute to the finalisation of the White paper and other developments for European HTA collaboration, as requested

Closing remarks

The next meeting will be hosted by EUnetHTA and will be scheduled for **Q2 2021**, most likely again in the virtual format.