

EMA / EUnetHTA meeting – Summary Report Final

9 December 2014, 10:30 – 17:00 CET

Host: Zorginstituut Nederland (ZIN)

Eekholt 4 | 1112 XH | Diemen
Room Kentaurus

AGENDA

Co-chairs: Finn Børlum Kristensen and Hans-Georg Eichler

Coffee – light refreshment	10.00 – 10.30
Welcome by the ZIN's member of the Executive Board (Bert Boer)	10:30
Adoption of draft agenda, review of minutes from the last meeting and update on action points (co-chairs)	10:40
Discussion theme: The roles of regulation and HTA in the life-cycle of a drug from innovation to healthcare practice / obsolescence (EMA, EUnetHTA): • Early dialogues: update on sharing information (F. Meyer, J. Moseley) • Additional data collection including areas of collaboration on pharmacovigilance and post authorisation efficacy studies (F. Meyer, P. Arlett) • Update on informing companies on the opportunities to participate in REAs (W. Goettsch, M. Berntgen) • REAs: update on possibilities to provide EUnetHTA with EPARs before EC decision (M. Berntgen, W. Goettsch) • ADAPTIVE LICENSING / MAAPs in general and the specifics of the EMA's current piloting (H-G. Eichler, W. Goettsch, other EUnetHTA partners)	10:50
Coffee break	11.45 – 12.00
Discussion theme: The roles of regulation and HTA in the life-cycle of a drug from innovation to healthcare practice / obsolescence – cont. (EUnetHTA, EMA)	12:00
Indication wording in the SmPC (E. George, T. Salmonson, M. Berntgen)	12:45
Lunch break	13.15 - 14.15
Update on the HTA Network development (F. Giorgio-DG SANCO representative)	14:15
Clarification of the possibility for pharmaceutical companies to use documents retrieved via EMA's "Policy on publication of clinical data for medicinal products for human use" for submission dossiers to HTA agencies (B. Wieseler, H-G. Eichler)	14:30
IMI 1: Get real and the relevance of its outcomes for HTA and regulators (W. Goettsch) IMI 2: topics of interest (F. Kristensen)	15:15
Coffee break	15:45 – 16.00
Disease-specific guidelines: involvement of EUnetHTA partners in EMA's public consultations; Contribution of EMA to the development of the first disease-specific guideline by EUnetHTA (M. Berntgen, F. Meyer, W. Goettsch, F. Kristensen)	16:00
Looking beyond 2015: practical and implementable areas for collaboration (co-chairs)	16:30
Any other business and closing remarks	16.45

1. Welcome by member of the ZIN's Executive Board, Bert Boer

Participants were welcomed by ZIN's member of the Executive Board, Bert Boer, who emphasized the importance of collaboration between the EMA and EUnetHTA for the connection between primary research, regulation, reimbursement, quality of care and the links with wider international collaborations.

2. Adoption of draft agenda, review of minutes from the last meeting and update on action points.

This was the ninth meeting between the European Medicines Agency (EMA) and representatives from the European network for Health Technology Assessment (EUnetHTA), led by co-chairs Finn Børlum Kristensen (EUnetHTA) and Hans-Georg Eichler (EMA).

The co-chairs welcomed all participants, and after a tour de table the draft agenda was adopted without changes. The action points in the minutes from last meeting had all been handled during the last half year. At the request of the EMA, the action point on Orphan drugs (MOCA developments) was postponed to the agenda of the next meeting (first half year 2015).

3. Discussion theme: The roles of regulation and HTA in the life-cycle of a drug from innovation to healthcare practice/ obsolescence

The life-cycle of a drug from innovation to healthcare practice was described, and the activities where HTA bodies currently have reactive/receiver role were outlined: Horizon scanning, rapid REAs, and HTA/REAs. For the other activities, a more pro-active approach can be taken: early scientific advice/ dialogue, additional data collection, and the identification of "unmet needs", i.e. health problems where no effective interventions have as yet been identified /developed. The regulatory bodies, the HTA bodies and EUnetHTA are moving into having a more proactive role, towards influencing and potentially improving data available for assessments. It may be anticipated that HTA and regulatory bodies will come up with new activities in this pro-active approach. The unmet needs could be responded to by regulatory processes which would stimulate companies to develop interventions/ medicines (e.g. new antibiotics). Identification of the "unmet needs" could be supported by information collection, e.g. horizon scanning. One existing example of ways to respond to unmet needs where licensing and HTA bodies could work more closely together is in the opportunities provided by the orphan drugs legislation.

A) Early dialogues: update on sharing information

EUnetHTA gave an update on the progress of the work in WP7 and SEED (European Commission (EC) tendered project) in early dialogues (ED) / early scientific advice. A model of how to conduct ED for drugs and medical devices will be presented for discussion during the EUnetHTA PA meeting in May 2015 and the final version will be included in the SEED report and sent to the EC.

EMA presented results of the consultation on the Best Practice Guidance for the EMA – HTA parallel scientific advice procedures. The participation of the HTA agencies is voluntary. The HTA bodies are selected by the sponsor. At present, a definitive response to the public consultation cannot be published until further testing of other elements of the procedure is carried out. In addition, the results of the SEED tender are also relevant and need to be taken into account and the most optimum and suitable procedure agreed by all relevant parties for the medium term. After receiving the final report from SEED it will be up to the EC to decide the next step. It should also be further clarified by the EMA, EUnetHTA and the EC that the early scientific advice is for the benefit of both parties: pharmaceutical companies and for the regulatory and HTA bodies.

The next steps in scientific advice should be proposed with the aim of accelerating patients' access to innovative therapies which have added value for patients and are affordable to the

EU Member States' health systems. Efficient procedures for providing scientific advice to the companies that are realistic and acceptable by all stakeholders will be further explored.

Action point(s):

- EMA and EUnetHTA will liaise on the evolution of the EMA – HTA parallel scientific advice pilot procedure
- EMA, EUnetHTA and the EC to agree on the form of the publication of the objectives of the ED/scientific advice, including information on the benefit of this process for all participating parties (both regulatory and/or HTA institutions as well as industry).
- EMA, EUnetHTA and the EC to continue discussions on appropriate ways of facilitating patients' access to innovative therapies by providing a scientific advice "service" for the pharmaceutical companies

B) Additional data collection including areas of collaboration on pharmaceuticals on pharmacovigilance and post authorisation efficacy studies

Enhanced input from EUnetHTA and HTA bodies is needed by the ENCePP HTA working group, where the main focus is now on capacity building of the medicines regulators and HTA bodies to contribute to the development of the post authorization studies. New opportunities for collaboration are foreseen within the next years. There are other opportunities for collaboration in terms of new initiatives in relation to regulatory science (e.g. PAES guideline), epidemiological methods, patient registries, and in the PROTECT IMI project (next workshop will be held on the 18-20 February, 2015). Currently three EUnetHTA member organisations expressed their interest in this collaboration: HAS, ZIN and AHTAPol. It was emphasized that in order to facilitate broader involvement of the HTA bodies in the collaboration, it would be important to clarify, map and prioritise tasks within already ongoing projects (e.g. ENCePP, GetReal, IMI2 consortia, PARENT).

Action point(s):

- EMA to explore how best include HTA bodies in the consultation on the PAES guideline
- EUnetHTA and EMA to map and prioritise tasks within other ongoing projects which involve additional data collection.

C) Update on informing companies on the opportunities to participate in REAs

There is progress in the involvement of the pharmaceutical industry in the rapid REA pilots. Recently, an information package was produced by EUnetHTA WP5 and it was discussed that the EMA could provide information related to the WP5 information package during the pre-submission meetings with applicants. It was discussed if this information should be provided to all companies that apply for market authorisation or only selected MAHs based on a topic selection process. The current broad scope in the topic selection used by EUnetHTA WP5 (topics selected based on the list of compounds under CHMP assessment, prior participation of the company in WP5 pilot, willingness of the authoring agencies to use the pilot for the national reporting) was noted. It was felt though that criteria should be developed to select candidates/application for which such leaflet should be handed out.

Action point(s):

- EUnetHTA to design a leaflet on rapid REA that can be provided by the EMA to prospective applicants in pre-submission meetings

- EUnetHTA and EMA to develop criteria for candidates/application for which such leaflet should be handed out

D) REAs: update on possibilities to provide EUnetHTA with EPARs before EC decision

There was a follow-up on the discussion during the previous meeting. The EMA explored a framework for providing the CHMP assessment report to EUnetHTA before the Commission Decision is being issued. Relevant parts of the reports are for EUnetHTA the introduction, clinical aspects and the benefit-risk section. There is a need to develop a robust framework under which such data sharing with HTA bodies could be envisaged. It will be explored and agreed upon between EMA, EUnetHTA and EC what type of agreements would be feasible and acceptable.

Action point(s):

- EC, the EMA and EUnetHTA to clarify options for data sharing agreements

E) ADAPTIVE licensing / MAPPs in general and the specifics of the EMA's current piloting

An update on the pilot project on adaptive licensing/pathways was presented by EMA. Thirty-four expressions of interest were received from industry. Six of these products were selected for piloting during the first half of 2015. EMA is looking for EUnetHTA partners as well as patient representatives to be involved in these pilots. Currently EUnetHTA has been appointed as an observer. Several EUnetHTA partners (e.g. EUnetHTA Secretariat, ZIN, HAS, AIFA and NICE) would participate in a teleconference organized by EMA on the next day (Dec 10th). Invited for this meeting were about 40-50 individual participants (including variety of Committees, e.g. PRAC). In the future there may be further division of the members between six planned working groups. Such a large involvement of the HTA bodies should be streamlined and coordinated by a permanent HTA structure in the future. Involvement of more payer representatives would be welcomed. An interest was expressed by a MEDEV member to act in this role. It was mentioned by the EMA that adaptive licensing/pathways may become a part of the parallel scientific advice process in the future.

Action point(s):

- EMA, EC to clarify the process of MAPPs pilots (particularly the issue of representatives of payers), and EUnetHTA members to consider participation

4. Indication wording in the SmPC

Comments from EUnetHTA partners (ASSR, IQWiG and NICE) during the public consultation on the "Reflection paper on the wording of indications for medicinal products for treatment of type 2 diabetes - EMA/CHMP/50673/2014" were presented by the EUnetHTA partner NICE. Based on comments with regard to legal and financial consequences in some Member States, there may be a need to develop criteria for a CHMP decision on therapeutic indications that are broader or narrower than the trial evidence supports. EMA provided an overall summary of the consultation feedback.

Action point(s):

- EMA to discuss possible criteria and general aspects of indication wording; a discussion paper to be shared with EUnetHTA preferably within 6 months' time

- In line with previous discussions on the EPAR, EMA to ensure that the finally approved indication (if the therapeutic indication(s) are broader or narrower than the pivotal trial population) is justified in the EPAR.
- EUnetHTA to comment on the EMA's discussion paper

5. Update on the HTA Network development

The representative of the EC provided an update on recent changes in the Commission, European Parliament and the EMA. The developments of the HTA Network Strategy and discussions on the next phase of JA3 in 2016 were summarised. The annual programme for 2015 of the Health Programme is planned to be adopted within the next three months. A JA3 will focus on joint HTA production, meeting national needs, and priorities for the sustainability of the activities. There is a clear recognition of the achievements of EUnetHTA in bringing this European HTA collaboration into the next step. A reflection paper on the reuse of the joint activities will be developed by March 2015 by an HTA Network working group. The EC also reported on the newly established group on Safe and Timely access to medicinal products (STAMP), the group will meet for the first time in early 2015.

Action point(s):

- none

6. Clarification on the possibility for pharmaceutical companies to use documents retrieved via EMA's "Policy on publication of clinical data for medicinal products for human use" for submission dossiers to HTA agencies

A summary of data requirements in the submission files submitted by pharmaceutical industry to HTA bodies was provided by the EUnetHTA partner IQWiG. In cases where no direct comparisons are available, indirect comparisons might be submitted in the dossiers. However often the detailed information needed for indirect comparisons is not sufficiently presented in published journal articles. This detailed information is generally available in clinical study reports. Therefore, availability of clinical study reports submitted to the EMA is important for HTA dossier preparation. It was unclear to HTA bodies and the pharmaceutical industry if based on the Terms of Use laid down in the "Policy on publication of clinical data for medicinal products for human use" companies can use clinical (study) reports of competitor companies for the preparation of dossiers for HTA bodies. EMA responded that enabling comparative effectiveness research is in the interest of public health. Usage of the data for scientifically sound relative effectiveness comparisons (produced by either HTA bodies or pharmaceutical companies) would not be reasonably deemed *per se* an unfair commercial use and therefore would not be considered by the EMA as in breach of the Terms of Use. An appropriate clarification will be included in the next version of the Q&A document on the Policy.

Action point(s):

- EMA to supplement the question regarding impact on HTA bodies in the Q&A document on the *Policy on publication of clinical data for medicinal products for human use* in order to add the above clarification

7. IMI

A) IMI1: GetReal and the relevance of its outcomes for HTA and regulators

The objectives, deliverables, benefits and obstacles of the IMI1 GetReal Project were presented by EUnetHTA partner ZIN. The framework for using real-world data and its relevance for HTA and EMA was emphasised. More input from both HTA agencies and the EMA is needed to facilitate the development of a common methodology for Network Meta-Analysis (NMA), modelling from efficacy to effectiveness, use of Individual Patient Data (IPD) and a standardized model for reporting. It was mentioned that there are societies and programmes where these issues are raised and methods developed (e.g. ISPOR Good Outcomes Research Practice Task Forces, the Cochrane Collaboration, PARENT Joint Action) and that coordination between these activities and GetReal is needed.

Action point(s):

- None

B) IMI2: topics of interest

Regarding the list of IMI2 potential topics developed by the EMA, an interest in participation in potential consortia collaborations, was explored by the EUnetHTA Secretariat among the EUnetHTA partners. Only very little response from partners was received. It was mentioned that a letter on the prioritization of HTA relevant topics in the Horizon 2020 will be sent by EUnetHTA to DG R&I and DG Sanco in early 2015. It was raised by the EMA that one topic in particular requires HTA bodies attention. A small consortium preferably composed of regulatory bodies, HTA agencies and industry is planned for *Call 4: Enabling platform on medicines adaptive pathway to patients*.

Action point(s)

- EUnetHTA to find out how HTA bodies could participate in the IMI2 Consortium on *Enabling platform on medicines adaptive pathway to patients* (through EUnetHTA or separately) jointly with EMA and potentially other partners

8. Disease specific guidelines: involvement of EUnetHTA partners in the EMA's public consultations; Contribution of the EMA to the development of the first disease-specific guideline by EUnetHTA

The EUnetHTA partners are continuously informed on the EMA's public consultations. Most of the guidelines submitted for public consultation are disease specific guidelines, however there are also some methodological guidelines, e.g. on analysis of subgroups of patients. It was decided that the information from the EMA on relevant consultations will be continued, however it was suggested by EUnetHTA to consult EUnetHTA partners earlier in the process, i.e. before public consultation. Even though it will not be possible to develop common responses, this would allow better distribution of the information among EUnetHTA partners (e.g. by publication in the EUnetHTA intranet)

EUnetHTA provided the timelines and an update on the development of a disease specific guideline (DSG) on Osteoarthritis. The EMA expressed an interest to contribute to this work by taking part in the consultation (in April 2015). It was decided that the draft guideline will be distributed internally by EMA and there will be a coordinated response given to EUnetHTA.

Action point(s):

- EMA to follow up on the possibility to share the draft guidelines with EUnetHTA members before public consultation. It will be explored if such a pre-consultation activity would be feasible.
- EUnetHTA to share the draft of the first disease-specific guideline on osteoarthritis with EMA

9. Looking beyond 2015: practical and implementable areas for collaboration.

The EMA and EUnetHTA future areas for collaboration were briefly discussed in the light of a likely JA3, where in one possible scenario the EMA would be an official partner in a EUnetHTA JA3. Details of this collaboration, beyond early scientific advice, will be explored in the later discussions.

10. Any other business and closing remarks.

EMA provided information of the current status of the Effect Tables, which are now included into the newly updated guidelines and will become a part of the EPAR.

The next meeting will be hosted by the EMA in London, most probably in the first week of June 2015.

PARTICIPANTS LIST

EMA / CHMP representatives

Attendee	Organisation
<i>Peter Arlett</i>	<i>EMA</i>
<i>Michael Berntgen</i>	<i>EMA</i>
<i>Hans-Georg Eichler</i>	<i>EMA</i>
<i>Jane Moseley</i>	<i>EMA</i>
<i>Tomas Salmonson</i>	<i>EMA /CHMP</i>

EUnetHTA

<i>Eva-Maria Zebedin</i>	<i>HVB, Hauptverband der Österreichischen Sozialversicherungsträger</i>	<i>Austria</i>
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<i>Finn Børlum Kristensen</i> <i>Lidia Becla</i>	<i>DHMA, Danish Health and Medicines Authority (EUnetHTA Secretariat)</i>	<i>Denmark</i>
<i>Francois Meyer</i>	<i>HAS, Haute Autorité de Santé</i>	<i>France</i>
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European Commission

Name	Organisation
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