EUnetHTA EFPIA Technical Meeting
Paris, June 7, 2016

European Federation of Pharmaceutical Industries and Associations

Address of venue:
Haute Autorité de santé, Paris, France
5, avenue du Stade de France

MINUTES OF MEETING

ACTION POINTS	Who
1. Identify areas or ways to build trust so reports are adopted at a national level	**All**
2. Circulate relevant information to members appropriately and timely	**EFPIA**
3. Develop Standard Operating Procedure (SOP) for the selection of authors and reviewers	**EUnetHTA**
4. Revise procedural documents relative effectiveness assessments (REAs): include involvement of patients	**EUnetHTA**
5. Consider revising the process of assessment, in particular the timing and breadth of the scoping meeting, on a case-by-case basis after discussions between authors and companies involved	**All**
6. Finalise the framework agreement for provision of final assessment reports by the European Medicines Agency (EMA) to HTA agencies in the context of rapid REA coordinated by EUnetHTA. Consider further in-person interactions beyond written arrangements for provision of final assessment reports	**EMA and EUnetHTA**
7. Refine the scope of the submission template	**EUnetHTA**
8. Discuss methodology of safety assessment using multiple data sources at the next upcoming EMA-EUnetHTA bilateral meeting.	**EUnetHTA/EMA**
9. Ensure relevance of products to HTA agencies priorities, through discussion between companies and EUnetHTA/HTA agencies	**EUnetHTA, EFPIA**
10. Consider opportunities for combined efforts in horizon scanning with regulators	**EUnetHTA/EMA**
11. Initiate national discussions between HTA authorities, industry and other relevant stakeholders to clarify opportunities of joint assessments and how to address any existing barriers at the national level	**EUnetHTA, EFPIA**
12. Patient organization to advocate at the national level to remove the legal barrier	**Patient organisations**
13. Continue dialogue around individual assessments and plan further interactions to build on today's outcomes	**All**

Participants:

See participant list in appendix I

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09:30 – 10:00	**Welcome and introduction** ➢ Introduction by Guido Guidi, Head of Pharma Region Europe, Novartis, member of EFPIA European Markets Committee ➢ Introduction of Co-chairs meeting: Wim Goettsch, EUnetHTA and Andrea Rappagliosi, EFPIA ➢ Introduction participants

Marc Guerrier, HAS, welcomed participants on behalf of the French Haute Autorité de Santé and informed participants that the new chair of HAS, Agnès Buzyn, would join at 4 pm.

Introduction by Guido Guidi (Novartis/EFPIA EMC)

On behalf of the EFPIA delegation, Guido Guidi underlined the importance of an open exchange between industry and Member State authorities. It is not obvious to find alignment on such important issues as the efficacy of medicines. He stresses that there are more commonalities than differences and we should aim to find common grounds on conducting joint scientific assessments on the clinical parts of HTA and discuss how to use them: we need to use (rather than re-use) what is produced jointly. Collaboration could focus first on a few countries only. It will not be easy; there will be differences of views, both within authorities and within companies. But it is important for an early and coherent access, as well as early evaluation. The technical discussion today would set the ground for a political discussion. We need to prepare for a stronger political endorsement by all relevant authorities.

Introduction of co-chairs

Wim Goettsch (EUnetHTA, ZIN) underlined the importance of having all relevant stakeholders present during the meeting today: HTA agencies, EFPIA, patient representatives, the EMA, the Commission. Unique that a stakeholder meeting takes place before any first official interaction of the Joint Action 3 (JA3) which shows commitment from all sides to move forward. He provided a brief historical perspective on JA, and stressed that JA3 is the bridge between JA2 and a more structured collaboration which can deliver quality, consistency, coherence and timeliness. The cooperation of all involved partners in JA3 requires open and realistic discussions and openness to clarify all opinions and balancing moving on and not going too fast. We need to understand who are in favour of joint assessments, and where problems lie in national settings to adapt joint reports. Before closing, he also welcomed the presence of the European Commission to the meeting as an additional sign of support to the overall objectives of the Joint Action.

Andrea Rappagliosi (EFPIA-Chair of the EFPIA HTA WG, SP-MSD) strongly believes that JA3 is critical in setting the permanent structure of HTA collaboration. The frame, as outlined by Guido Guidi, is the clinical part of HTA. We now need to generate evidences demonstrating that collaboration is doable and maintained through time. It is important to de-ideologise the debate. How can we make the system more efficient, and benefit of the joint work?

10:00 – 10:45	**Introduction Joint Action 3** ➢ Feedback and follow-up on JA2 Technical meeting, Oct 2015. EFPIA, EUnetHTA ➢ Plans and activities EUnetHTA JA3: focus on REA WP4. NIPHNO, ZIN

Feedback and follow up

Ansgar Hebborn, Roche and Vice-Chair of the EFPIA HTA WG, reflected on the historical involvement of stakeholders in EUnetHTA. He stressed that the focus of JA3 should be on the Member States, to identify barriers and drivers of using the output of European collaboration at the country level. He underlined the importance of lead authors coming from the national evaluation team. In order to ensure this increases over time, we need to build trust in the system; regular meetings will help to brief additional companies in that sense.

He presented the industry views (slides attached):

- Joint reports need to be adopted one to one in the national process.
- JA3 and Member States need to identify ways in which this adoption can happen, and therefore relevant national agencies need to be involved directly.
- Potential barriers for adoption need to be identified and addressed, in order to avoid any duplication of assessment.
- It is important to identify the Member States which are willing to use the reports, before assessments start, in order to manage expectations, also on the industry side

Wim Goettsch, and **Hedi Schelleman**, Advisor, ZIN,
Presented the outcomes and follow-up to the JA2 meeting with EFPIA in October 2015 (see slides). In particular, the first meeting of Work Package 4 (WP4, Joint Assessments) in September 2016 with all the WP4 partners will discuss how to refine the process of joint assessments to integrate comments previously expressed.

Marianne Klemp, EUnetHTA JA3 WP4 leader (NIPHNO),
Presented the work plans for JA3 WP4 (see slides). She underlined that WP4 has a total of 60 active partners for authors and co-authors, including a large number of regional agencies and non-for-profit organisations. 33 Joint assessments and 4 collaborative assessments on pharmaceuticals are planned in 4 years. No prioritisation process will be needed for collaborative assessments, as the interest of at least two partners (Member states) is sufficient to trigger an activity.

During the discussion, the following items were raised:
- How to reach the target of 33 assessment? Hopefully WP4 will receive many letters of interest from which to pick the best one, contribution of the Industry and specifically EFPIA to achieve the target is crucial.
- The importance of choosing topics that are of interest/relevant for all countries, and timely for national decision-making.
- Other initiatives have a role to identify potentially suitable compounds for joint assessments such as early dialogue or PRIME; consider opportunities for horizon scanning in collaboration with regulators.
- In order to ensure company interest it is important that authorities use the joint reports produced; showing that reports are used will create a positive spiral.
- To clarify the content of joint assessment, not only process.

11:00 – 12:30	**Process of joint REA (WP4)** ➢ Priority setting: selection of health tech for REA aimed at implementation (NIPHNO) ➢ Criteria for selection of authors and reviewers (NIPHNO) ➢ Organisation and timelines of Scoping phase and Assessment phase (ZIN, EFPIA) ➢ Provision of regulatory assessment reports by EMA (EMA) ➢ Involvement other stakeholders (patient representative)

<u>Priority setting, criteria for selection of authors and reviewers</u>

Ingvil Saeterdal (EUnetHTA JA3 WP4, NIPHNO) presented the process of priority setting in JA3, and what the criteria are for selecting authors and reviewers. She stated that both the selection of products and authors will be based on the needs of Member States. This also means that those Member States volunteering to author joint assessments will need to commit to use the joint reports. Furthermore, more experienced partners will take the lead in the beginning to support less experienced Member States moving forward.

<u>Timelines of scoping and assessment</u>

Hedi Schelleman (ZIN) presented the scoping timeline and stressed the importance of achieving the timeline in JA3 (reference to submission 180 days prior to CHMP opinion).

Louise Timlin (Eli Lilly) presented the EFPIA views on the assessment process (see slides). EFPIA proposed to include an early scoping meeting in order to determine PICO, complemented by a final draft

submission review meeting before the CHMP positive opinion to ensure completeness of the submission.

The ensuing discussion/questions round on scoping covered the following:

- Potentially influence the timelines of the evaluation (plan for an earlier submission, e.g. around 240 days prior to CHMP opinion).
- The difficulty to have a scoping meeting without some preparatory work from the company.
- An informed scoping meeting could lead to a draft submission and a final discussion. In order to avoid too many meeting, technical tools such as e-meetings could be used.
- What is the optimal timing of availability of the joint report in order for HTA agencies to be able to use it?
    - NICE (2-3 months prior to CHMP opinion for cancer medicines);
    - ZIN (at time of EPAR would be sufficient);
    - FIMEA, TLV and NOMA (time of CHMP decision);
    - France (at time of company submission; for ATU[1] products this is compulsory one month after market authorisation (MA)),
    - Italy (at time of company submission; for orphan medical and exceptional therapeutic relevance products as defined by AIFA committee, the company submission can be as early as CHMP positive opinion)
    - Poland, Croatia and Italy (the reimbursement process starts on initiation by the manufacturer after MA);
    - Germany the process starts at MA.
- In order to start the assessment earlier than CHMP positive opinion and handle change of indications between the regulatory 180-day and 210-day reports, constant contact and communication with industry representatives are required.

Provision of regulatory assessment reports by EMA

Michael Berntgen (EMA) presented an update of the collaboration between EMA and EUnetHTA (see slides). Specific for the topic on the provision of assessment reports, he indicated that a framework agreement is currently being finalized by EMA in collaboration with the European Commission to enable the sharing directly by the EMA of certain parts of the final CHMP assessment report (introduction, clinical aspects and benefit risk section; the quality part will not be provided) at time of CHMP opinion directly with individual HTA bodies involved in joint assessment coordinated by EUnetHTA. Such agreement cannot be entered with EUnetHTA itself as it is currently not a legal entity. The Commission clarified that this agreement is currently limited to agencies actively contributing to joint assessments.

In the Q&A round, these points were discussed:

- Is the sharing of assessment reports enough? It could make more sense to initiate meetings between EMA rapporteur and co-rapporteur with EUnetHTA authors and co-authors.
- The framework agreement would be a general agreement to support JA3 activities (i.e. there would not be a need to negotiate for each individual product/assessment).
- If anything changed in the EPAR, compared to the CHMP assessment report, this will be flagged to EUnetHTA appropriately.

Involvement other stakeholders

François Houyez (Eurordis) presented the patient perspective on bringing value to the joint assessment process (see slides). He made concrete proposals building on the regulatory experience at both the national and European levels. He underlined that involvement of patients could take place at the national level; complementary to the European process, if that could make it easier to identify relevant expert patient representatives. He also underlined that patient representatives could help to make European reports more accessible to the lay public.

[1] ATU is Autorisation Temporaire d'Utilisation de Cohorte or Temporary Authorization for Use. It is the regulatory mechanism used by ANSM (the French Regulatory Agency) to make non-approved drugs available to patients in France when a genuine public health need exists.

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13:30 – 14:30	**Methodology and Quality Management (WP6)** ➢ Explanation of activities (IQWIG) ➢ Other Methodological issues, e.g. submission template (EFPIA) ➢ Discussion of Challenges and Solutions with the HTA Core Model application for REAs

Methodology and Quality management

Alric Rüther (EUnetHTA JA3 WP6, IQWIG) presented the JA3 plans on methodology and quality management (see slides).

The discussion focused on methodological concerns:

- Could we identify the minimum quality set that can be accepted by all agencies in their work to ensure the use of reports at the national level?
- Implement improvements to ensure that the reports are reliable.

Other methodological issues

Louise Timlin presented the industry views on issues that would need to be further considered in the methodological space, in particular around safety evaluation that will complement the EMA assessment and be relevant and useful to national HTA bodies. She suggested this is taken up in further discussions involving safety and statistical experts.

The discussion focused on the following items:

- The importance of information on adverse events when establishing the benefit profile of a new treatment.
- The importance of indirect meta-analysis of relative safety.
- The REA HTA core format and its focus on the most important issues for the joint REA.

14:30 – 16:00	**National implementation and impact (WP7)** ➢ Explanation of activities focused on joint REA's for pharma (NICE) ➢ Barriers to implement EUnetHTA reports (individual countries) ➢ Company barriers and possibilities in European Market (EFPIA, individual companies) ➢ Discussion

National implementation and impact

Zoe Garrett (EUnetHTA JA3 WP7, NICE) presented the work plan of WP7. She indicated that partners from all European countries except Bulgaria and Estonia (see slides) participate in WP7.

Barriers to implement EUnetHTA reports

- England/NICE: The next 2 years will be a critical period to collect evidence to build case for change for NICE, the experience from JA2 is too limited to make such a change (out of 5 JA2 joint assessments, 3 did not enter the NICE process; only one of the remaining two could be used for comparison at the national level). Joint assessments need to be on relevant products and timely, evidence in the REA assessment needs to be consistent with cost effectiveness assessment (CEA).
- Norway/NOMA: the lack of the economic model from the company is a challenge for the process.
- Netherlands/ZIN: Timing was a major problem with JA2 pilots as national assessments had already been completed, the new arrangements for provision of regulatory assessment reports between EMA and HTA bodies involved in completing joint REA may help. Need right reports on time to build trust within their agency.
- Poland: Similar circumstances as NICE around CEA, specifically the need to assess in REA the indications claimed (sometimes different than all registered).
- Croatia: the legal framework, as the MoH and health insurance fund need to request HTA but it is not

mandatory. However the necessary change of legislation is in process.

- Sweden: any HTA report needs to be relevant to the ultimate payer; the legal barrier is not as strong as the reluctance to talking to the ultimate payer.

These issues were discussed:

- How will the agencies adapt the joint REA reports, as use and appraisal are two different things.
- How critical topic selection is, and any product put forward for European assessment needs to be high on HTA agencies' agendas.
- What is the definition of success? For example simple metrics such as reduction of national processes by X% would be motivating for both companies and agencies and number of agencies that implement the EU REA .

16:15 – 17:00	**What's next** ➢ Further activities, timing of first pilots (individual companies) ➢ General Discussion

Timing of first pilots

- The importance of selecting relevant pilots that can be used.
- Take the lessons learned and modify accordingly.
- The first two assessments will need to focus on products that are important for both companies and agencies, acknowledging that the process might not be perfect to start with.
- The vision for a sustainable HTA cooperation after 2020.
- The call for a joint assessment to be solution oriented and looking at public health needs.

Speech by the new chair of HAS, Agnès Buzyn

She underlined the importance of the EUnetHTA JA3 initiative, and assured that France is fully taking part, in particular the contribution of HAS to a better evaluation. Now with JA3, we need to show that joint work is utilized locally and is viable in the long term. She noted that stakeholders are represented at the meeting and welcome the efficient dialogue with stakeholders. However the first aim of the collaboration should be to respond to health needs. In the framework of the Directive on cross-border healthcare, the principle of independence of expertise is key. This is positive for all stakeholders, in order to ensure sustainable trust from patients and citizens. She also referred to a recent meeting she attended of the Commonwealth fund which showed the interest of US colleagues on how Europe and EUnetHTA evaluates medicines.

Richard Bergström/EFPIA expressed their full commitment to the process, and expects more collaborations whilst respecting the competence of Member States.

On behalf of the European Commission Dominik Schnichels also thanks Ms Buzyn for her comments and for the leadership HAS provided to the cooperation in the past and look forward to further leadership in the new phase of cooperation. This third Joint Action is key to implement in real life working methods and tools piloted in the past and has a major responsibility for proposing a sustainable model of cooperation. To achieve this the leadership and commitment of all key players is essential.

What is next?

EMA is awaiting concrete proposals on:

1) Post authority data requirement
2) Identifying relevant topics

Summing up the day, **Wim Goettsch** underlined the many positive ideas that were brought forward. Based on the discussions of the day EUnetHTA will discuss with interested companies products that could be suggested; contacts will be established also through EFPIA to discuss what can be done regarding implementation and use at the national level.

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Appendix I: Participant list

List of Participants EUnetHTA Technical Meeting 7th June, 2016, Paris, France	
EUnetHTA Coordinator + partners responsible for national pharma assessments	
ZIN (Netherlands) (EUnetHTA JA3 coordinator)	Wim Goettsch (co-chair) Hedi Schelleman Marcus Guardian Aileen Yang
NIPHNO (Norway) (WP4 leader)	Marianne Klemp Ingvil Saeterdal
AAZ (Croatia)	Mirjana Huic
HVB (Austria)	Anna Nachtnebel
HAS (France) (WP5 leader)	Francois Meyer Marc Guerrier Agnes Buzyn Chantal Berlorgey Anne d'Andon Nathalie Merle Margaret Galbraith
GBA (Germany)	Antje Behring
IQWiG (Germany) (WP6 leader)	Alric Ruether
TLV (Sweden) (WP3 leader)	Niklas Hedberg
NICE (UK) (WP7 leader)	Nick Crabb Zoe Garrett
NOMA (Norway)	Kristin Svanqvist
FIMEA (Finland)	Tuomas Oravilahti
AOTMiT (Poland)	Anna Zawada Anna Zaremba

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AEMPS (Spain)	Laura Oliveira
AIFA (Italy)	Agnese Cangini
Uniba FoF (Slovakia)	Tomas Tesar
EFPIA + members willing to be involved in assessments	
EFPIA	Andrea Rappagliosi (co-chair) Edith Frénoy Richard Bergström
AstraZeneca	Chris Hoyle
Boehringer Ingelheim	Ingolf Griebsch
Bristol Meyers Squibb	Patrick Hopkinson
Celgene	Adam Parnaby
GlaxoSmithKline	Aikaterini Fameli
J&J	Eric Braun
Eli Lilly	Louise Timlin
Novartis	Guido Angelo Guidi (Head of Pharma Region Europe) Gesa Pellier
Roche	Ansgar Hebborn
LEEM	Thomas Borel
Sanofi	Hélène Afflard
Stakeholders	
DG SANTE	Flora Giorgio Dominik Schnichels
EMA	Michael Berntgen
Eurordis / EPF	Francois Houyez (Patient representative) Valentina Strammiello