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Final Minutes of EMA/EUnetHTA meeting

14 May 2013 – chaired by Hans-Georg Eichler and Finn Børlum Kristensen

Role	Name
Chairs	Hans-Georg Eichler and Finn Børlum Kristensen
Participants	<p><u>EMA</u>: Peter Arlett, Michael Berntgen, Hans-Georg Eichler, Ana Hidalgo-Simon, Jordi Llinares, Luis Prieto, Guido Rasi, Spiros Vamvakas</p> <p><u>EUnetHTA</u>: Lidia Becla, Finn Børlum Kristensen, Agnese Cangini, Julia Chamova, Elisabeth George, Wim Goettsch, François Meyer, Simona Montilla, Mira Pavlovic, Robert Saueremann, Simone Warren, Beate Wieseler</p> <p><u>European Commission</u>: Flora Giorgio</p>

Item	Draft agenda	Name
1.	Welcome by the EMA's Executive Director	Guido Rasi
2.	Adoption of draft agenda	Hans-Georg Eichler (HGE), Finn Børlum Kristensen (FBK)
3.	Scientific Advice / Early dialogue <ul style="list-style-type: none"> EMA-HTA workshop on parallel scientific advice in drug development: 26 November 	Spiros Vamvakas (SVA) François Meyer (FM), FBK
4.	Post-authorisation collaboration	Ana Hidalgo-Simon (AHS)
5.	Scientific guideline development <ul style="list-style-type: none"> EUnetHTA input on EMA's consultations (EUnetHTA to develop joint position on EMA public consultations of relevance to EUnetHTA strategic matters) EMA's input into the disease-specific guidelines process (JA2 WP7) 	Wim Goettsch (WG), FBK Michael Berntgen (MBER) FM, MBER
6.	EPAR improvement <ul style="list-style-type: none"> Data on the relevance of Clinical Study reports for HTA 	Beate Wieseler (BW)

Item	Draft agenda	Name
7.	EUnetHTA-EMA cooperation on JA2 WP5 pilots (rapid REAs) <ul style="list-style-type: none"> Request from EUnetHTA (Letter 11 March) 	WG / HGE / MBER
8.	Orphan medicinal products	Jordi Llinares (JLG)
9.	Development of a EUnetHTA-EMA 3-year work plan	HGE, FBK
10.	Any other Business: <ul style="list-style-type: none"> Publication of joint meeting minutes 	AOB
11.	Closing remarks	HGE, FBK

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

The Agency's Executive Director, Guido Rasi, welcomed the participants highlighting the importance of this ongoing dialogue between regulators and HTA organisations from a public health perspective.

The draft agenda was adopted with the addition of an update from the EC representative on the development of a network in accordance with Article 15 of the Cross-border Healthcare Directive, as well as the request from EUnetHTA for a discussion on a planned workshop regarding parallel EMA/HTA scientific advice.

Update on the future HTA network according to Article 15 of the Cross-border Healthcare Directive

The European Commission is in the process of finalising the drafting of a Implementing Act for setting up the future network on cooperation and exchange of information amongst Member States authorities and bodies responsible for HTA, as foreseen by article 15 of the Directive on patients' rights for cross border healthcare (Directive 2011/24). This draft will shortly be submitted to the Member States for adoption. The aim is to have the first meeting of this new strategic committee in the third/fourth quarter of 2013. The draft Implementing Act foresees that regular guests are invited to the committee meetings to ensure appropriate exchange of information, and explicitly mentions the EMA as invitee.

Scientific Advice / Early dialogue

EMA provided a brief update on the status of parallel EMA/HTA scientific advice, also known as multi-stakeholder consultations. So far 18 such procedures have been completed involving HTAs and payers from UK, Sweden, France, Italy, Netherlands, Spain, Germany, Belgium; further applications are currently in pre-submission phase. With regard to the EUnetHTA early dialogue an overview was provided highlighting that these procedures are one element of EUnetHTA's initiatives for improvement of initial and additional evidence generation for all health technologies, next to disease-specific guidelines, methodological guidelines, and templates for submissions by manufacturers. Four early dialogue procedures have been completed with voluntary participation of Germany, UK, Austria, Belgium, Italy, Netherlands, and France. The procedural workflow is similar to the EMA scientific advice. Important is however the preparatory work amongst HTA participants facilitated by the lead (HAS). EMA has recently started as an observer to the process. Additional pilots for six more drugs and

one device/procedure are scheduled for 2013. Feed-back and input from companies and HTA bodies is expected by the end of 2013 through a survey to improve the process. For the future financing of early dialogue procedures, a call for tender has recently been launched (n° EAHC/2013/health/09), to which a consortium of HTA bodies closely linked to EUnetHTA and led by HAS will apply.

Based on the experience gained so far, the EMA plans hosting a workshop on parallel scientific advice in drug development in November 2013; an invitation for expressions of interest was recently circulated to all HTA bodies that participated already to these procedures. During the discussion it was indicated that it might be an opportunity to broaden the scope of the workshop and also cover the first experiences with EUnetHTA early dialogue procedures; this was agreed in principle and the details should be developed outside the meeting.

Having seen the early dialogue procedures a potential improvement in the parallel scientific advice could be the facilitation of HTA input prior to the meeting. Due to resource constraints this appears not feasible for EUnetHTA at this point hence alternative ways might need to be identified in the ongoing improvement processes. The future involvement of EUnetHTA as observer to the parallel EMA/HTA scientific advice was mutually agreed with the aim at improving and aligning the two processes for obtaining advice.

In a wider discussion the attractiveness of a “one-stop shop” for drug developers was explored since the key obstacle is to have more than one entry door to interactions with decision makers. Scientific advice is generally considered an important element for success rate and speed to market. Both industry and patients are asking for aligned discussions covering end-to-end processes. Apart from overlapping data requirements the access to a similar (and limited) pool of experts need to be considered. There was general agreement that provided different remits and obligations are respected, much better synergy in terms of inputting into development plans from regulatory and HTA perspective at an early stage can be envisaged hence a “one-stop shop” vision could be a positive opportunity. The aim should be to identify evidence requirements and methods to define clinical development plans that cover both the regulatory and HTA perspective. In case specific evidence criteria for either regulators or HTAs drive certain scientific data requirements then these should be identified early in the process, to avoid delays in decisions on patient's access to the medicine. It was noted however that for this to become successful in the future it will be necessary to discuss to what extent the information for decision making in terms of benefit/risk (regulators), relative effectiveness/cost effectiveness (HTA), and affordability (Payers) can be aligned. To achieve this, interactions have to go beyond HTA and regulatory agencies, would involve the national health care systems and industry.

Actions:

- For the planned EMA-HTA workshop on parallel scientific advice in drug development, expand the scope to also cover experience with EUnetHTA early dialogue – Spiros Vamvakas and Finn Børlum Kristensen /Mira Pavlovic
- Finalise the web announcement for the workshop by end of May based on feedback from EUnetHTA – Spiros Vamvakas
- Explore EUnetHTA observer status or even more active role with a view to collect information from the EUnetHTA partners – Finn Børlum Kristensen /Mira Pavlovic

Post-authorisation collaboration

An introductory overview summarised the first eight months of operation of the Pharmacovigilance and Risk Assessment Committee (PRAC) in terms of activities and outputs, developments with regard to the review of post-authorisation safety studies (PASS) and the legal framework for post-authorisation efficacy studies (PAES), as well as the ENCePP HTA working group. It was highlighted that the concept

of 'Best evidence regulation' is expected to drive up the quality of the decisions, in the interests of public health. In this context it is necessary to fully use the evidence hierarchy and ensure that regulatory decisions for public health are based on all relevant data, information and knowledge.

With regard to the legal framework for PAES, a Commission Expert meeting will be held in June 2013 and the Commission 'Delegated Act' is expected for autumn 2013. For the EMA scientific guidelines on efficacy study methods, a draft is expected by end of year 2013 and a preparatory scientific workshop on methodologies is in planning. In terms of post-authorisation evidence generation, through both PASS or PAES, there was the shared view that efforts should be made to design studies that to a point could satisfy needs of both regulators and HTA bodies. A possible platform for having such discussions could be a parallel scientific advice, and expressions of interest from industry for such discussions on post-authorisation study programmes should be sought. EMA offered to host such parallel "late stage" scientific advice sessions with industry.

The ENCePP Working group on HTA is in operation since October 2012 and is co-chaired by François Meyer as EUnetHTA representative. Since other HTA bodies would be interested in participating in these discussions, it was agreed that additional nominations should come from EUnetHTA. Ongoing initiatives include the review of specific proposals on the development of methodological guidance for studies on HTA and the writing of a Working Document aimed at bridging, through study design, the gap between HTA and Regulators requirements with regard the requests for additional evidence generation. During the discussion it was indicated that – before embarking into concrete work - it would be important to clearly identify already existing work on methodological guidance and to see where this particular working group can make itself most relevant. It was agreed that it is essential not to duplicate existing work. For this purpose it was generally agreed that available results and work programmes from the EUnetHTA work packages will be shared.

Actions:

- For the ENCePP HTA WG to clarify activities by mapping out existing guidance and where additional guidance could be useful – Luis Prieto and François Meyer
- Additional participants to the HTA WG to be identified – Finn Børlum Kristensen/François Meyer
- Encourage companies to come forward and request parallel advice on post-authorisation data collection – EMA
- Send to EMA the work programme of EUnetHTA JA on methodological guidelines– François Meyer

Scientific guideline development

Following up on the agreement from the previous meeting to provide EMA guidelines and concept papers for commenting, an update on the documents under consultation and the received comments was provided to EUnetHTA. Overall, comments on guidelines were only provided by a very limited number of HTA organisations. EUnetHTA confirmed that they will continue to alert their members about guidelines under consultation but it appears not feasible to establish a process to systematically provide formal consolidated comments from EUnetHTA. Individual HTA bodies might send in comments; also if there was a guideline with relevance to a EUnetHTA early dialogue then there might be some consolidated commenting. It was therefore agreed to continue with the scheduled alert by EMA to EUnetHTA on guidelines (not concept papers) under development.

In terms of EUnetHTA guidelines, following the first set of nine methodological guidelines there are plans to prepare further Guidelines for methodology assessment of medical devices and procedures and disease-specific guidelines, like on Internal validity of observational studies, cost-effectiveness

assessment (economic evaluation), and Information retrieval in study registries and bibliographic databases. Furthermore, a topic for a disease-specific guideline for technology developers is currently being identified. The input from EMA is foreseen on these disease-specific guidelines; this can either occur in parallel to the consultation of the stakeholder advisory group or to the public consultation.

Actions:

- EMA to continue providing overview of EMA guidelines under public consultation – Michael Berntgen
- EMA to express when they want to contribute to the EUnetHTA disease-specific guidelines – Michael Berntgen
- EUnetHTA to explore / discuss ways to maintain contribution to EMA guidelines under consultation – Finn Børlum Kristensen /Mira Pavlovic

EPAR improvement

A review on the completeness of information for study outcomes in clinical study reports, registry reports and journal publications was performed by IQWiG. These data, which are currently in preparation for publication, clearly demonstrate the relevance of clinical study reports for HTA bodies since relevant information is not always publicly available. This information also supports the initiatives by the EMA to proactively make information from clinical studies publicly available. This initiative has already received important support from many stakeholders, and the draft policy, which is due to be published end of June for consultation, will certainly be of interest for HTA bodies.

With regard to the EPAR improvement project, the draft manuscript for publication of this initiative has been prepared and will shortly be circulated to colleagues from EUnetHTA and EMA. Having considered various options, the publication will summarise the entire project as a policy paper starting with the comments received, the way they were addressed as well as the first impact analysis. In this way it is planned to provide an account how the task stemming from the High-level Pharmaceutical Forum 2008 was addressed and completed. This approach was agreed and the benefits of a fast manuscript finalisation for publication was emphasised.

Action:

- Commenting on draft EMA CT data Publication Policy - EUnetHTA
- Draft manuscript on EPAR project to be finalised – Michael Berntgen and Anne Gourvil

EUnetHTA-EMA cooperation on JA2 WP5 pilots (rapid REAs)

Under Joint Action 2 one of the objectives in Work Package 5 is to test the capacity of national HTA bodies to produce structured core HTA information (full core/rapid HTAs) together and apply it in national context (including collection of data on costs and overall efficiency of the production in the network. The output (products) oriented work package is intended to prove the capacity of cooperation for increased efficiency of European HTA-production. In this context pilot reports will be produced in order to critically review the applicability of the work done by Joint Action 1. To prepare for these pilots, particularly the scoping exercise, EUnetHTA enquired whether EMA could provide early information on the timing of final meeting of decision of CHMP, the direction of outcome of assessment before final CHMP decision. Furthermore, information on the availability of report after positive CHMP decision was requested. EMA clarified that at time of CHMP Opinion the applicant receives the final CHMP assessment report and that the applicant is free to share this document with HTA bodies. If the manufacturer agrees then also EMA should be in a position to provide the CHMP assessment report to EUnetHTA. In terms of the actual timing and expected outcome, issues around practicability,

predictability, and legality would prevent EMA to share this information unless the applicant agrees. EUnetHTA therefore would need to work with the manufacturers for the scoping of the pilots.

Orphan medicinal products

Transparency with regard to significant benefit evaluation for orphan medicinal products was subject of an overview provided by EMA. Public summaries of opinion at time of designation and maintenance review are made publicly available. Summary of COMP position on the review of the orphan status at time of authorisation includes information on prevalence, seriousness, and significant benefit if applicable, as well as a link to EPAR. Furthermore, since Sept 2012 minutes of the Committee for Orphan Medicinal Products (COMP) are being published.

Regarding the existence of other satisfactory methods of treatment, this only refers to products authorised for the condition, i.e. no "off label" is considered and no standard therapies discussed unless having authorised indication. The basis for assumption of significant benefit over existing treatments is clinically relevant advantage / major contribution to patient care with quantification of effect and clinical relevance. HTA representatives confirmed that it would be important to have the data that was supporting the significant benefit, as well as the information why a medicine is no longer considered to have a significant benefit. EMA is currently working on further improving these publicly available documents and in particular to add more qualitative information. Overall, it is important that the outcome of the assessment regarding orphan status is well described in the publicly available document. For the future pilots on REA, EUnetHTA will also include orphans.

Actions:

- Updates on transparency proposals for orphan medicinal products at future meetings – Jordi Llinares

Development of a EUnetHTA-EMA 3-year work plan

It was agreed that it would be beneficial to develop such work plan specifying the overall objective and areas of collaboration together with identified activities. EUnetHTA will prepare a draft for review by EMA.

Actions:

- Draft to be developed with an aim to finalise it by September 2012 - EUnetHTA

Publication of joint meeting minutes

In view of transparency, it was agreed to make the final minutes of this meeting publicly available on the websites of EMA and EUnetHTA. A joint press release will be prepared informing external stakeholders about this initiative. In addition, the minutes of previous meeting should be made publicly available; it was noted that they will be annexed to the EUnetHTA report on Joint Action 1.

Actions:

- Prepare draft minutes of the meeting for review by all participants – EMA
- Prepare draft press release for review by EUnetHTA and EC - EMA
- Review of previous meeting minutes in view of publication – EMA and EUnetHTA

Next meeting: in 4Q13 at the premises of a EUnetHTA member organisation
