EMA / EUnetHTA meeting – Summary Report FINAL

23 November 2015, 10:30 – 17:00 CET

Danish Health Authority (DHA)
Islands Brygge 67| DK-2300 | Copenhagen S
Room 501

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

Coffee – light refreshment	***10.00 – 10.30***
Welcome to DHA *(Finn B Kristensen)*	10:30
Adoption of draft agenda, review of minutes from the last meeting and update on action points (co-chairs) *(Finn B Kristensen/ Hans-Georg Eichler)*	10:40
Update and contribution of HTA institutions to initiatives under the leadership of EMA: the Adaptive Licensing Pilot project, ADAPT-SMART, activities regarding registries (ENCEPP), guidelines (PAES), *(Wim Goettsch / Nick Crabb; Hans-Georg Eichler / Peter Arlett / Michael Berntgen)*	10:50
Cooperation on initiatives related to evidence generation (early dialogues and PAES) *(Francois Meyer; Giovanni Tafuri / Peter Arlett)*	11:50
Lunch break	***13.00 - 14.00***
DG Santé update on the development of the HTA Network and JA3 preparations (including the involvement of the EMA) *(Jerome Boehm/Hans-Georg Eichler)*	14:00
Cooperation on joint HTAs: -status of data sharing for REAs in JA2 *(Michael Berntgen/Wim Goettsch)* -joint production of HTAs with a view to the involvement of EMA in the process *(Wim Goettsch)*	14:20
Coffee break	***15.30 – 15.45***
Engagement with patients during EMAs processes and HTA processes: discussion of experiences and future developments *(Beate Wieseler / Isabelle Moulon)*	15.45
Three-year work plan (and reporting of its implementation) *(Lidia Becla/Michael Berntgen)*	16.30
Any other business and closing remarks	16.45

1. Welcome

Participants were welcomed by Prof. Finn Børlum Kristensen, Director of the EUnetHTA Secretariat, to this 11th meeting of the EMA with EUnetHTA. He informed the participants about the re-organisation of the institution hosting the EUnetHTA Secretariat. The DHMA (Danish Health and Medicines Authority) has been divided into three agencies: The Danish Health Authority, the Danish Medicines Agency and the Danish Patient Safety Authority. The Danish Health Authority (DHA) carries forward the responsibility for the EUnetHTA JA2 coordination from the former DHMA to its finalisation in 2016, with no further commitment of budget allocation to activities in EUnetHTA JA3.
This meeting between the EMA and EUnetHTA was chaired by Finn Børlum Kristensen (EUnetHTA) and Hans-Georg Eichler (EMA).

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

The draft agenda was adopted without changes. It was agreed that the list of the action points will be updated, attached to the Summary Report from this meeting and circulated among participants for their checking of the status and provision of exact timelines for a planned delivery of the remaining outputs.

3. Update and contribution of HTA institutions to initiatives under the leadership of EMA: the Adaptive Pathways Pilot project, ADAPT-SMART, activities regarding registries (ENCEPP), and guidelines (PAES)

Adaptive Pathways pilot project: An update was provided by the EMA. Several substances have been chosen out of 60 compounds proposed by the industry for the pilots. Several EUnetHTA members participated in various pilots.

ADAPT SMART (IMI project): Three EUnetHTA members participate in the project: ZIN, HAS and NICE, where the latter is the leader of a WP: “Evidence generation throughout the life cycle”. Engagement of a larger number of HTA institutions is needed to ensure more systematic collection of HTA views and perspectives.

Some drawbacks may possibly prevent involvement of HTAs and payer organisations in the ADAPT-SMART and other activities led by EMA were indicated and further discussed:

- big number and a wide variety of competing activities drawing upon resources within the HTAs
- lack of sufficient resources to support the HTA organisations’ participation (no fee for service options, this is relevant for participation in the Adaptive Pathways pilots projects; limited European Commission (EC) funding, limited number of experts available “in house”)
- concerns related to the lack of well-developed down-stream section of the access pathway
- lack of effective mechanisms for discontinuation of coverage of drugs that have proven not to provide value for money in real world settings (“exit schemes” fostered by payers during the life cycle of a product)
- reluctance of some HTA institutions to invest resources and public funding in procedures and projects which involve private entities

- not sufficient focus on methodological challenges (e.g. type of data) of the development of adaptive pathways

It was suggested that the majority of the many HTA organisations would prefer to be involved by providing a constructive critique and comments to draft procedures as developed by WP1 the ADAPT-SMART project, where the discussion on methods is already facilitated.

The post-authorisation regulatory initiatives related to additional data collection were summarised by EMA. Some EUnetHTA partner organisations participate in these initiatives and provide the following contribution:

- comments on the PAES guidelines,
- participation in the ENCePP meetings (next meeting to be held at EMA on Nov 24),
- revision of the existing ENCePP guidelines by providing comments,
- individual participation in IMI projects (e.g. IMI Get Real).

Ongoing initiatives to support the collection of data and information on products on the market include the EMA initiative on patient registries, ENCePP, collaboration on common studies based on electronic health records (EHRs) and harnessing new technology for product surveillance. An objective of the collaboration on registry initiatives is to agree on methods and terminology and to look into tools that would drive up data quality and help to data collected in different registries and in different countries and settings.
Regarding collaboration on common studies using EHR data, EU regulators already have access to EHR from a number of EU Member States and there are current pilots to use a common protocol in different data sets where studies are run by national regulators and EMA. Efforts are also underway to facilitate access to data and the conduct of studies. Regarding new technology the Web-RADR project includes participation of EMA and a number of national regulators and the project will support ADR reporting from mobile phones and analysis of the utility of social media data for product monitoring.
Recommendations from the PARENT Joint Action (JA) will be taken forward by EUnetHTA JA3. The PARENT recommendations document will be circulated after the meeting.

Action point(s):

- EUnetHTA to continue encouraging its partners to participate in the initiatives related to additional data collection
- EUnetHTA to circulate recommendations of the PARENT JA
- EMA to consider how to facilitate EUnetHTA involvement in initiatives on use of EHR data.
- EMA to regularly update “note on the regulatory post-authorisation data collection”

4. Cooperation on initiatives related to evidence generation (early dialogues and PAES)

EMA provided an outline of a possible cooperation with EUnetHTA on Shaping European Early Dialogues (SEED) and EMA Parallel Regulatory HTA Scientific Advice under Best Practice Guide (BPG).
Preliminary results of an EMA initiated content analysis based on SEED procedures and EMA Parallel Regulatory HTA Scientific Advice procedures, under BPG was presented by EMA. The objective was to explore the level of alignment reached by the EU Regulator and HTA bodies, and among HTA bodies themselves, for the recommendations provided when applicants obtain simultaneous scientific advice from both a regulatory and an HTA perspective.
The methods used for the analysis were commented by EUnetHTA participants. Differences between SEED and the Best Practice Guide initiative on parallel advice (procedures, preparatory work, coordination and participating bodies) were noted. The definitions used were explained in the meeting. Potential limitations of a pooled analysis were underscored.

With regards to the SEED project, its pilot status was emphasised – i.e. the evolution of the process from the first pilot to the last one. EUnetHTA participants further noted that to come to single conclusions and to an alignment between EU Regulators and the HTA bodies and among HTA bodies themselves is not a main goal of the SEED initiative. Instead, the SEED initiative was undertaken to help companies to understand what the needs of the HTA and decision bodies are. It was noted that the outcome is never legally binding even if the advice is resulting in an official document. All the above reservations as well as further consultation with the SEED consortium (which is coming to an end) and EUnetHTA will be taken into account by the EMA in relation to the content analysis.

Action point(s):

- EMA to take into account comments on the content analysis EMA to further consult the SEED consortium regarding methods to be used and procedural developments to be included in the analysis.

A scientific guidance on post-authorisation efficacy studies was shared with EUnetHTA partners for comments. Before the new EU Regulation ((EU) 357/2014) was introduced, PAES could be requested in the context of certain Marketing Authorisations (conditional, exceptional circumstances, ATMPs), paediatric use and referral procedures. At this moment PAES can be required for medicines with standard MA either at the time of granting authorisation or after. This requirement to conduct additional studies will reflect uncertainties regarding (sub-) populations, endpoints, other results of the long term treatment, co-treatment with other products, real-life use, a change in the understanding of a disease or drug or change in scientific factors for previous efficacy evaluations.
Ways to involve the HTA organisations and payers were discussed. Their input should be included together with the regulator's input (e.g. as an additional investigational arm), provided that there is no impact on study primary objectives.
The following limitations of the approach were expressed by HTA bodies and further discussed:

- Lack of transparency on the side of the companies asked for additional evidence generation.
- The options to withdraw compounds which may have added value but where submitted information was not sufficient, has not been developed yet.

5. DG Santé update on the development of the HTA Network and JA3 preparations (including the involvement of the EMA)

An update on the HTA Network and decisions made during the meeting that was held on Oct 29, 2015, in Paris, was provided by the DG Santé representative, Jerome Boehm. Two subgroups, one consisting of 5 Member States (MS) and the other consisting of 10 MSs were established to adequately take forward:

- A long-term multi-annual work programme
- interaction between regulatory and HTA areas

At the level of the HTA Network, an initiative by 2018 will be prepared with the following aims:

- financial sustainability,
- established Secretariat for the cooperation,
- promotion of the re-use of the HTA reports in the national settings.

Other areas of discussion included integration of the HTA cooperation into pathways of health care products' development, more active involvement of payers, governance of early dialogues (including Conflict of Interest procedure), synergies regarding the evidence generation and access to CHMP data.
There does not seem to be willingness to provide substantial EU Health Programme resources into the research area of the HTA collaboration. Instead it is advised to work with other research consortia, e.g. IMI. There had also been discussions within the HTA Network

on involving economic aspects in the HTAs. The latter issue was commented by EUnetHTA participants in the meeting. Even though there is no clear willingness among all partners to use the HTA Core Model domains outside REA at the local level, domains such as organisation and economic analysis should not be left out as many countries need to include economic, social or organisational aspects in their analyses, and therefore it would be advised to have the possibility to include them in the Network's activities.

6. Cooperation on joint HTAs: status of data sharing for REAs in JA2 and joint production of HTAs with a view to the involvement of the EMA in the process

An ongoing discussion in previous meetings was continued on the sharing of final CHMP assessment reports with EUnetHTA to be used in rapid REAs of pharmaceuticals, before decision of the European Commission (EC) and consequently the EPAR is published. Because the EMA sends the CHMP assessment reports to the applicant and to the Member States soon after they are finalised, they could be made available to the HTA bodies by the pharmaceutical companies directly. It has however proven to be not always easy for the HTA bodies to timely (i.e. shortly enough after opinion of CHMP) receive the document either from the relevant Member States recipient institution or from the involved manufacturers, and is practically impossible to get this information in case the manufacturer does not want to be involved in the REA process at all. This generates strong dependency of the REA process on the industry, so that the process of the assessments cannot be started early and raises the risk of assessing only products that are of the lowest-risk for the companies. Untimely the REAs cannot then be re-used nationally by HTA organisations which in turn prevents effective national adaptation of the EUnetHTA output, prevents decrease in duplication of work across Europe and delays patient access to the effective therapies. Therefore it seems to be crucial for the EU cooperation and cooperation between EUnetHTA and the EMA to timely share the CHMP assessment reports. It was further emphasised during the discussion that to go back from a European level to the national levels in order to get access to this information, is non-contemporary, non-practical and non-realistic option.
Although a conceptual framework of sharing this early regulatory information has already been determined and substantial legal analysis has been provided by the EMA, the legal framework still needs to be confirmed by the European Commission. Therefore it is suggested that these activities be included into the agenda of the next meeting of STAMP in order to initiate the debate on sharing data across European institutions before start of the JA3.

Action point(s):

- European Commission to include point on information sharing in the agenda of the next STAMP meeting and to provide further clarifications and options for establishment of appropriate legal framework

7. Engagement with patients during EMAs processes and HTA processes: discussion of experiences and future developments

An overview of patient involvement in the German health care system and on the European, regulatory level was presented respectively by IQWIG and the EMA. Presentations included categories of patient participation, selection of patient representatives, and framework of interaction with patients. In addition, NICE provided information about its practices related to involvement of both patient organisations and patient experts, usually in the scoping and appraisal phases. Evidence submitted by patient organisations may also be taken into account in the production of the HTA report. EUnetHTA is looking for more patient involvement in the future pilots, and therefore different options for involvement (either by participation in scoping meetings or by filling in questionnaires on patient relevant aspects) were discussed in more detail.

Exchange of information was followed by the discussion about concrete solutions used in terms of conflict of interest procedures, confidentiality issues, resources and reimbursement of patient involvement in the procedures. It was agreed that standards and procedures for use during the patient involvement will be collected for the discussion at the next meeting.

Action point(s):

- to compile information on criteria for patient organizations to be involved at the EMA or HTA organisations

8. Three-year work plan (and reporting of its implementation)

A report on the implementation of the work plan is under development. The document will include achievements of the collaboration between the EMA and EUnetHTA within the last three years. The first version containing the outline of the report has already been agreed between the EUnetHTA Secretariat and the EMA. Production of the second version is ongoing and the document will be sent for consultation within the EMA and EUnetHTA by the EUnetHTA Secretariat and the EMA in February so that document is finalised in March.

9. Any other business and closing remarks.

This was the final meeting organised within EUnetHTA JA2 and follow-up and continuation is in the hand of the EMA and EUnetHTA JA3. It was noted that future topics for the regular dialogue may include the specifics of paediatric medicines as well as aspects of product labeling.

The meeting was adjourned at 16.55.

STATUS OF ACTION POINTS: Nov 23, 2015

*[Note: Action points from the previous meeting are in **BOLD**]*

Who	What	Status	When
EMA (SVA/JM) and EUnetHTA (FM)	to liaise on the evolution of the EMA – HTA parallel scientific advice pilot procedure	ongoing	continuous
EMA (SVA/JM), EUnetHTA (FM) and EC (JB)	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 (JM)/ (GT) EUnetHTA (FM)	-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 -**further consult SEED consortium regarding methods to be used and procedural developments to be included in the analysis**		
EMA (GT)	**to take into account comments provided on the content analysis**		
EMA (JM) EUnetHTA (FM) and EC (JB)	to continue discussions on appropriate ways of accelerating patients' access to innovative therapies by providing a scientific advice for the pharmaceutical companies	ongoing	continuous
EMA (JL)	To share with EUnetHTA an outline of the scheme for unmet-needs-drugs		
EMA (JM)	to explore how best include HTA bodies in the consultation on the PAES guideline to provide draft PAES guideline to EUnetHTA, once this has been reviewed by its scientific committees	done done	**x**
EUnetHTA and EMA (PAR)	to map and prioritise tasks within ongoing projects which involve additional data collection.	done	**x**
EMA (PAR)	**to regularly update "note on the regulatory post-authorisation data collection"**	**ongoing**	**Ahead of each meeting**
EMA (PAR) EUnetHTA (FM)	EMA to engage EUnetHTA in any activities regarding registries	?	
EUnetHTA	EUnetHTA to circulate recommendations of PARENT related to registries		
EMA (PAR)	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 focused on HTA studies)		
EMA (MBER)	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.	ongoing	
EMA (PAR)	**EMA to consider how to facilitate EUnetHTA involvement in initiatives on use of EHR data**		
EMA (HGE/Legals)	to amend the Q&A document on the Policy on publication of clinical data for medicinal products for human use in order to clarify intended use of the data published by EMA for pharmaceutical	done	**x**

	submission dossiers		
EMA (FP/AK)	to trigger a joint review of experience in "Effect Tables" development and consider preparation of a joint publication		ahead of the May 2016 meeting
EUnetHTA (WG)	to design a leaflet on rapid REA that can be provided by the EMA to prospective applicants in pre-submission meetings	ongoing	**to be addressed again in JA3**
EUnetHTA (WG) and EMA (MBER)	develop criteria for candidates/application for which leaflet on rapid REA should be handed out	ongoing	
EC EMA (MBER/Legals) and EUnetHTA	-to clarify options for data (i.e. CHMP assessment report) sharing agreements -to continue work on a legally robust framework for data sharing with individual HTA organisations **-EC to include point on information sharing in the agenda of the next STAMP meeting and to provide further clarifications and options for development of sufficient legal framework**	Ongoing	
EUnetHTA (WG)	to provide list of HTA bodies involved in REA including information on their legal entity, based on query to be received from EMA		
EMA (HGE, SVA) EC (JB)	to clarify the process of MAPPs pilots (particularly the issue of representatives of payers)	done	**x**
EUnetHTA members (particularly the representatives of payers?)	to consider participation in the MAPPs pilots	done	**x**
EUnetHTA (Secretariat + partners separately)	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	done	**x**
EUnetHTA	-to facilitate contribution of different HTA institutions to the initiatives on Adaptive Pathways / MAPPs **-to keep encouraging its partners to participate in the initiatives related to additional data collection**	ongoing	continuous
EUnetHTA	to continue exploring with payers how they can be involved in the development of Adaptive Pathways	continuous	
EUnetHTA	to continue to clarify how to get information exchange with additional HTA organisations including from new Member States (MS)	continuous	
EMA	to explore feasibility of defining "sample" scenarios to be discussed with HTAs in the context of the ADAPT-SMART project		
EMA (MBER, TS)	To discuss possible criteria and general aspects of indication wording in the SmPC; a discussion paper to be shared with EUnetHTA		
EUnetHTA (all partners?)	to comment on the EMA's discussion paper on indication wording in the SmPC		

EMA (MBER)	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	continuous	continuous
EUnetHTA (WG) EMA (KL)	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	postponed	
EMA (IM) EUnetHTA (IQWIG)	to continue the discussion with a view to allow HTA bodies to get practice in the engagement with patients during rapid REA **to compile information on criteria for patient organizations to be involved at EMA or HTA organisations**	continuous done	X x
EC	Topic [*patient interactions*] to be included in the future Joint Action 3		

EMA	**=**	**European Medicines Agency**
AK	=	Andreas Kouroumalis
FP	=	Francesco Pignatti
GT	=	Giovanni Tafuri
HGE	=	Hans-Georg Eichler
IM	=	Isabelle Moulon
JM	=	Jane Moseley
KL	=	Kristina Larsson
MBER	=	Michael Berntgen
PAR	=	Peter Arlett
SVA	=	Spiros Vamvakas
TS	=	Tomas Salmonson
EUnetHTA	**=**	**European Network for Health Technology Assessment**
FM	=	Francois Meyer
WG	=	Wim Goettsch
EC	**=**	**European Commission**
JB	=	Jerome Boehm

PARTICIPANTS LIST

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Peter Arlett	***EMA***
Michael Berntgen	***EMA***
Hans-Georg Eichler	***EMA***
Harald Enzmann	***EMA /CHMP***
Isabelle Moulon	***EMA***
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Regina Skavron	***GBA, Federal Joint Committee***	*Germany*
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Luciana Ballini	***ASSR, Regional Agency for health and social care – Emilia Romagna***	*Italy*
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Wojciech Wysoczanski	***AOTMIT, Agency for Health Technology Assessment and Tariff System***	*Poland*
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European Commission

Name	Organisation
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