19 January 2024
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Minutes of Concluding EMA – EUnetHTA bilateral meeting: "Celebrating joint achievements - progressing future collaboration"

14 September 2023

Role	Name
Co-chairs:	Michael Berntgen and Niklas Hedberg
Present:	EUnetHTA: Roisin Adams, Ines Costa, Judith Fernandez, Naomi Fujita-Rohwerder, Wim Goettsch, Gianluca Grimaldi, Marcus Guardian, Niklas Hedberg, Krystyna Hviding, Marco Marchetti, Gergo Meresz, Helena Monteiro, Eleni Pitta, Sonia Pulido, Stephanie Said, Hedi Schelleman, Johanna Seeger, Merle Tenberg, Camille Thomassin, Beate Wieseler, Anne Willemsen EC: Maya Matthews, Valentina Barbuto EMA: Gaelle Andriantafika, Miguel Antunes, Alex Barbosa Correia, Ralph Bax, Michael Berntgen, Fabrizio Boccacci, Laurent Brassart, Francesca Cerreta, Emer Cooke, Silvy Da Rocha Dias, Francesca Day, Juan Garcia, Iordanis Gravanis, Hans Hillege, Carla Jonker, Dominik Karres, Kristina Larsson, Jane Moseley, Thorsten Olski, Elias Péan, Steffen Thirstrup, Enrico Tognana, Spiros Vamvakas, Machteld van Egmond, Sandra Vanlievendael, Patrice Verpillat Committees: Brian Aylward, Pierre Demolis, Ilona G. Reischl, Violeta Stoyanova-Beninska

Item	Draft agenda	Name	Time
1.	**Welcome and opening address** Outline of the day and adoption of the draft agenda	Emer Cooke Michael Berntgen and Niklas Hedberg	20 min
2.	**Keynote address**: "Policy shaping through technical cooperation: the experience with the EMA/EUnetHTA collaboration as nucleus for the HTA Regulation"	Maya Matthews (DG SANTE)	20 min

Item	Draft agenda	Name	Time
3.	**The regulatory / HTA interface in the context of decision-making** Opening statements: 1. Experience from managing Joint Clinical Assessment and its precursors 2. Mutual learnings from respective decision criteria and methodologies Discussion topic: Translating experience into future operations	 Anne Willemsen (EUnetHTA) Johanna Seeger (EUnetHTA) and Hans Hillege (EMA) Facilitated by Steffen Thirstrup (EMA)	 15 min 10 min 25 min
Interactive coffee break "Do you make the connections?"			30 min
4.	**The regulatory / HTA interface in the context of evidence planning** Opening statements: 1. Learnings of good procedural practices 2. Review of impact: measured so far and yet to be measured Discussion topic: Translating experience into future operations	 Thorsten Olski (EMA) Stephanie Said (EUnetHTA) and Jane Moseley (EMA) Facilitated by Gergo Meresz (EUnetHTA)	 10 min 15 min 25 min
Lunch break (Sky lounge, floor 18) **incl. group photo**			70 min
5.	Introduction to the initial work of the HTA Coordination group and its subgroups	Roisin Adams (HTACG chair)	15 min
6.	Implementation planning from the European Commission perspective	Valentina Barbuto (DG SANTE)	15 min
7.	**Identification of priority areas for future technical collaboration between regulators and HTA** Break-out sessions (groups rotating every 20 minutes): A. Evidence planning B. Assessment methodologies C. Planning for capacity and capability, medicinal products and medical devices	 Rapporteur A – Spiros Vamvakas Rapporteur B – Beate Wieseler Rapporteur C – Marcus Guardian	60 min
8.	**Planning for the future** • Report from the break-out sessions • Report of the EMA/EUnetHTA work plan and next steps	 Rapporteurs from session 7 Anne Willemsen (EUnetHTA) and Francesca Cerreta (EMA)	 30 min 15 min
9.	Closing remarks	Michael Berntgen and Niklas Hedberg	10 min

This was the 25th and concluding 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.

Emer Cooke welcomed the participants to this event under the theme "Celebrating joint achievements - progressing future collaboration". An era comes to an end since the European-level cooperation between the regulatory and HTA communities started in 2010. During this time regulators and HTAs have learned from and about each other, and these experiences are also an energiser for continued joint work, under the new legal framework. Three workplans have been established throughout the years and through their delivery the value of regulatory/HTA cooperation was demonstrated. The regulatory/HTA collaboration will continue on a new footing, now enshrined into European law, with more participants, additional responsibilities and high expectations by stakeholders.

The objectives of the meeting were to review the achievements under the work plan 2021-2023 and identify priorities for future collaborative regulatory/HTA work. The draft agenda was adopted without changes.

Keynote address: "Policy shaping through technical cooperation: the experience with the EMA/EUnetHTA collaboration as nucleus for the HTA Regulation"

Maya Matthews delivered a keynote address providing reflections how technical cooperation helps and shapes policymaking, eventually leading to new legislation in the European Union. Starting from the perspective of the "Heath Union" from the recent State of the Union address by the President, several elements supporting patient-focused policy were outlined.

The regulatory / HTA interface in the context of decision-making

Experience with joint clinical assessment by EUnetHTA concerned medicinal products as well as medical devices. In Joint Action 3 16 JCA (so-called REA "Relative Effectiveness Assessments") were performed for medicinal products. Specific confidentiality agreements with EMA allowed receiving information after CHMP opinion was adopted; furthermore, webinars between rapporteurs and HTA assessors were conducted. In EUnetHTA 21, two joint clinical assessment were performed on medical devices as well as three PICO exercises on medicinal products. Furthermore, in absence of applications from developers for joint clinical assessments for medicinal products, a product-specific webinar was held on an approved ATMP. Such product-specific exchange was highly valued by both regulators and HTAs as it allowed insight in key learnings on evidence and uncertainties with enhanced mutual understanding e.g. on PLEG requirements and indirect comparisons. It was therefore recommended to continue interactions, to facilitate mutual understanding, learning and awareness and facilitate timely decision-making.

The difference in scope of benefit/risk assessment versus additional benefit assessment was acknowledged. From a regulatory perspective an overview of the benefit/risk methodology was provided alongside a comparison of uncertainties that regulators and HTAs need to address noting that they differ in nature and mitigation strategies. It was noted that to maintain credibility in decision-making, it is crucial to uphold the distinct principles and mandates of each entity involved and increase dialogue, predictability, transparency and consistency in data presentation and decision-making. This includes from regulatory perspective a robust approach to risk/benefit analysis and utilizing state-of-the-art data presentation, assessment and decision-making methodology, while incorporating multi-stakeholder input. Transparent description of similarities and differences of EMA and HTA assessment scopes in EPAR / JCA report to increase awareness of stakeholders. Exchange on requirements regarding study design aspects, e.g. population and endpoints, is valuable. This also includes post-

authorisation studies where early exchange between regulators and HTAs on requirements allow communication to developers. Furthermore, more detailed discussions on methodologies, such as indirect treatment comparisons, should be pursued.

The discussion on translating experience into future operations touched on several aspects such as opportunities to facilitate earlier exchange on uncertainties and how these can be addressed with additional evidence, importance of robustly documenting the assessment considerations and value judgements, as well as challenges with evidence generation for innovative treatments addressing unmet needs.

The regulatory / HTA interface in the context of evidence planning

An overview was provided on the evolution of the parallel scientific advice framework and the various iterations. For the initial EMA/HTA parallel scientific advice in 2010 the EMA procedure adjusted to the needs of the HTAs and applicants contacted HTA bodies individually. It was from the outset important that EMA and HTAs were equal partners with dedicated project managers on either side. In 2017 a more structured and streamlined process for Parallel Consultation (PC) was created, with a single platform, central HTA recruitment, establishment of the EDWP and the options for consolidated or individual consultations. This was changed towards a single call for interest in 2020, when applicants received consolidated feedback from HTAs. From 2021 the EMA-HTA parallel Joint Scientific Consultations (JSC) discontinued the written-only procedure and the EDWP was replaced by the JSC CSCQ. In 2023 the parallel Scientific Advice during "interim period" was launched, modelled on the PCI process. This will be in place until the operations under the HTA Regulation. Key learning were that continuous improvement was key to deliver best results, respect for roles and remits is paramount and that joint technical work as the foundation for establishing mutual trust and understanding.

Drilling into the seven joint scientific consultations conducted during EUnetHTA 21, all were for First in Class products, 3 out of 7 were orphan medicinal products, 4 out of 7 products were oncology or oncology-related products, 2 out of 7 products were ATMPs, and 2 of the 7 applicants were SMEs. In 6 out of 7 JSCs patient (representatives) and in 4 out of 7 JSCs clinical experts have been involved at European level. "Population" and "Outcome" were subject to all requests; 4 requests concerned questions on PLEG. There was very high alignment between regulators and HTAs in all 7 joint scientific consultations, preparatory bilateral meetings before the discussion meetings did not reveal any clearly divergent positions. A publication of the detailed results is foreseen. Furthermore, refence was made to the two previous publications analysing the degree of concordance between regulatory and HTA positions in parallel scientific advice and the uptake of the guidance by developers.

In the discussion it was stressed that the earlier the interaction the better particularly in challenging areas such as rare diseases and unmet medical needs. The importance of the transitional arrangements was noted as this prepares for the future parallel JSC framework and also enables optimised evidence generation for products under future joint clinical assessment (Guidance on Parallel EMA/HTA body (HTAb) Scientific Advice for the Interim Period). A follow-up analysis to the study in 2018 was encouraged. Finally, it was noted that elements of the proposed revision of the pharmaceutical legislation are also relevant for enhanced discussions between regulators and HTAs on evidence plans.

ACTIONS:

- Joint publication of the analysis of experience with parallel Joint Scientific Consultation under the EUnetHTA21 framework

- Consider follow-up analysis of the scientific advice cases from the earlier publications, focusing on insights into decision making on the basis of the generated evidence

Introduction to the initial work of the HTA Coordination group and its subgroups

The governance under the HTA Regulation is being established. At the core is the Member States Coordination Group on HTA (HTACG), which had four meetings so far. The HTACG will adopt guidance on procedures and methodological guidance, and have exchanges with EMA and the Heads of HTA Agencies Group (HAG). Four subgroups have been established and they will develop and validate procedural and methodological guidance. A workplan was approved for 2023 and 2024. The 1st HTA Stakeholder Network meeting was held and a series of Information Days, organised by the EC together with the HAG, will be held to inform stakeholders.

Implementation planning from the European Commission perspective

Key areas of implementation work concern setting up the governance (HTACG and subgroups) as well as the Stakeholder network, training and capacity building, developing the IT platform, drafting the Implementing Acts and facilitate collaboration with the EMA (Implementation of the Regulation on health technology assessment). The 1st Stakeholder Network meeting was held in June 2023; EMA was also present. Upcoming meetings will cover consultations on main concepts of first Implementing Act; also there will be a workshop on oncology and ATMPs. The HTA IT platform is based on SharePoint in the EC datacentre and the go-Live of release 1 is planned in September / October with the onboarding of HTA Stakeholder Network in November. The interface with EMA systems is yet to be developed. Work on the six Implementing Acts is scheduled between 4Q23 and 4Q24. With regard to guidance development, methodological guidance on joint work, procedural steps and the timeframe for the conduct of JCA and JSC, as well as guidance on the appointment of assessors and co-assessors for JCA and JSC are progressing. Training and capacity building is financed under EU4Health as well as Horizon Europe (SUSTAIN HTA to University of Utrecht to support the uptake of innovative HTA methodology and advancing HTA expertise across EU).

Finally, in terms of collaboration at the regulatory/HTA interface the EC will facilitate the identification of key areas of technical collaboration between EMA and the HTACG, to continue the close collaboration with EMA on the implementation of the HTA regulation, and ensure synergies between the implementation of the HTA Regulation and the development of the legislation on pharmaceuticals and medical devices.

Identification of priority areas for future technical collaboration between regulators and HTA

Priorities for future technical collaboration between regulators and HTAs were discussed in break-out sessions. The objective was to inform future discussions on technical cooperation between EMA and the HTACG and its subgroups.

In terms of "Evidence planning", the potential use of horizon scanning reports / business pipeline data to identify needs and capacity for parallel joint scientific consultation was noted, also to facilitate priority setting and predictability for developers. Going further, early awareness through horizon scanning activities can facilitate interaction on potentially significant innovative technologies through other frameworks. More in-depth exchanges on suitable comparators, also in view of pharma review, should be held. Continued collaboration on registries as example of real-world evidence is valuable to ensure relevance and usability of data. Finally, it is important to disseminate positions on evidence needs from both regulatory and HTA perspective not only through guidelines but also in scientific papers and Q&A's, where relevant.

Collaboration on "Assessment methodologies" should foster methodological exchanges on various topics, such as indirect comparison, including their relevance for evidence from single arm trials, uncertainties from studies/data, their characterisation and management within the different assessment frameworks by HTAs and regulators, as well as PROs / patient experience data and endpoints more generally. There are opportunities through the access to individual patient data. Other topics included continued collaboration on real-world evidence, better understanding of the application, opportunities and challenges of artificial intelligence, exchange on indication-specific guidance as well as extrapolation / evidence transfer within the different assessment frameworks.

Regarding "Planning for capacity and capability" cooperation on horizon scanning to identify capacity / capability needs, prepare for changes in processes / procedures, and influence R&D ecosystems is advantageous. Mutual discussion on application / volume planning can facilitate understanding of respective capacities. Joint capability building eg through training sessions involving HTAs and EMA, allowing exchange of expertise and providing a framework where experts can learn from each other. Also, incremental learning, such as research programmes (eg Erasmus) and observer status can be relevant. Specific focus on areas with sparse experience of joint work, such as medical devices and combination products.

Planning for the future

The EMA/EUnetHTA 21 work plan 2021-2023 had nine topics with 17 activities, progressed by joint topic leads from EMA and EUnetHTA. Medical device related activities were added in March 2023. Examples were provided on progress with methodologies for engagement of patients and healthcare professionals, continuous optimisation of regulatory outputs as reference for down-stream decision making, as well as establishing working practices in the context of TISP (topic identification) for JCA on Medical Devices. Throughout the collaborative work, both sides appreciated the sharing of perspectives.

It was agreed that it is important to foster this collaboration in the future. Basis for such collaboration should be the priorities identified in the three break-out sessions.

ACTIONS:

- Publication of the achievements under the current work plan as Report on the implementation of the EMA-EUnetHTA 21 work plan 2021 - 2023 .
- EMA and HTACG, facilitated by the EC, to identify priorities for future technical collaboration, also considering the primary focus on implementation work for the HTA Regulation

Closing remarks

The EMA and EUnetHTA cooperation, which started in 2010, was driven by commitment, curiosity and pragmatism. The work has been a forward-looking and progressive endeavour on project-level, which is now been enshrined into European law. Thank you to all contributors along the journey, as chairs, topic leads, discussants, meeting participants, work plan coordinators, and organisers.