EMA-EUnetHTA Meeting Minutes
08 June 2017 – 11:00 to 16:00 CET
Meeting Venue: ZIN Offices - Eekholt 4 | 1112 XH | Diemen

Role	Name
Chairs	Wim Goettsch and Hans-Georg Eichler
Present	EUnetHTA: Chantal Belorgey, Hannah Brühl, Irina Cleemput, Wim Goettsch, Marcus Guardian, Niklas Hedberg (by TC), Pall Jonsson, François Meyer, Michelle Mujoomdar, Margarida Oliveira, Tuomas Oravilahti, Alric Rüther, Tomáš Tesař, Anne Willemsen, Wojciech Wysoczanski EMA and CHMP: Michael Berntgen, Hans-Georg Eichler, Harald Enzmann, Jordi Llinares (by TC), Jane Moseley, Tomas Salmonson European Commission: Ioana-Raluca Siska, Helen Lee (by TC, Item 5), Olga Solomon (by TC, Item 5)
Regrets	Rui Santos Ivo, Marianne Klemp, Christoph Künzli, Simona Montilla

Item	Description	Name
1	Introduction to the day and adoption of agenda	Wim Goettsch and Hans-Georg Eichler
2	Update from DG SANTE on activities related to the EMA-EUnetHTA interaction	Ioana Siska
3	General update on EUnetHTA Joint Action 3 (JA3)	Wim Goettsch
4	Recent developments / Progress on EMA-EUnetHTA activities: • Parallel Scientific Advice / Early Dialogue, including developing perspectives for "late dialogue" • Collaboration at time of market entry (from regulatory opinion to joint REA production)	Topic Co-Leads: Jane Mosely & François Meyer Michael Berntgen & Michelle Mujoomdar
5	"Unmet medical need" as prioritisation criterion: • Review of different approaches to the interpretation of the concept • Identifying and prioritising compounds targeting an unmet medical need along the product lifecycle (pipeline analysis → SA/ED → horizon scanning → prioritisation → joint assessment)	Topic Co-Leads: Niklas Hedberg (with Irina Cleemput) & Jordi Llinares / Michael Berntgen
6	Discussion and agreement of work plan and identification of topic leads, deliverables and timelines	Michael Berntgen & Michelle Mujoomdar
7	Action points from previous meetings	All
8	Closing remarks	Wim Goettsch and Hans-Georg Eichler

1. Welcome & Introductions

This was the 13th meeting between the European Medicines Agency (EMA) and representatives from the European network for Health Technology Assessment (EUnetHTA).

The draft agenda was adopted without changes.

2. Update from DG SANTE on activities related to the EMA-EUnetHTA interaction

HTA Network Meeting
The 8th HTA Network (HTAN) meeting was held on 29 March. The morning session open to members only, provided an opportunity to discuss the results of the public consultation on the Inception Impact Assessment. Members of the HTAN also were provided with summary of findings from the commissioned study on the impact analysis of policy options for EU cooperation on HTA beyond 2020. The afternoon session also included representatives from the HTAN Stakeholder Pool and EMA. Topics covered in the afternoon session included presentation of findings from the two mapping studies that were commissioned to inform the Impact Assessment and a discussion of the next steps of the Ad-hoc Synergy group which was created following the adoption of the reflection paper on synergies between regulatory and HTA issues on pharmaceuticals.

Follow-up of the Reflection paper on Synergies between Regulatory and HTA Issues
A summary of the proposed next-steps for the Ad-hoc Synergy group (hereafter referred to as the Synergy group) was presented. The Synergy group was created following the adoption of the reflection paper on synergies between regulatory and HTA issues by the HTAN in Nov 2016. The Synergy group will be composed of equal number of HTA representatives and regulators. As a first activity, the Synergy group will undertake a mapping of planned or on-going activities at the EU level relevant to the topics identified in the Reflection Paper. A kick-off meeting for the Synergy group has been scheduled for June 2017 where a chair will be elected, the work will be organised, and a timeline for the group's activities will be established. There was some discussion regarding the scope of the group's work and it was clarified that at this time, the focus of the mapping exercise is on EU-level activities rather than national activities; however, it was noted that there may be some learning from on-going national activities that could be of benefit.

Public Consultation on the Inception Impact Assessment
DG SANTE provided an overview of the results from the public consultation on the Inception Impact Assessment. Nearly 250 responses were received during the three month public consultation period with 63 responses coming from citizens representing 21 member states. The majority of responses (150) were received from public administrations, organisations, and associations. Thirty-six responses were received from small and medium-sized enterprises (SMEs). Overall, 87% of respondents were supportive of EU cooperation on HTA beyond 2020 with 80%, 72%, and 54% noting that cooperation on the assessment of pharmaceuticals, medical technologies, or other technologies, respectively, would be useful or to some extent useful.

In terms of governance for such a mechanism, a majority of respondents reported that either an existing EU agency, a new EU agency, or the European Commission itself, would be most

suitable. Results from the consultation suggested that a hybrid funding model including contributions from Member States (MS), the EU budget, and industry application fees would be preferred.

Next steps will include the finalisation of the supporting studies for the Impact Assessment, finalisation of the Impact Assessment in Q2 2017, and a development of a proposal on the future of HTA beyond 2020 to be published in Q4 2017. It was noted that consultation with MS, the HTAN, EUnetHTA, and stakeholders will be on-going throughout.

3. General update on EUnetHTA Joint Action 3 (JA3)

June 2017 marks one year of EUnetHTA JA3 –a summary of the progress to date and key achievements within Work Package (WP) 4 (Joint Production), WP5 (Evidence Generation), WP6 (Quality Management), and WP7 (National Implementation) was provided. Within WP4, there are two on-going pharmaceutical joint assessments and six on-going or completed collaborative assessments of non-pharmaceutical technologies. The call for expressions of interest for Multi-HTA Early Dialogues (ED) for pharmaceutical technologies was launched by WP5 Strand A and the first ED is scheduled for Q3 2017. The collaboration between EUnetHTA and EMA is progressing towards a single platform for Parallel Consultation by Q3 2017. WP6 is coordinating the development of SOPs, related to the joint and collaborative assessment procedures. These SOPs will be integrated in the EUnetHTA Companion Guide – a web-based tool to facilitate the production of joint work. A report detailing the HTA and reimbursement processes in EUnetHTA partner countries has been drafted by WP7. A more complete understanding of such processes will help to understand how MS can engage in and use EUnetHTA's work. It was also noted that EUnetHTA's Executive Board is engaged in the discussions regarding the post-2020 scenarios. Upcoming events like the HTAi meeting in June and the EUnetHTA Forum in September, both with contributions from EMA, were noted.

4. Recent developments / Progress on EMA-EUnetHTA activities

<u>Parallel Scientific Advice / Early Dialogue, including developing perspectives for "late dialogue"</u>
A joint presentation was provided by EMA and EUnetHTA WP5 describing a new platform for multi-stakeholder evidence generation interaction with EMA and HTA bodies (HTABs) as equal partners. This new platform, known as Parallel Consultation, will build on the experience gained from the multi-stakeholder Parallel Scientific Advice (PSA), EUnetHTA Joint Action 2, and the Shaping European Early Dialogues (SEED) project.

EUnetHTA has created the Early Dialogue Working Party (EDWP)[1] which includes HTABs with experience in EDs and that are committed to participate in EUnetHTA EDs. Applicants interested in receiving Parallel Consultation will notify simultaneously EMA and EUnetHTA. A subset of applications will be selected for a Parallel Consultation that involves the EDWP –known as Consolidated Parallel Consultation. To conduct this selection, EUnetHTA has developed criteria[2].

[1] The EDWP includes members from France (HAS), Germany (G-BA), the United Kingdom (NICE), Italy (AIFA with Emilia Romagna as an alternate), Hungary (NIPH), and shared seat between the Netherlands (ZIN) and Belgium (RIZIV INAMI).

[2] The product should aim to bring added benefit to The product should aim to bring added benefit to patients i.e. by: a new mode of action for the indication, AND targeting a life-threatening or chronically debilitating disease, AND responding to unmet need (no treatment or only unsatisfactory treatment available).

The output of a consolidated HTA process will be a single written report including: consolidated written answers for shared positions amongst the HTABs, and individual HTA answers to those questions for which a common answer/recommendation from HTABs was not possible. Regulators will also issue a written CHMP letter in line with CHMP procedures.

Applications not selected by the EDWP will proceed with an Individual Parallel Consultation. As with Consolidated procedures, Individual Parallel Consultations are supported by the EUnetHTA Early Dialogues Secretariat, thereby benefiting from HTA scientific and administrative coordination with centralised HTA recruitment, consolidated HTA List of Issues, albeit with individual HTA written responses as the final product.

The new process will be launched in early Q3 2017; it was agreed to have a joint press release in relation to this launch. A process review of the new platform will be undertaken as needed.

An overview of EMA's registries initiative was provided. The initiative aims to facilitate impartial discussions at an early stage in the marketing authorisation procedure with a view to increase the use of existing patient registries. As part of the EMA registry initiative registries that have demonstrated high-quality data collection methods, governance, and have multi-stakeholder relevance can apply for a qualification procedure. The first parallel EMA EUnetHTA qualification advice procedure on a registry (non-product-specific) is underway and involves HTABs either participating formally or observing. In instances where a suitable registry that could support the authorisation procedure is not available, the initiative aims to facilitate the creation of a new registry that is based on standardised methodological approaches and that can be used by downstream (e.g., HTABs and payers) users. EMA also highlighted forthcoming public EMA workshops in Multiple Sclerosis and Cystic Fibrosis registries to which EUnetHTA representatives were invited. Work within EUnetHTA WP5 – Strand B aims to enhance the use of high-quality registries through the adaptation of existing quality standards for registries (PARENT) into a practical tool to be applied to registry data in HTA.

EMA shared an update on experience with a new framework for the provision of Scientific Advice on peri-/post-licensing studies. Limited, but growing experience exists for providing advice on registries or non-randomised studies. Provision of advice may be prior to marketing authorisation or in the context of imposed post-authorisation data collection requirements. Within WP5B, efforts are on-going to identify products for post-licensing evidence generation (PLEG) pilots. Selection criteria will be the same as those used for Early Dialogues with the additional that the data generated would be used for subsequent reassessment and decision-making.

The optimal timing and conditions for engaging in multi-stakeholder discussions on registries, or additional data generation needs, was discussed. There was general agreement that products for which a Conditional Marketing Authorisation (CMA) may be suitable candidates for the PLEG pilots. Furthermore, Advanced Therapy Medical Products (ATMPs), may lend themselves to a collaborative approach on evidence generation throughout the lifecycle –from early Parallel Consultation to dialogues on registries and PLEG needs. An opportunity are products in the PRIME scheme where the planning of the interactions during development should contain engagement with HTAs as part of the definition of evidence generation plans.

Collaboration at time of market entry (from regulatory opinion to joint REA production)

An update on the collaboration between EUnetHTA and EMA in the context of joint REA production was provided. This collaboration facilitates the provision of specific parts of the final CHMP assessment report to the authors of EUnetHTA joint REAs. This exchange respects the respective remits of EMA and EUnetHTA and is done under strict confidentiality arrangements. A "dry-run" e-meeting between select HTA bodies and the CHMP rapporteurs for a recently approved product was held in May 2017. Feedback following the e-meeting indicated that participants found the experience positive and that the exchange helped to better understand the views of HTABs and regulators, including providing clarity on the approved patient population. The exchange allowed for product-specific discussion, but also identified topics that are relevant more broadly to the therapeutic area and would benefit from follow-up discussions. The first two joint REAs within EUnetHTA JA3 will be pilots in this initiative. An update on the initiative will be provided at two upcoming meetings with the pharmaceutical industry.

5. "Unmet medical need" as prioritisation criterion

An exchange was held regarding the concept of unmet medical need (UMN). The discussion aimed to promote a deeper understanding of and clarity on how HTABs and regulators operationalise the concept of UMN, by which criteria UMN is determined, and how UMN is applied in the assessment and review activities.

The EMA provided an overview of how the concept is interpreted from a regulatory perspective. The definition of UMN is provided within the regulation for conditional marketing authorisation (CMA) and is implicit in the accelerated assessment (AA) procedure. Accepting a CMA or AA represent two ways in which UMN is used by regulators and while the criteria for acceptance is consistent, fulfilment of the criteria may be different. In addition, the concept is used to incentivise development and the marketing of products via activities including the PRIority MEdicines (PRIME) scheme, adaptive pathways, the designation of orphan medicines, and paediatric investigation plan waivers.

When considering UMN, a number of issues need to be addressed by regulators including a patient-level focus rather than a population-level focus; a focus on a single medicine and how it addresses a need rather than how the medicine compares to others. Deciding on UMN is generally a binary decision and the degree of need is not necessarily further quantified.

An overview of how the concept of UMN is used by some HTABs was provided. The output was derived from a questionnaire provided to EUnetHTA partners within WP4. Ten of 19 organisations who responded to the survey stated that the concept of UMN was used in their organisation. Of these, six indicated that this concept was used within the context of prioritisation of innovation procedures and two stated that they used it for select for early dialogues. It was noted by some respondents that the criterion of UMN was too vague. In addition to UMN, responding HTABs noted other prioritisation criteria used included: the potential to offer a major advantage, SME/academic origin of the proposal, disease severity and rarity, and high clinical effectiveness coupled with fair price.

An example of how UMN is applied in the HTA context was provided by TLV. In Sweden, UMN is

often considered in decision making as it influences the willingness to pay. TLV does not have a formal cost-effectiveness threshold; however, historically approvals that exceed 500K-600K SEK/QALY have been uncommon. Where a high UMD has been demonstrated, TLV has accepted higher costs per QALY. In these instances, the wiliness to pay may be higher if the following criteria are met: the condition is very rare, very severe, no alternative treatments exist, and the treatment demonstrates significant clinical effectiveness.

KCE provided an overview of the UMN programme in Belgium. The programme was established in 2014 and allows for reimbursement of medicines that fall under a Compassionate Use or Medical Needs programme. Medicines also need to target an UMN and for which marketing authorisation in Europe will be sought. The impetus for the programme is to promote a shift from a supply-driven reimbursement scheme to one that is needs-driven.

KCE was assigned to develop an approach through which ranked list of UMNs could be established. A multi-criteria decision analysis (MCDA) approach was chosen that included both patient and public involvement and accounted for both therapeutic and societal needs. The procedure and tool was piloted with eight conditions and overall the resulting ranking was deemed to have face validity by members of the UMN Commission within Belgium. Further information, including a summary report, the tool, and template is available on the KCE website.

The discussion focused on the reason to engage into this topic in the first place. There was a shared view that exchange on this concept is beneficial in view of prioritisation of resources. It was therefore agreed to further explore synergies in two distinct areas: identification of products for the PRIME scheme as well as product-related discussions on evidence generation plans where unmet medical need is particularly relevant (e.g. conditional marketing authorisation).

6. Discussion and agreement of work plan and identification of topic leads, deliverables and timelines

A detailed joint EMA/EUnetHTA work plan was presented and the following areas for collaboration were confirmed:

1. Parallel Multi-HTA/EMA early dialogues
2. “Late dialogues” / peri-licensing advice on post-licensing data generation plans
3. Registries and real world evidence
4. Facilitating the exchange of information between regulatory outcome and HTA
5. Methodologies to identify and document the eligible population for a treatment
6. Approaches for significant benefit vs. added therapeutic value for orphan medicines
7. Exchange on concepts including unmet need and therapeutic innovation for priority setting
8. Collaborative approaches to horizon scanning
9. Sharing of methodologies and approaches for patient and clinician engagement
10. Methodological approaches of clinical trials and observational studies;
11. Population-specific or Intervention-specific areas

Development of the work plan was guided by the HTA Network's reflection paper on "Synergies between regulatory and HTA issues on pharmaceuticals." The work plan will be posted on both EMA and EUnetHTA's websites by the end of 2017.

7. Action planning

The action items from previous meetings were reviewed and follow-up activities noted.

8. Closing remarks

The next meeting will be hosted by the EMA and will be scheduled for Q4 2017.

Action Points	Responsible
Finalise procedure for the new platform for Parallel Consultation. Issue a joint press release by Q3 2017	EMA/EUnetHTA
Identify candidates for late dialogues – e.g., products going through PRIME process	EMA/EUnetHTA
Identify co-leads for activities within the joint EMA/EUnetHTA work plan and support progress on activities between bilateral meetings.	EMA/EUnetHTA
Publish joint work plan on respective websites in Q3 2017	EMA/EUnetHTA