EUnetHTA JA Stakeholder Forum and Executive Committee
e-meeting
November 24, 2010
1:00-3:00pm CET

E-meeting
Organised by EUnetHTA Secretariat
National Board of Health, Denmark

Participants:
Chair of the meeting: Finn Børlum Kristensen, NBoH, Denmark (Secretariat)

Stakeholder Forum representatives:
Andrea Rappagliosi, EFPIA
Ilaria Passarani, BEUC
Magdalena Machalska, AIM
Nicola Bedlington, EPF
Nicole Denjoy, COCIR
Pascal Garel, HOPE
Pascale Brasseur, EUCOMED
Rita Kessler, AIM
Ursula Hofer, CPME

EUnetHTA Executive Committee representatives:
Alric Ruether, IQWIG, Germany
Christoph Künzli, SNHTA, Switzerland
Eleanor Woodford Guegan, NETSCC, United Kingdom
Elisabeth George, NICE, United Kingdom
Inge Merete Skov, NBoH, Denmark (Secretariat)
Julia Chamova, NBoH, Denmark (Secretariat)
Marianne Klemp, NOKC, Norway
Marina Cerbo, AGENA's, Italy
Sarah Kleijnen, CVZ, Netherlands
Sun Hae Lee Robin, HAS, France

European Commission
Anders Lamark Tysse, DG Sanco, EU

Apologies:
Bert Boer, CVZ, Netherlands
Andrew Cook, NETSCC, United Kingdom
Carole Longson, NICE, United Kingdom
Eva Turk, NIPH, Slovenia
Gro Jamtved, NOKC, Norway
Kristian Lampe, THL, Finland
Raf Mertens, KCE; Belgium
Urs Brügger, SNHTA, Switzerland
Wim Goettsch, CVZ, Netherlands
Jerome Boehm, DG Sanco, EU
ESIP

ECPC
EURORDIS

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1. **Practical implementation of the Stakeholder Involvement/SAGs in WPs**

2. **Efficacy and effectiveness – what is the difference?**

3. **Other issues**

    a. **Draft SF activities plan 2011-2012**

Finn B. Kristensen (FBK) welcomed participants to the 2nd EUnetHTA JA Stakeholder Forum e-meeting. Since Bert Boer, CVZ was unable to attend the meeting; FBK chaired this e-meeting. The meeting was scheduled to last 1½ hour. FBK presented the agenda of today's e-meeting.

1. Practical implementation of the Stakeholder Involvement/SAGs in WPs

Julia Chamova (JUCH) presented the general principles of implementation of the stakeholder involvement in the work packages and briefly outlined specific details of stakeholder advisory group work in WP 4, 5 and 7.

General Principles (Part B, Stakeholder Involvement SOP):

- The Executive Committee is overseeing the stakeholder involvement in the WPs. The Work Package Lead Partners and Co-Lead-partners are responsible for appropriate, practical implementation and planning of the work in the WP's which is dedicated to Stakeholder-involvement. They are responsible for implementing the general principles.
- The face-to-face and e-meetings of the Stakeholder Forum (SF) will be used to update the members on the general issues of implementation (eg, WP SAGs)
    - **more frequent updates of the respective umbrella organisations in the SF on the WP SAGs activities is the responsibility of the SF representatives in the WP SAGs (confidentiality undertaking to be observed)**
- The WP LPs (and Co-LPs when applicable) are responsible for appropriate practical implementation of general principles

- **Modes of participation**
- WP Stakeholder Advisory Groups (SAGs)
- WP4, 5 and 7
- provision of specific subject-matter knowledge on specific technical questions, eg, specific technologies, research methodologies, practical matters in conducting data collection, etc
- review and provide feedback to draft final documents undergoing public consultation

Procedures

- WP LPs' plan for stakeholder involvement (based on the 3-year Work Plan)
- Both members and participants of the Stakeholder Forum may appoint (up to 3) individuals for representation in each of the WP SAGs and shall inform the EUnetHTA Secretariat of their names

- WP LPs manage the SAGs
- The Composition of SAGs can change over time due to changing topics. If an organisation changes representative in SAGs the EUnetHTA Secretariat shall be informed.
- Each member of the SAG must sign a confidentiality undertaking document prior to commencing the his/her work
- If more than one individual is appointed to represent an organisation, a collated singular response on major documents is requested per each Forum organisation represented in the advisory group. This means that if an organisation e.g. 3 members in WP4, the organisation is asked to send one response only to the WP-Lead Partner, covering the response from all 3 members.
- standard period of response from SAGs will be 2(3) weeks
- no comments will be accepted after the deadline
- electronic means of communication will be the mode of providing input; if necessary and depending on the budget available, face-to-face meetings my be convened (there are no resources allotted for this in the budget for the EUnetHTA Joint Action).
- a compilation document containing all received feedback from SAG's members and comments from LP/Co-LP will be shared within the respective WP and the respective SAG as well as the EUnetHTA Executive Committee. This document will not be publicly available.

JUCH outlined the overall timeline for the SAG in WP4, WP5 and WP7. Each WP has already sent initial information on the activities in the WP SAGs to the SAG members.

WP4 SAG

December 2010: review of the first draft of the HTA Core Model application for Screening Technologies.
January 2011: HTA Core Model Handbook
April 2011: 1st Draft of Policies on the Core HTA Structure (i.e. HTA Core Model and information produced through using it)
June 2011 : 1st Draft of core HTA protocols
May 2012 : Review of Policies on the Core HTA Structure

- WP4 SAG mailing list will be set by THL (Finland) – WP 4 LP. *The mailing list is not yet ready;*
- meanwhile please use eunethta@thl.fi for contacting the THL team and hta@agenas.it for AGENAS team (WP4 Co-LP)

WP5 SAG

Jan 2011: draft background review
Mar 2011: selection of pharmaceuticals for piloting the rapid and full REA model
Apr 2011: concept guidelines
Dec 2011: results of the pilot experiments
Jun 2012: 2nd versions of rapid and full REA model

- Details on the specific deadlines and contact details for sending SAG's input will be provided to the WP5 SAG's members before December 15.

WP7 SAG

Next 6 months:
Stakeholder involvement will be limited to strand A (strand B concerns exchange of information on planned and ongoing HTA projects)

WP7/strand A;
Jan 2011 the first draft of relevant items that will define the content (the nature of information to be shared) of the database for additional evidence generation on new technologies
Feb 2011: the first draft of criteria to select and prioritize new technologies for additional evidence generation
Mar 2011: the draft of the dataset, following completion of the Delphi activity, on prospective data collection in development
- response to be sent to sh.leerobin@has-sante.fr

FBK commented that the SAGs in the WPs is a result of the interaction with the Stakeholder Forum this spring and summer.

Pascale Brasseur, EUCOMED, had 2 questions for clarification. 1st question was why the compiled document should not be publicly available – any specific reason for that? 2nd question was why there is no SAG involvement in WP7, strand B - the strand where there is exchange of information – why couldn't stakeholders be involved in that.
JUCH responded to the 1st questions that the documents that will be made available to SAG for commenting are draft documents that are not publicly available at that point of time or may never be publicly available. Therefore the comments on the confidential documents will not be made publicly available. After the SAG review and eventual adjustments, some draft documents will undergo public consultation and the comments received during the public consultation will be made publicly available.
FBK responded to the 2nd question that the WP7, strand B covers planned and ongoing projects in the participating agencies in EUnetHTA, this information is shared confidentially since e.g. some of the projects may eventually not be implemented in practice. Within EUnetHTA, the access to this database is also restricted only to those who supplied information to this database. It should be seen as an instrument that should help sharing information and collaboration as well as to help implementation of tools. Additionally, some institutions have an internal policy of not sharing this type of information publicly.

Andrea Rappagliosi, EFPIA asked to be verified that his understanding of the SAG role is correct, ie that members of SAG may be called an early-stage consultees, and be able to comment on the work in WPs at an early stage (eg, draft documents). Is there any other interaction that is foreseen?
JUCH confirmed that one may call SAG members "early consultees". The SAG members can also be approached by the WP LP to identify appropriate contacts for soliciting and to be able to provide specific subject-matter knowledge on specific technical questions, eg, specific technologies, research methodologies, practical matters in conducting data collection, etc

FBK emphasized that the management of these groups are in the hands of the LPs of each group. FBK invited the WP-leaders to provide any additional comment.

Andrea Rappagliosi, EFPIA requested further clarification from each WP chair how they want this co-operation to work in practice – it would be interesting to hear from LPs how they want the approach to be in the future.
FBK asked for additional information from LPs that could be provided at this time, however emphasised that it is important to get the work started and see a practice evolved. The work will be happening in SAGs, so the SAG members can report back to the umbrella organisations they represent.
Sarah Kleijnen, CVZ commented that with regards to the 2nd bullet-point at slide 4 (ie, provision of the specific subject-matter knowledge) that this is not planned at present, but can be evolving at a later stage when WP5 moves into the production of pilots on specific pharmaceuticals. Then WP5 LP may ask SAG members to facilitate that specific pharmaceutical companies provide input. With regards to the 3rd bullet-point, the public consultation is planned on the background review, guidelines, the pilot experiments and of the full and rapid model that WP5 will be developing.
FBK commented that when moving to piloting it would be an option to use patient organisations representatives to point to a specific expertise in that area to solicit patient perceptions and views. So it is not limited to manufacturers, but also include other stakeholder groups, eg, patients, healthcare providers.
Sun Hae-Lee Robin, HAS commented that for WP7 HAS will send specific document for review and ask specific questions to SAG-members as indicated in previous slides. With regards to the 2nd bullet-point WP7 will ask SAG-members to give feed-back on e.g., studies in development to collect additional evidence for new technologies with regards to which items are the most relevant ones to be shared within the EUnetHTA database. WP7 envision that there will be many occasions when the SAG members will be asked specific questions to provide focused feedback. For the 3rd bullet-point, WP7 will define selection criteria to identify the most relevant new technologies for which it is valuable to request more data collection. At that point WP7 will ask SAG members to give feed-back on the criteria for these items. Specific questions will be formulated and asked to the SAG members.
Marina Cerbo, AGENAS, informed that due to the dynamic nature of the work in WP4 it will be possible to specify the modes of interaction and timing for specific questions regarding the provision of the subject-matter knowledge on technical questions when the work on pilots is starting. She foresees many occasions when SAG members will be involved.

JUCH informed on the procedure of collecting confidentiality undertakings form the SAG members:

- Standard text of the document must be signed by each appointed individual prior to commencing work in the WP SAG.
- The document will be e-mailed by the Secretariat to all individuals on the WP SAGs **on November 25**
- Each individual shall print out the Confidentiality Undertaking (CU), sign it, scan it and send the scanned document to the Secretariat (eunethta@sst.dk) **by December 7**, 2010
- The Secretariat will inform the WP LPs on the names of those whose signed CU documents have been received.

Andrea Rappagliosi, EFPIA asked if it will be possible to receive the documents sent to members of the SAG in copy.
JUCH responded that the SAG members can update their respective umbrella organisation on the activities within SAGs, however, the members must adhere to the confidentiality requirements, specifically respecting point 3 of the Confidentiality Undertaking. Only in cases when the SAG member need to seek consultation with the employees/directors/officers at his/her place of

employment or at the main office of the umbrella organisation in order to be able to provide input as a SAG member, is she/he allowed to disclose confidential information to third parties*. The Lead and Co-Lead Partner must be informed about such consultation.
**) Secretariat comment:* As a consequence each individual third party must sign the Confidentiality Undertaking before the SAG member can share confidential information with him/her.

JUCH confirmed that confidential documents will be marked as "confidential".

Pascale Brasseur, EUCOMED asked if it will be possible to assist the Stakeholder Forum members/participants in the administration of this confidentiality undertaking by putting together a list of all who will be potentially involved once and for all, e.g. the names of the colleagues that a SAG member will always consult with*..
*) *Secretariat comment:* A procedure of up front signing by potentially involved individuals will be welcomed.

Pascale also asked if a SAG member has to sign the undertaking every time she/he receives a new confidential document.
JUCH commented that each member will sign the confidentiality document before the start of his/her work in the SAG, which will last for the whole period of his/her work. However, should a new member step in; he/she will need to sign the document.

FBK made clear that in a situation where a SAG-member would like to involve his/her umbrella organisation or his/her own organisation of employment, this person needs to send a message to the Lead Partner informing that this happens.

Rita Kessler, AIM clarified that AIM representatives normally share with colleagues and AIM members before providing input. The timelines for SAGs' input are very strict. Thus, there will be nearly no time to share information. AIM recommends that colleagues and AIM members should be consulted in situations like this. Rita therefore asked if the AIM-appointed individual on the SAG will have to inform the Lead Partners of the names of those she/he consults with..
FBK emphasized that the work in SAGs is a more focused work requiring certain competence on the subject and therefore EUnetHTA JA has asked the Stakeholder Forum members/participants to appoint people who should be able to perform such work. In order to perform according to the contract with the Commission and deliver accordingly WPs need to have short deadlines for input from SAGs. He further mentioned that consulting the colleagues might not be necessary for the competent appointed individuals to provide their input as SAG members. FBK invited the Lead Partners to provide any further considerations. There was no immediate response form the Lead Partners present.
JUCH responded that from point of view of EUnetHTA JA the appointed individuals should possess necessary competence to provide input, and only in cases when they find it is needed to have access to additional competence of their colleagues at the place of employment or the main office of the umbrella organisation should they seek such consultation.

FBK commented that the issue of the progress in and management of the SAGs will be a recurring item in the Stakeholder Forum communication. It is important to start the work and gain some experience with stakeholder involvement in work packages.

2. **Efficacy and effectiveness – what is the difference?**

FBK pointed to the need to keep clarity on the definitions of and the differences between efficacy and effectiveness when carrying out HTA. Therefore this issue was brought up in the Stakeholder Forum. The issue has been discussed in several fora, most recently, e.g., at the ISPOR-conference in Prague with special reference to pharmaceuticals. The slides on the subject used during the e-meeting are from the issue panel on the topic that was held at the ISPOR conference. FBK said that Sarah Kleijnen and Elisabeth George were present in this e-meeting and could provide clarifications if needed.

FBK presented the definitions of efficacy, relative efficacy, effectiveness and relative effectiveness with relation to pharmaceuticals. The definitions were agreed by the High Level Pharmaceutical Forum and the follow-up work on relative effectiveness assessment of pharmaceuticals is taken forward by the EUnetHTA JA WP5.

According to the Pharmaceutical Forum:

- **Efficacy:** is the extent to which an intervention does more good than harm under ideal circumstances. (*WP5 comment:* Information is used for decisions in *MARKET AUTHORISATION*)
- **Relative efficacy:** can be defined as the extent to which an intervention does more good than harm, under ideal circumstances, compared to one or more alternative interventions.

Both concepts above are applicable during the research situations, and not in the regular/every day clinical practice.

- **Effectiveness** is the extent to which an intervention does more good than harm when provided under the usual circumstances of health care practice.
- **Relative effectiveness** can be defined as the extent to which an intervention does more good than harm compared to one or more intervention alternatives for achieving the desired results when provided under the usual circumstances of health care practice. (*WP5 comment: Information is used for the decisions on REIMBURSEMENT)*

**RELATIVE EFFICACY AND RELATIVE EFFECTIVENESS: DO REGULATORY AGENCIES AND REIMBURSEMENT AGENCIES HAVE THE SAME NEEDS? IP8 Mo 8-11, 10.15-11.15. George, Abadie, Rappagliosi, Goettsch*

Nicole Denjoy, COCIR commented that discussion on effectiveness already took place previous to the Pharmaceutical Forum. From the slides it is obvious that we here talk about pharmaceuticals. The notion of efficacy is not applicable to medical devices. When referring to medical devices we are looking at minimum safety requirements. However, effectiveness could consider to be applicable. Efficacy versus effectiveness is only valid to pharmaceuticals. For medical devices claims are made and it should be ensured that the claims are followed.
FBK replied that in the work of EUnetHTA JA the issue of relative effectiveness is explicitly addressed with regards to pharmaceuticals in WP5. However, the concept of efficacy and effectiveness is also an issue in WP4 about the HTA Core Model where the aim is to get as close as possible to estimating the real life effect of an intervention. If a medical device should undergo a rigorous study that is designed as a randomised controlled trial, this would be determining the efficacy of that device. Establishing efficacy of a device is indeed not a regulatory requirement. However, efficacy is not exclusively a regulatory concept, but also a methodological concept, a research design concept. Efficacy and Effectiveness can be seen as methodological research concepts. Although there are no regulatory requirements regarding efficacy beyond the regulatory requirements with regards to pharmaceuticals, it is still relevant

to keep the concepts of efficacy and effectiveness clear and separate. Our goal is to put across that HTA is interested in the effectiveness, even if sometimes the effectiveness is estimated based on the efficacy data.

Sun Hae Lee Robin, HAS commented that she agrees with FBK – there is no regulatory requirements of efficacy of medical devices, but as an agency for HTA looks at benefits, efficacy or effectiveness of medical devices, those concepts and definitions are to some extent applicable to assessment of medical devices as well. When we carry out HTA we look at benefits and harms. Therefore, the discussion is not about the regulatory requirements only.

FBK commented that during the EUnetHTA Project, there was development of two versions of the HTA Core Model and its application on the basis of two concrete medical technologies. One was addressing drug eluding stents. It is a device. One can go to the EUnetHTA website and see how the work was done and how the issue of benefits and harms was addressed as well as the issues of effectiveness.

Nicole Denjoy, COCIR, agreed to keep the concepts, however, pointed out that other references (than the Pharmaceutical Forum) should be used for this purpose.

Andrea Rappagliosi, EFPIA, commented that in order to be politically correct it needs to be clarified that the wording MARKET ACCESS and REIMBURSEMENT were not in the definitions agreed by 27 Member States, EU Commission, EU Parliament and stakeholders*.
*) See Secretariat comment above.

Pascale Brasseur, EUCOMED, commented that the issue is more complex with regards to devices and more connected to the performance of a device, however, for the sake of the discussion, these definitions can be kept, especially if the words MARKET AUTHORISATION are removed, these definitions are helpful.

FBK confirmed that the explanatory additions of MARKET AUTHORISATION and REIMBURSMENT to the definitions of efficacy and effectiveness should not be seen as the text from the Pharmaceutical Forum.

Andrea Rappagliosi commented that it might be an explanatory but not a shared interpretation.

Nicole Denjoy, COCIR, commented that the definitions should be kept, but even in this context of HTA a correct reference should be made for medical devices, which is totally different from pharmaceuticals. When we talk about market authorisation for medical devices, we are talking about CER marking requirement. Regarding the efficacy of medical devices we are talking about safety and performance.

FBK suggested that this issue could be up again in this forum for the specifics of devices and pharmaceuticals. We should also have an update on the current developments in the area of regulation of medical devices that are going on in the EU. The essential message is that HTA is ideed addressing all kinds of interventions and devices and when doing this HTA makes use of all best evidence available to estimate the benefits of the interventions in the real life application of medical technology (be it a pharmaceutical, device or medical procedure, etc),i.e. the real effects in clinical practice.

Nicola Bedlington, EPF supported FBK's suggestion to look at the current developments with regards to medical devices, perhaps looking at the report coming out of the exploratory process on medical devices that was adopted at the beginning of this year, and other developments that are happening currently at the EU level.

Sun Hae Lee Robin, HAS agreed that each technology has its specificity, however, we should avoid to multiply definitions. Maybe we can refer to the INHATA definitions of health technology, efficacy, effectiveness, etc . Sun found that his topic deserves more in depth discussion.

Pascale Brasseur, EUCOMED; disagreed with Nicole Denjoy . EUCOMED would propose to avoid several definitions. The present definitions of efficacy and effectiveness are broadly, generally accepted.

Nicole Denjoy commented that we need broader definitions, but we should not refer to the Pharmaceutical Forum as a reference.

Andrea Rappagliosi, EFPIA; emphasised that the definitions developed during the Pharmaceutical Forum have been endorsed by the 27 member states, the European Commission, etc and should not be ignored. We should not go into an exercise of redefining, reshaping, etc of definitions agreed. The effect of various interventions (medical devices, pharmaceuticals, etc) should be compared in order to identify the best intervention in the interest of the patient.

FBK clarified that the WP5 takes the definitions of the Pharmaceutical Forum forward – there is a plan for this work. It is related to the work in WP4, however, in WP5 the work is a focused on pharmaceuticals. Thus, throughout the 3 years of the EUnetHTA JA the definitions inherited from the Pharmaceutical Forum will be used. There might be discussions about the concepts, etc, but it is simply a given that we use these definitions for the work of WP5. The Stakeholder Forum can take up the issue of relative effectiveness for discussion again and expand the discussion to other interventions, but for now these concepts have been addressed sufficiently. The Forum may take the definitions up again later for further discussions.

Andrea Rappagliosi, EFPIA, requested clarification on why the topic of the efficacy and effectiveness was brought to the agenda of this e-meeting. FBK reiterated that this is an issue that is currently being discussed in various forums. It is being discussed who should do what and when – especially when it comes to looking at efficacy and effectiveness. More specifically, when it concerns pharmaceuticals, what is the legislative basis for the activities of EMA, the medicines agencies and HTA agencies. Besides the issue was prompted by a recent public communication from one of the member organisations of the EUnetHTA JA Stakeholder Forum..

3. Other issues

JUCH briefly informed that the draft activity plan for the Stakeholder Forum is yet to be developed and be made available in January 2011 to the Stakeholder Forum.

The timetable of the e-/meetings in the Stakeholder Forum and the WP1 /Executive Committee is available below.

E-meetings are always scheduled 13:00-15:00 CET (if not noted otherwise on case by case basis)

Year	WP1 / Exec Comm	Stakeholder Forum	Notes
2010	Sept 8, e-meeting	Sept 22, e-meeting	
	Oct 14-15, Brussels meeting	Nov 24, e-meeting	
	Dec 9, e-meeting		
2011	Jan 26, e-meeting	March 2, e-meeting	
	March 21-22, Paris meeting		
	April 13, e-meeting	May 3, Brussels meeting	
	May 25-26, EUnetHTA JA Plenary Assembly meeting in London	*May 25-26, EUnetHTA JA Plenary Assembly meeting in London*	*4 EUnetHTA JA Stakeholder Forum observers each representing a specific stakeholder group in the EUnetHTA JA Stakeholder Forum can participate in the Plenary Assembly meeting*
	June 15, e-meeting	June 8, e-meeting	
	Sept 7, e-meeting	Sept 20, e-meeting	
	Oct 5, Warsaw meeting		
	Nov 16, e-meeting	Nov 22, e-meeting	

The Secretariat needs to know the names of the four Stakeholder Forum representatives who will be attending the Plenary assembly meeting in London in May.

a. Next Stakeholder Forum e-meeting – March 2, 2011, 13-15 CET