Minutes of EMA/EUnetHTA meeting
21 November 2019

Role	Name
Co-chairs:	Hans-Georg Eichler and Giovanni Tafuri
Present:	**EUnetHTA:** Luciana Ballini – RER (dial-in) Nick Crabb - NICE Jadwiga Czeczot - AOTMiT Brad Groves - NICE Marcus Guardian - ZIN Chantal Guilhaume - HAS Irena Guzina - HAS (dial-in) Krystyna Hviding - NOMA Tuomas Oravilahti - FIMEA Chaienna Schreuder - ZIN Regina Skavron - G-BA Giovanni Tafuri - ZIN Beate Wieseler - IQWiG Claudia Wild - LBI-HTA **European Commission**: Flora Giorgio **EMA**: Michael Berntgen Emil Cochino (dial-In) Pierre Demolis (dial-in) Falk Ehmann Ralf Herold Xavier Kurz Jordi Llinares Garcia Maria Mavris Jane Moseley Elias Péan (dial-in) Armin Ritzhaupt Bruno Sepodes Anna Tavridou (dial-in)

Item	Draft agenda	Name
1.	Introduction to the day and adoption of the draft agenda	Hans-Georg Eichler and Giovanni Tafuri
2.	Update on Joint Action 3	Marcus Guardian
3.	Update from the European Commission	Flora Giorgio
4.	Exchange on recent developments regarding better utilization of patient-reported outcomes as part of evidence generation plans: - Experience gained in Parallel Consultation on PROs - Reporting on patient-reported outcomes (PRO's) in assessment reports and the SmPC for oncology products - Reporting on PROs in REAs and national HTA reports	**EMA:** Francesco Pignatti, Elias Pean, Ralf Herold, Spiros Vamvakas, Jane Moseley, Pierre Demolis **EUnetHTA:** Chantal Guilhaume (HAS), Regina Skavron (G-BA), Beate Wieseler (IQWIG)
5.	Follow-up discussion on registries: - Update on the REQueST tool - Update on the EMA reflection paper on registries - Multi-stakeholder workshop on cancer registries	**EMA:** Peter Arlett, Xavier Kurz **EUnetHTA:** Brad Groves (NICE)
6.	Practices and experiences with combination products/companion diagnostics: - Overview of activities from the EMA-EUnetHTA combination products / companion diagnostics work stream - Latest information on the implementation of the MDR/IVDR legislation - Upcoming events for engagement	**EMA:** Falk Ehmann **EUnetHTA:** Nick Crabb (NICE), Claudia Wild (LBI)
7.	Experience with Post-licensing Evidence Generation (PLEG): - Update on PLEG pilots from HTA bodies - Review of latest discussions on PLEG in Parallel Consultation	**EMA:** Jane Moseley, Xavier Kurz, Anna Tavridou, Emil Cochino **EUnetHTA:** Irena Guzina (HAS), Chantal Guilhaume (HAS)
8.	Review of the operational arrangements between EMA and EUnetHTA in the context of REA activities: - Fine-tuning of the operations - Latest experiences and estimates for	**EMA:** Michael Berntgen **EUnetHTA:** Chaienna Schreuder (ZIN)

	upcoming REAs	
9.	Progress of the EMA/EUnetHTA work plan activities	**EMA:** Michael Berntgen **EUnetHTA:** Giovanni Tafuri
10.	Closing remarks	Hans-Georg Eichler and Giovanni Tafuri

This was the 18th meeting between the European Medicines Agency (EMA) and representatives from the European Network for Health Technology Assessment (EUnetHTA) and attended by the European Commission. The draft agenda was adopted without changes.

Update on Joint Action 3

Within the current Joint Action, the production of Joint and Collaborative Assessments as well the Early Dialogue programme are successfully proceeding with continued efforts to refine processes and procedures. Continued improvements are also in progress for the recently established EUnetHTA policy on conflict of interest, a key tool for the involvement of patients and health care professionals in the Joint and Collaborative Assessments, Early Dialogues and projects on Post-Launch Evidence Generation.

Furthermore, EUnetHTA has triggered an open discussion with its partners about the future model of cooperation post 2021 in light of new possible scenarios in the European HTA landscape.

Update from the European Commission

The state of play on the HTA proposal at the European Parliament and at the Council as well as an overview of the progress under the Romanian and the current Finnish Presidency (July-December 2019) was presented. Participants were also informed that the new designated Health-Commissioner reiterated her commitment to the HTA Proposal.

An overview of the new Partnership on Health Innovation (IHI) was presented. Building on the Innovative Medicines Initiative (IMI2), IHI would significantly revise its governance, scope and expand its partners, (including not only medicinal products but also other medical technologies). Such initiative shall fund actions of joint relevance to both EU public health and healthcare systems and the private sector.

Industry is organising an online consultation on the Draft Strategic Research Agenda for such new partnership, which represents an important opportunity for public authorities to provide their inputs. Further possibilities to provide input to the Commission services on the IHI's agenda will be available shortly.

Exchange on recent developments regarding better utilization of patient-reported outcomes (PROs) as part of evidence generation plans

PROs represent an important area of common interest to both EMA and EUnetHTA. EMA conducted an analysis on EMA-HTA Parallel Consultation procedures finalised between January 2013 and December 2018. The aim was to quantify and characterise the nature of

such advice procedures, and specifically questions to CHMP relating to use of PROs. Results showed that 68% (80 of 118) of parallel consultation procedures had questions related to PROs addressed to CHMP. Overall, 115 different instruments were identified in the questions, both generic and disease specific.

A similar analysis focussing specifically on PRO related questions in Early Dialogues is currently under way. EMA and EUnetHTA participants agreed to perform a joint EMA/EUnetHTA review of the experience with PROs in Parallel Consultation

The second part of this session focussed on the use of PROs at the regulatory and HTA level. A presentation on PROs in assessment reports and SmPCs for oncology products was provided by EMA. The importance of disease-specific PRO data in submissions as well as an adequate reporting in the EPAR (with potential reflection of relevant elements in the SmPC section 5.1) was highlighted given their role to determine B/R as well as in health care professional's decision-making.

A dedicated workshop on PROs in oncology is being prepared by EMA in cooperation with EORTC in 2020. Furthermore, PROs are part of the activities for the EMA Regulatory Science Strategy (2020-2025). Discussion focusses on which PRO elements can be systematically reported in a way that is useful for HTA and on whether the CONSORT PRO may be used as a starting point.

From an HTA perspective, PROs also play a key role in the assessment. For the 5 completed EUnetHTA Joint Assessment Reports, PRO data were requested by EUnetHTA to manufacturers for each product and for 4 out of 5 products such data were submitted and assessed. At the national level, examples from France (HAS), Germany (IQWiG) and Norway (NOMA) were presented, all of which showed the importance attributed to such data by the three bodies.

Action Points:

- Perform a joint EMA/EUnetHTA review of the experience with PROs in Parallel Consultation

- Progress with the enhancement of assessing and reporting of PROs in EMA outputs (such as assessment reports) based on CONSORT-PRO and the internal guidance developed by the Oncology office.

Follow-up discussion on registries

An update on the use of the REQueST tool was provided by EUnetHTA. REQueST is being used by different registry holders in the UK to evaluate the quality and the potential use of their data by HTA bodies.

From the regulatory side, an overview of the EMA discussion paper on registries was presented. The document stems from a public consultation ended in June 2019. Key elements of the document were presented. EMA has also organised a Workshop on the role of registries in the monitoring of cancer therapies based on genetic and molecular features in November 2019 with the participation of representatives from the EUnetHTA consortium.

The primary objective of the workshop is to agree on recommendations about i) core data elements that should be collected in cancer registries, ii) quality assurance to ensure registry data are of suitable quality and to permit registries interoperability, iii) governance, to discuss practical considerations for accessing/sharing data and clarify roles of all involved stakeholders.

Action Points:

- Follow-up discussion on the use of the REQueST tool and the forthcoming guidance on use of registries for regulatory purposes, to ensure they are complementary

Practices and experiences with combination products/companion diagnostics

An update on activities related to the EMA/EUnetHTA workplan item on combination products/companion diagnostics was presented. Main areas of collaboration are the next generation sequencing, the evaluation of genetic signature tests, new treatment paradigms (e.g. highly personalised cancer treatments), histology independent indications of cancer drugs and operational issues around patient access to companion diagnostic tests. The experience gained at the national level in relation to these points are discussed within this forum. Mutual commenting was facilitated through the collaboration (e.g. joint HAS, IQWiG and NICE response to the EMA concept paper on development and lifecycle of personalised medicines and companion diagnostics).

An update was provided on the status of the implementation of the Medical Device and the In vitro Diagnostics Regulations. Key elements relevant to EMA./Eunethta include the new classification for high risk devices, work on Common Specifications and collaboration on the evaluation of IVD/MP (co-)developments.

The need for more specific guidance and collaboration for the evaluation and life cycle management of IVD and MP has been highlighted and the tools available to EMA highlighted including labelling and EPARs. EUDAMED's launch will occur at the time of the In vitro Diagnostics Regulation implementation, i.e. May 2022.

The EC MDEG is a relevant stakeholder and participation from the pharmaceutical (regulators) side and Eunethta should be considered.

The challenge of adequacy of data in the context of application dossiers for regulatory/HTA decision making was raised.

Action Points:

- Further refinement of the type information on companion diagnostics to be included in the CHMP assessment report in order to enhance the usefulness of this output for HTA

- Possibility to engage with the medical device community though the Medical Device Coordination Group (MDCG), subject to discussion with the EC

Experience with Post-licensing Evidence Generation (PLEG)

An update on ongoing PLEG pilots was provided by EUnetHTA. General features of PLEGs as well as specificities of the PLEGs on Spinraza and on CAR-T therapies were presented. In particular, the latter PLEG aims to provide HTA advice on the quality and usability of the EBMT registry for post-launch follow-up of CAR T therapies to inform HTA re-assessment at the national level. The assessment of EBMT quality is done by using the REQueST tool.

Subsequently, EMA presented preliminary findings from a qualitative analysis based on questions on post licensing evidence generation within EMA/HTA Parallel Consultations.

In the discussion it became apparent that the early identification of post-licensing evidence needs in the context of conditional marketing authorisation is a particular challenge. There are different perspectives on this concept that aims to facilitate medicines addressing unmet medical needs. It was therefore agreed to have a dedicated discussion at the next bilateral.

Action Points:

- Review opportunities for product-specific interaction in the context of joint REA production using the established information exchange, to inform PLEG pilots

- Discussion at the next bilateral on the CMA concept and the perspective from regulators and HTAs, respectively, in order to reflect on the ecosystem of decision making from patient's perspective

Review of the operational arrangements between EMA and EUnetHTA in the context of REA activities

The latest operational experiences of collaboration between EMA and EUnetHTA in the context of REA activities were discussed. Recently, in order to facilitate the process of REA production, refinement to the operational framework between EMA and EUnetHTA were introduced. The main changes are:

1. Provision of the final adopted SmPC together with the relevant sections of the CHMP assessment report

2. Update of EUnetHTA on timelines of the regulatory review from products with planned REA

3. Debrief on final CHMP outcome immediately after CHMP opinion

4. Clarification regarding the citation of CHMP assessment report in the REA

Action points:

- Implementation of the new process for products with CHMP opinion from December 2019 onwards

Progress of the EMA/EUnetHTA work plan activities

Progress of each activity within the current work plan was discussed This was to ensure that the work plan will be delivered as expected. Most activity areas are either progressing or showing at least some progress.

Action points

- Prolongation of the work plan to 2021 following the JA3 extension

Closing remarks

The next meeting will be hosted by EMA and will be scheduled for mid-2020.