28 November 2022
EMA/908798/2022

Minutes of EMA/EUnetHTA 21 virtual meeting

25 November 2022

Role	Name
Co-chairs:	Michael Berntgen and Niklas Hedberg
Present:	EUnetHTA 21: Anja Schiel (NoMA), Anne Willemsen (ZIN), Annelie Blumrich (G-BA), Antje Behring (G-BA), Antoine VANIER (HAS), Beate Wieseler (IQWiG), Chantal BELORGEY (HAS), Chara Kani (EOPYY), Cornelia Rüdig (IQWiG), Daniel Ritter, Eleni Pitta, Frank Hulstaert (KCE), Giovanni Polimeni, Hanna Zirath (TLV), Irene Urbina, Irina Cleemput (KCE), Jelena Ivanovic, Jelena Ivanovic (AIFA), Krystyna Hviding (NoMA), Luca Tomassini, Marcus Guardian (ZIN), Margaret Galbraith (HAS), Merle Tenberg (ZIN), Nico Fischer (G-BA), Niklas Hedberg (TLV), Olesja Rissling, Petra Galusová (SUKL), Pier Paolo Olimpieri, Pier Paolo Olimpieri (AIFA), Roisin Adams (TCD), Sara Couto, Sonia Pulido Sanchez, Stephanie Said, Yvonnne Schmidt (G-BA) EC: Valentina Barbuto, Jose Valverde Albacete. EMA: Juan Jose Abellan Andres, Gaelle Andriantafika, Peter Arlett, Michael Berntgen, Milton Bonelli, Francesca Cerreta, Harald Enzmann, Juan Garcia, Rosa Gonzalez-Quevedo, Thorsten Olski, Elias Pean, Francesco Pignatti, Kelly Plueschke, Andrej Segec, Spiros Vamvakas, Machteld van Egmond.

Item	Draft agenda	Name	Time
1.	Welcome / introduction to the day and adoption of the draft agenda	Michael Berntgen and Niklas Hedberg	5 min 10.00-10.05
2.	Update from the European Commission on the progress with the implementation activities for the HTA Regulation	Valentina Barbuto	15 min 10.05-10.20
3.	Learnings from the workshop on patient experience data (Executive summary)	EMA: Juan Garcia	10 min 10.20-10.30

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000
An agency of the European Union

Item	Draft agenda	Name	Time
		EUnetHTA 21: Beate Wieseler, Maggie Galbraith	
4.	Collaboration in the context of patient relevant data for decision making a. IQWIG study on the use of PROs in HTA reports and related information in SmPCs b. Project NEED (Needs Examination, Evaluation and Dissemination) c. ICH activities regarding guidance on patient preferences	EUnetHTA 21: Beate Wieseler (a.), Irina Cleemput (b.) EMA: Milton Bonelli (c.)	30 min 10.30-11.00
5.	Update on the EMA funded registry-based study on Spinal Muscular Atrophy	EMA: Kelly Plueschke EUnetHTA 21: Yvonne Schmidt, Beate Wieseler	20 min 11.00-11.20
6.	Progress with the identification of use cases for DARWIN EU	EMA: Juan Jose Abellan Andres EUnetHTA 21: Niklas Hedberg	15 min 11.20-11.35
7.	Overview of EUnetHTA 21 deliverables with potential relevance for EMA	EMA: Michael Berntgen EUnetHTA 21: Roisin Adams	15 min 11.35-11.50
8.	Status update on the delivery of the EMA/EUnetHTA21 work plan	Anne Willemsen	5 min 11.50-11.55
9.	Closing remarks	Michael Berntgen and Niklas Hedberg	5 min 11.55-12:00

This was the 23rd 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.

The draft agenda was adopted without changes.

Update from the European Commission on the progress with the implementation activities for the HTA Regulation

The European Commission reported from the inaugural meeting of the HTA Coordination Group (HTACG) in June 2022, which will be followed by a second meeting on 28 November 2022. A rolling plan is published to guide the implementation of the operations under the HTA Regulation. Key activities in 2023 are the establishment of the subgroups, as well as the development of the IT platform. Other priority areas are establishing governance and operational structures to ensure new system in place by 2025, drafting and adopting the implementing legislation ensuring exchange of information with the EMA, as well as engaging in communication and dissemination, ensuring training activities in Member States.

The activities under the EMA / EUnetHTA 21 work plan will contribute to this implementation work. In the discussions it was noted that exchange of confidential information will be an important aspect for collaboration between EMA and the HTACG under the Regulation. Also highlighted was the importance of continued engagement on evidence and methodologies.

Learnings from the workshop on patient experience data

EMA reported on latest activities regarding Patient Experience Data (PED). Although there has been much progress in the EU in recent years, PED are still not systematically included in all aspects of medicines development and regulation. Reinforcing patient relevance in evidence generation is a key priority in the EMA's Network Strategy and the Regulatory Science Strategy. It was noted that PED is relevant in the context of the implementation of the HTA Regulation. Guidance work is also ongoing at ICH for global harmonisation of PED.

Against this background a multi stakeholder workshop on patient experience data in medicines development and regulatory decision-making was held in September 2022. The objectives were discussions on a common understanding on PED definition in the EU, including patient engagement (PE), patient preferences (PP) and patient reported outcomes (PROs); current methods for collecting and incorporating patient data into medicines development and regulatory assessments; how direct patient data collection from real-world healthcare can be leveraged and used; and priorities to enhance the collection and use of patient experience data. Key outcomes included the need for resources and technical expertise and development of an overall strategy on PED. An executive summary from the workshop has been published: Patient experience data in EU medicines development and regulatory decision-making workshop.

In the discussions it was emphasised that this an important topic for further discussions. Developing a clear terminology is valuable and using PEP with three subparts (PROs, PP, PE) is helpful. In the context of HTA PROs are used for many years. It is also important to clearly distinguish between PP and PRO in terms of evidence. Further collaboration on the topic of PED would be valuable.

ACTIONS:

- EMA to engage with HTA representatives in the context of the development of a reflection paper on PED.

Collaboration in the context of patient relevant data for decision making

Three initiatives were presented. IQWiG reported on research in collaboration with the Drug Committee of the German Medical Association on reporting of patient-reported outcomes (PROs) in HTA reports and SmPCs. For this research HTA reports (including RCTs) of drugs entering the market in Germany between 1/2014 and 7/2018 were reviewed, identifying RCTs with evaluable PRO data in the HTA reports, if these RCTs are reported in the SmPC, and if evaluable PROs from the RCTs included in the SmPCs are reported in the SmPC. In conclusion, only part of the available PRO data is presented in the SmPCs, PRO presentation seems to differ between indications and PRO presentation might be different between PRO categories (symptoms and HRQoL) and outcomes (positive vs. negative results). The study is published here: Results on patient-reported outcomes are underreported in summaries of product characteristics for new drugs | Journal of Patient-Reported Outcomes

KCE presented a study proposal for research infrastructure called NEED (Needs, Examination, Evaluation and Dissemination) to identify unmet patient and societal needs for a more needs-driven health policy and product development. The objectives are to develop, host and maintain an evidence database on patient and societal needs in different disease areas, and to coordinate unmet needs research. An invitation to support the objectives of the project was expressed.

Finally, EMA provided an update on ICH activities related to Patient-Focused Drug Development. A reflection paper was co-sponsored EMA/FDA and the draft underwent public consultation in 2021. Aims are to improve the quality, relevance, safety and efficiency of drug development and inform regulatory decision making. Specifically, it addresses patient-meaningful COAs and endpoints as well as patient

preference information for preference-sensitive benefit/risk assessments. EMA will collaborate with FDA on drafting topic proposal and advance public consultation and engagement aspects. Comments received so far will be considered for further steps of the ICH process (i.e., guideline work) and there will be further opportunities for non-ICH stakeholder input during guideline drafting work. More information here: ICH Reflection Paper on patient-focused drug development

ACTIONS:

- Topic leads from the work plan item "Continue sharing experience on labelling and EPARs information, e.g. regarding information on subpopulations" to review learnings from the IQWIG research
- HTA community to comment on ICH guidances included under the Patient-Focused Drug Development initiative during the public consultation

Update on the EMA funded registry-based study on Spinal Muscular Atrophy

EMA provided an update on a study on spinal muscular atrophy disease (SMA) that aims at describing SMA patients' characteristics at baseline and throughout course of disease, as well as clinical management and its evolution over time across the multiple disease phenotypes and genotypes in at least 5 European countries. A secondary objective is to learn about how we can work with registries to improve evidence generation. The study plan was recently provided by the service provider and accepted by EMA. For the study 4 clinician-based registries (Belgium, Sweden, Switzerland and Czech Republic/Slovakia) and 3 patient-based registries (Spain, Germany & Austria, and UK & Ireland) have been selected. The draft protocol is under review and engagement with interested HTA bodies took place in the context of the review. The study report is expected in 2Q23.

G-BA reported on a registry-based SMA study they required for onasemnogen-abeparvovec and a comparison with the EMA-funded study. It was noted that the objectives of the EMA study are broader, however there is overlap between the studies concerning comparative effectiveness and safety of DMTs. The G-BA study investigates specific comparisons (onasemnogen vs. nusinersenin specific patient populations) rather than in untreated vs. all treated patients. It primarily uses the SMArtCARE registry with the option to include other (international) registries if registry and data quality is sufficient. Further details were elaborated.

During the discussion it was highlighted that there are opportunities for mutual learning on registry-based methodologies and what is the place of different types of evidence in decision making.

ACTION:

- EMA to facilitate follow-up discussions with HTA representatives on the protocol and the later study results
- Joint follow-up in terms of sharing the experience from this work as part of the EMA / EUnetHTA 21 work plan activities

Progress with the identification of use cases for DARWIN EU

EMA together with the HTA representative in the DARWIN EU Advisory Board reported on the workshop "How can DARWIN EU® support HTA/Payer decision-making?" held in October 2022. More than 30 representatives from HTA and Payers organisations across the EU took part. The objectives were to raise awareness of the possibilities of RWE generation via DARWIN EU; better understand the HTA/payers research questions of interest suitable for RWE analyses; and identify simple and complex

use cases from HTA/payers perspective that could lead to studies conducted by DARWIN EU. In terms of specific studies to be conducted, two studies were agreed subject to the feasibility assessment:

- Natural history of multiple myeloma. Off-the shelf study to characterise MM patients, including treatments/treatment sequences received and survival;
- Effectiveness study to assess overall survival of patients with non-small cell lung cancer treated with immunotherapies (pembrolizumab, nivolumab and atezolizumab) as first line.

The opportunities of collaboration in the RWE space through DARWIN EU were acknowledged.

ACTION:

- Joint follow-up in terms of sharing the experience from this work as part of the EMA / EUnetHTA 21 work plan activities

Overview of EUnetHTA 21 deliverables with potential relevance for EMA

An update was provided on the EUnetHTA 21 deliverables and the review and commenting by EMA. Of the EUnetHTA 21 deliverables (https://www.eunethta.eu/jointhtawork/) the following were identified for EMA review: D4.3.1 practical guideline direct and indirect comparators and comparisons, D4.6 practical guideline validity of clinical studies, D7.1 practical guideline HTD and HTA interaction, D7.2/7.3 patient and HCP guidance and templates for interaction, D4.5 practical guideline applicability of evidence, D4.4 practical guideline endpoints. EMA feedback was feedback under the framework of the EMA/EUnetHTA 21 workplan, and focused solely on technical observations or input, respecting the different remit, or covered editorial considerations in view of processes for collaboration. In terms of uptake of this input by EUnetHTA 21, the following was noted:

- Suggestions to address other or additional HTAR articles/recitals, where relevant, this was added.
- Technical suggestions referencing ICH, e.g. suggestion to better incorporate the estimand framework with reference to the ICH E9(R1) addendum led to changes in the EUnetHTA 21 deliverable.
- For the practical guidelines on involvement HTD & Experts (patients & HCPs), the input of EMA was accompanied with exchanges. This helped to understand legal procedures, and EMA standpoints (e.g. with confidentiality and redaction possibilities in EMA reports). It also helped to understand the current practice at EMA and certain procedural obligations.

Status update on the delivery of the EMA/EUnetHTA21 work plan

EMA and EUnetHTA provided a joint update on the status of the work plan activities. The majority of activities were on track (17 of the 25 with report from the topic leads), three were progressing but some obstacles are experienced, and five were currently behind schedule. A call for continued focus on the delivery of the work plan was jointly made towards all topic leads.

ACTION:

- Follow-up review at the next EMA/EUnetHTA 21 bilateral, to ensure full delivery

Closing remarks

The next meeting will be hosted by EUnetHTA and will be scheduled for **Q2 2023**, most likely again in the virtual format.