30 June 2015
EMA/353327/2015

Minutes of EMA/EUnetHTA meeting - Final

8 May 2015 – chaired by Hans-Georg Eichler and Finn Børlum Kristensen

Role	Name
Chairs:	Hans-Georg Eichler and Finn Børlum Kristensen
Present:	EUnetHTA: Luciana Ballini, Lidia Becla, Finn Børlum Kristensen ,Wim Goettsch, Simone Warren, Thomas Kaiser, François Meyer, Leeza Osipenko, Robert Sauermann, Anna Zawada EC: Jerome Boehm EMA: Peter Arlett, Michael Berntgen, Francesca Cerreta, Hans-Georg Eichler, Andreas Kouroumalis, Kristina Larsson, Jordi Llinares, Jane Moseley, Isabelle Moulon, Douwe Postmus, Spiros Vamvakas, Sandra Vanlievendael
Apologies:	Marianne Klemp, Simona Montilla, Pierluigi Russo, Christoph Künzli, Eva-Maria Zebedin, Harald Enzmann, Robert Hemmings, Alar Irs, Francesco Pignatti, Tomas Salmonson, Almath Spooner

Item	Agenda item	Lead
1.	Welcome and opening by the co-chairs	Hans-Georg Eichler (EMA) Finn Børlum Kristensen (EUnetHTA)
2.	Adoption of draft agenda, review of minutes from last meeting	All
3.	EC update on the development of the HTA Network	Jerome Boehm (EC)
4.	Update on: a) MAPPs and Adaptive Pathway Pilots b) Procedural support for unmet-need-drugs c) Parallel Regulatory/HTA Scientific Advice d) Support to REA pilots through provision of regulatory assessment reports e) On-market evidence collection f) Principles for indication wording	a) Hans-Georg Eichler, Francesca Cerreta (EMA) and Finn Børlum Kristensen (EUnetHTA) b) Jordi Llinares (EMA) c) Jane Moseley (EMA) and François Meyer (EUnetHTA) d) Michael Berntgen (EMA) and Wim Goettsch (EUnetHTA) e) Peter Arlett (EMA) and François Meyer (EUnetHTA) f) Michael Berntgen (EMA), and Leeza Osipenko (EUnetHTA)

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5.	Orphan Drugs	Kristina Larsson (EMA) and Wim Goettsch (EUnetHTA)
6.	“Effects tables” - First feedback from the joint recent exchange	Andreas Kouroumalis and Douwe Postmus (EMA), and Wim Goettsch (EUnetHTA)
7.	Initial experience with patient interactions (eliciting patient values, preferences)	Isabelle Moulon (EMA), Thomas Kaiser and Leeza Osipenko (EUnetHTA)
8.	Three-year Work Plan Summarising the implementation RESULTS of the three-year work plan as a contribution to the final reporting from JA2 and as a basis for recommendations to JA3	Jerome Boehm (EC), Finn Børlum Kristensen (EUnetHTA), and Hans-Georg Eichler (EMA)
9.	Action points from previous meetings (see annex)	All
10.	Any other Business	All
11.	Closing remarks	Hans-Georg Eichler (EMA) Finn Børlum Kristensen (EUnetHTA)

1. Welcome and opening by the co-chairs

This was the 10th meeting between the European Medicines Agency (EMA) and representatives from the European Network for Health Technology Assessment (EUnetHTA).

2. Adoption of draft agenda, review of minutes from last meeting

The draft agenda was adopted without changes. The already published minutes from the last meeting were noted.

3. EC update on the development of the HTA Network

The EC provided an update on the development of the HTA network. It was noted that the strategic position paper on the re-use of relative effectiveness assessments at national level has been finalised and is about to be published. The main activities are now targeting the preparation of Joint Action 3 to implement what has been agreed in the strategy paper; the next preparatory meeting will be convened on 12th June.

4. Updates

a) MAPPs and Adaptive Pathway Pilots

The EMA provided an update on the Adaptive Pathways pilots, a safe harbour initiative within the existing legal framework. Currently the review of stage 2 proposals is ongoing. The discussion covered several aspects of engagement across stakeholders. From a payer perspective it is particularly important to focus on the economic model, which is assumed to be documented with limited evidence

and likely high costs. The development of the price over the life-cycle of the technology with additional evidence becoming available needs to be considered. It was noted that it was already discussed in some stage 2 discussions that one has to work out different pricing models for reimbursement in member states as well as the options for exit strategies.

If, especially due to short timelines, it is not sufficiently possible to involve payers in the AP discussions at such an early stage, the initial experience in the AP pilot could be used to outline a series of scenarios on which the payers could give feedback, to support the AP discussions (e.g. compatibility of annuity payments with national frameworks, feasibility of registry for regulatory and reimbursement purposes...)

Participation in the pilots is of interest for HTA and payer organisations, however resourcing becomes a bottleneck. In this respect these activities are competing with involvement in parallel EMA/HTA scientific advice. To ensure adequate funding it needs to be considered to have such involvement covered by the future Joint Action 3, along with scientific advice.

Better involvement of payers could be explored with organisations that wear both hats, i.e. HTA and payer. Furthermore, preliminary exchanges between EUnetHTA and MEDEV have taken place and it would be welcomed if MEDEV could also be involved further to allow reflection of the payers. At the same time, EUnetHTA retains its focus on the scientific aspects.

Regarding MAPPs, the EMA reported on the progress with the IMI proposal ADAPT SMART that was submitted in response to the "coordination and support action" call topic on MAPPs, for which EMA is willing to lead the consortium. The goal is to establish a platform for horizon scanning and gap analysis for the future development of MAPPs, and to prepare a comprehensive scientific plan for development and exploration of tools. Four HTA partners are consortium partners; it was noted that for other HTA organisation the resourcing was a challenge as well as the fact that some of them cannot have any contact with industry. The need for wider involvement of HTA organisations, including from new Member States (MS), was recognised.

Action points:

- EUnetHTA to facilitate contribution of different HTA institutions to the initiatives on Adaptive Pathways / MAPPs
- EUnetHTA to continue exploring with payers how they can be involved in the development
- EUnetHTA will continue to clarify how to can get information exchange with additional HTA organisations including from new Member States (MS)
- EMA to explore feasibility of defining "sample" scenarios to be discussed with HTAs in the context of the ADAPT-SMART project

b) Procedural support for unmet-need-drugs

EMA provided an outline of a new scheme under development aiming at providing better support for the development of medicinal products with the potential for addressing unmet needs. It was noted that HTAs should have an important role in such development.

Action point:

- EMA to share with EUnetHTA an outline of the scheme once available

c) Parallel Regulatory / HTA Scientific Advice

Updates on both the parallel EMA/HTA scientific advice as well as the SEED project were provided. It was generally noted that a challenge is the definition of objectives of early dialogue given the different backgrounds and remits of the organisations involved. At the next EUnetHTA plenary assembly, an update of the SEED project will be presented and feasibility of a permanent model discussed based on the experience with the early dialogue procedure. For this purpose a report will be prepared and it was agreed to involve EMA in the drafting given that some of the procedures are run jointly. At the same time a report from the EMA/HTA scientific advice pilot is foreseen.

Action point:

- Coordination between EMA and EUnetHTA with regard to the drafting and review of reports on the EMA/HTA parallel scientific advice and the Early Dialogue under SEED, respectively

d) Support to REA pilots through provision of regulatory assessment reports

Previously a request was received by EMA from EUnetHTA to obtain regulatory assessment reports at time of Opinion (before EC Decision) to support REAs. Specific parts of the reports that are of particular interest were identified. It was agreed that a robust framework for data sharing was needed and the parties were clarifying the options. Discussions are currently ongoing between the EMA and the EC. It was generally noted that the ultimate aim would be for companies to voluntarily share these reports with requesting HTA bodies at time of opinion; this would reflect the principle of seamless reviews which is also requested by industry. Experience so far was however that companies provided reports only with delay impacting their usefulness for rapid REA. Therefore, as a transitional measure to facilitate progress with WP5 pilots the framework to allow such sharing directly from EMA to the respective HTA bodies performing the REA review is being explored. As soon as the legal framework is agreed EMA might need further information concerning the legal status of the specific HTA organisations, i.e. to establish if such HTA has the legal authority/capability according to its founding act to conclude/enter into agreements with the EMA.

Action points:

- EMA and EC to continue work on a legally robust framework for data sharing with individual HTA organisations
- EUnetHTA to provide list of HTA bodies involved in REA including information on their legal entity, based on query to be received from EMA

e) On-market evidence collection

An overview of opportunities for regulatory involvement and for potential HTA-regulatory collaboration for on-market evidence generation was provided. Of particular interest was the use of registries and their conduct in countries with interest from a clinical practice perspective. With regard to the ENCePP working group it was considered that the functioning of the HTA studies group would be enhanced by merging it with the existing ENCePP Working Group 1 which focusses on developing methodological guidance. This is particularly relevant as the existing experience of the ENCePP Working Group has highlighted methodological challenges for studies which might serve both regulators and HTA as being the most important area upon which to focus. For the PAES scientific and procedural guidance EUnetHTA expressed high interest in reviewing and commenting on a draft, once available. This topic should be identified for the next meeting.

Action points:

- EMA to engage EUnetHTA in any activities regarding registries,
- EMA to further develop the ENCePP working group 1 on methods by including experts with experience in studies to serve HTA (rather than having a separate group focussed on HTA studies).
- EMA to provide draft PAES guideline to EUnetHTA, once this has been reviewed by its scientific committees

f) Principles for indication wording

EMA reported that the CHMP is developing principles for indication wording, with particular reflection when to go broader and when to go narrower compared to the study population investigated in the clinical trials supporting the application. Starting point is the existing legal/regulatory framework. Key elements are the study population (e.g. inclusion criteria, representativeness) and benefit risk assessment (e.g. effect size, uncertainties, concerns in subpopulations, pharmacogenomic considerations, knowledge of mechanism of action). Further fine-tuning is based on factors like disease characterising, predictability of biomarkers, etc.

HTA bodies emphasised the importance of the indication wording for their evaluations, including the understanding why the regulators came to a certain decision. Based on the approved label and the trial data it is important to have clarity why a certain indication was approved. This concerns situations where the patient population covered by the approved indication is narrower compared to the study population, but also the rationale in case of a “broader indication” compared to the study population. It was noted that the aspects of patient population that are crucial from a regulatory perspective are of relevance for HTA assessments and should be clearly stated in the approved SmPC and explained in the EPARs.

Action point:

- EMA to share with EUnetHTA draft principles ahead of the next meeting, where they will then be discussed.

5. Orphan Drugs

Focus of the discussion was on the framework for orphan designation and particularly the significant benefit criterion at the time of MAA. From the exchange it emerged that the evaluation of "significant benefit" as assessed by the COMP appears to have a lower/different hurdle than expected by HTA bodies. It was noted that major contribution to patient care or "ease of use" as a criterion can be used by the COMP to support significant benefit and maintain the orphan status at the time of MAA. However, for the HTAs this could only be done exceptionally and would normally require a demonstration of improved effectiveness as a result of the “ease of use”. This should be further explored in a joint evaluation by EMA and EUnetHTA.

Action point:

- Develop further understanding regarding the similarities and differences between the regulatory significant benefit assessment and the joint REAs in terms of objective and content by performing a scientific comparison based on real-life examples of orphan drug assessments, for presentation at the next meeting.

6. “Effects tables” - First feedback from the joint recent exchange

The CHMP recently completed the pilot on the Effects Table and agreed its implementation into routine work. Therefore, all initial MAAs and Extensions of indications from February 2015 onwards will have the Effects Table in their assessment reports. Representatives from EUnetHTA have previously been involved in the work. It was agreed to revisit the experience in May 2016 with a number of examples; a joint publication could be considered. Also this work could be considered as part of Joint Action 3.

Action point:

- EMA to trigger a joint review of experience ahead of the May 2016 meeting and consider preparation of a joint publication

7. Initial experience with patient interactions (eliciting patient values, preferences)

EMA provided an overview of the various initiatives to obtain patient views in the context of evaluation activities. The discussion centered on how this experience found was? used in the context HTA work. Involvement can occur through direct meeting participation but also in writing and though teleconferencing. Particularly in the context of rapid relative effectiveness assessments where time is limited the engagement through a targeted questionnaire might be an option. NICE reported of their experience when asking manufacturers about patients involvement during development, which seems often not to be the case.

Benefit from the engagement of patients is not only by obtaining their valuable input but also by providing patients with a better understanding of the decision-making process, promoting transparency about the regulatory systemThe professionalism of patients in their engagement was highlighted.

The EMA framework of interaction provides a robust structure including specific processes (e.g. for evaluation of public and private funding of patients’ organisations); the one developed by EMA can be shared with EUnetHTA for information. At present EMA is usually working through European patient organisations to identify patients; in the future it might be considered to have a pool of patient experts, with a call for expression of interest.

Action point:

- EMA and EUnetHTA to continue the discussion with a view to allow HTA bodies to get practice in the engagement with patients during rapid REA (for reporting at the next meeting)
- Topic to be included by the EC in the future Joint Action 3

8. Three-year Work Plan

To document the achievements of the collaboration between EMA and EUnetHTA a report on the work plan, which runs out in 2015, will be produced. For the future it was envisaged this collaboration to become part of Joint Action 3 to make it a formal engagement. Aspects like governance and non-drug technologies would need to be discussed how to address within such framework.

Action point:

- EUnetHTA and EMA to develop report on the implementation of the work plan in autumn 2015

9. Action points from previous meetings

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

Action point:

- Updated listing to be circulated to participants.

10. Any other Business

No additional points were raised.

11. Closing remarks

The next meeting will be hosted by the Danish agency in Copenhagen, likely in 4Q2015 (date TBD).