HTA cooperation in Europe: Early Dialogues and beyond

Dr François Meyer, MD
TOPRA Brussels – 14th October 2015
Muti HTA early dialogues: Why they are necessary
Early engagement in health technology assessment (HTA)

- 3 options to get the HTA advice in Europe
  - National
    - HTA advice from national HTA body
  - Parallel EMA HTA
    - Advice from EMA and some HTA bodies on regulatory and HTA issues
  - Multi-HTA
    - Cooperative advice from EU national HTA bodies
    - Projects sponsored by European Commission
The EUnetHTA network 2012 – 2015
28 Member States, Total budget: € 9,428,550

• Production of **common assessment reports** (Core HTA information)
  – for full HTA
  – for rapid HTA, with template for the submission of data by industry

• **Methodological guidelines**

• Actions to improve quality and adequacy of the **development of new products**
  – Early dialogues
  – Disease specific guidelines

• Coordinated **requests for additional date collection**:
  – Common core protocol
Multi-HTA advice

• Principles
  – Voluntary activity of HTA bodies
  – Sponsored by European Commission – no fee for companies
  – Capacity building
  – Exchanges between HTA bodies
    • Consensus
    • Different views
  – Non-binding
  – Confidentiality
Multi HTA Early Dialogues
(1) 2012 - 2013

- 2 preparatory pilots (2012) and 8 pilots (2013)
  - Coordinated and hosted by HAS, France
    Dr Mira Pavlovic
  - 12 HTA bodies, 9 companies involved
  - Both small and big companies
  - EMA invited as observer
  - One-day face-to-face meeting
  - 10 drugs in various therapeutic fields
Multi HTA Early Dialogues
(1) 2012 - 2013

Outcomes

– Successful experience: 3 pilots planned, 10 done
– **Dialogue** between HTA bodies, to reach consensus when possible
– A **survey** was done among participants to refine the procedure
– A **consolidated procedure** has been produced
– Related activity: production of **disease specific guidelines**
Multi HTA Early Dialogues
(2) 2014 - 2015

Context

– Call for tenders issued by the European Commission

– SEED Shaping European Early Dialogues = Consortium of 14 partners, led by HAS
  • UK, Italy, Netherlands, Spain, Germany, Belgium, Austria, Ireland, Hungary, France

– Regulators, payers, patient representatives as observers
14 SEED Partners, led by HAS

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<thead>
<tr>
<th>#</th>
<th>Abbrev.</th>
<th>Institution</th>
<th>Country</th>
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<tbody>
<tr>
<td>1</td>
<td>HAS</td>
<td>Haute Autorité de Santé (Leader)</td>
<td>France</td>
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<tr>
<td>2</td>
<td>RER-ASSR</td>
<td>Regione Emilia-Romagna, Agenzia Sanitaria e sociale Regionale</td>
<td>Italy</td>
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<td>3</td>
<td>AIFA</td>
<td>Italian Medicines Agency</td>
<td>Italy</td>
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<tr>
<td>4</td>
<td>AVALIA-T</td>
<td>Conselleria de Sanidade de Galicia</td>
<td>Spain</td>
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<tr>
<td>5</td>
<td>GB-A</td>
<td>Gemeinsamer Bundesausschuss (Federal Joint Committee)</td>
<td>Germany</td>
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<td>6</td>
<td>GYEMSZI</td>
<td>National Institute for Quality and Organizational Development in Healthcare</td>
<td>Hungary</td>
</tr>
<tr>
<td>7</td>
<td>HVB</td>
<td>Hauptverband der Österreichischen Sozialversicherungsträger</td>
<td>Austria</td>
</tr>
<tr>
<td>8</td>
<td>ISCIII</td>
<td>Instituto de Salud Carlos III</td>
<td>Spain</td>
</tr>
<tr>
<td>9</td>
<td>AETSA</td>
<td>Regional Government. Fundación Pública Andaluza Progreso y Salud</td>
<td>Spain</td>
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<tr>
<td>10</td>
<td>CVZ</td>
<td>Health Care Insurance Board</td>
<td>Netherlands</td>
</tr>
<tr>
<td>11</td>
<td>IQWIG</td>
<td>Stiftung für Qualität und Wirtschaftlichkeit im Gesundheitswesen</td>
<td>Germany</td>
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<tr>
<td>12</td>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
<td>United Kingdom</td>
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<td>13</td>
<td>KCE</td>
<td>Belgian Health Care Knowledge Centre</td>
<td>Belgium</td>
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<tr>
<td>14</td>
<td>HIQA</td>
<td>Health Information and Quality Authority</td>
<td>Ireland</td>
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10 Early Dialogues

- 7 drugs and 3 Medical Devices (including IVD)
- Drugs: 4 multi-HTA ED (HTA bodies only)
  - 3 parallel EMA-SEED ED
- Different therapeutic fields: oncology, cardiology, haematology, etc.
- Orphan and non-orphan diseases, small and big companies
- 1st ED on May 2014 (drug), June 2014 (MD)
- 1st EMA SEED parallel advice: 8th October 2014
- Last ED expected March 2015
Documents available on website

- 3 Briefing Book Templates
  - Medical device: [http://www.earlydialogues.eu/has/?p=35](http://www.earlydialogues.eu/has/?p=35)
  - Drugs for multi-HTA: [http://www.earlydialogues.eu/has/?p=51](http://www.earlydialogues.eu/has/?p=51)
  - Drugs for Parallel EMA-HTA: [http://www.earlydialogues.eu/has/?p=248](http://www.earlydialogues.eu/has/?p=248)
- 2 Procedures
  - Parallel EMA HTA: [http://www.earlydialogues.eu/has/?p=271](http://www.earlydialogues.eu/has/?p=271)
  - Multi-HTA: [http://www.earlydialogues.eu/has/?p=1](http://www.earlydialogues.eu/has/?p=1)
How to manage the list of candidates

- More than 10 candidates
- Possible cancellations (for instance due to delays in product development)
- Waiting list for products
- To date: one delay, one cancellation, one product finally non eligible
  - EARLY DIALOGUES ARE NOT PRE-SUBMISSION MEETINGS
- Change in development plans possibly affecting the appropriateness of an early dialogue (not sure anymore to conduct a phase III trial...)
SEED: Shaping European Early Dialogues

Input from the company

– The company provides a structured submission file (Briefing book) containing:
  • Development strategy, cost-effectiveness studies: planned studies
  • Prospective questions and company’s position for each question relevant to the development plan

– Issues related to the relative effectiveness and/or economic aspects

– Questions up to the choice of the company
Main topics

– Population

– Comparator

– Design of the trial (duration, dosing)

– Endpoints

– Statistic analysis (subgroups, stratification)

– Economic data (population, comparator, model, utility values, resource utilisation)
SEED: Shaping European Early Dialogues

SEED features: Exchanges among HTA bodies

1. E-meeting to identify the need for additional information or clarification in the briefing book
2. Written draft positions of each HTA body exchanged
3. E-meeting to identify key issues
4. Face-to-face meeting among HTA bodies:
   • Prior to the meeting with the company to discuss divergent views
   • After the meeting to make conclusions and proposals for further improvements
SEED: Shaping European Early Dialogues

Procedure

– Letter of intent to be sent by the company at least 4 months before the intended date of the meeting

Day -90: Pre-validation by HAS
Day -60: Validation by HTA bodies
Day 0: Meeting
Day +10: Minutes of the meeting

– Meeting:
  • Morning session = discussion among HTA bodies
  • Afternoon session: discussion with the company focused on key issues.

– Outcome: Minutes of the meeting produced by the company, reviewed by participating HTA bodies
SEED outputs

• **10 Early Dialogues + 10 reports**
  – On various products (including devices) at various stages of development
  – Including orphan drugs, advanced therapies, co-diagnostic development
  – Various sizes of companies, including SMEs
  – Testing EMA-HTA procedure in this context
  – Participation of payers, patients.. (exploratory phase)

• **Report to propose permanent model** for Early Dialogues in Europe

• To be delivered to the European Commission by August 2015
What after SEED?

• Implementation of a permanent network of HTA bodies in Europe

• Strategic level in place: HTA Network (art 15 Directive 2011/24)— (2 meetings yet, 10/2013 and 4/2014)
  ▶ MS representatives (mainly MoH); EMA associated

• EUenetHTA (Joint Action HP)— scientific level – on-going until October 2015
  ▶ HTA doers (mainly HTA Agencies)

• Two levels in synergy and complementary
• Involvement of stakeholders - both @ strategic level and scientific level
Some challenges ahead

• From a EU sponsored model to a self-sustainable model.
• Fee for service?
• Choice of participating HTA bodies
• Relatives roles of national vs international
• Production of disease specific guidelines when necessary
SEED Consortium: 14 European HTA agencies

Abbreviation Institution Pays 1 HAS Haute Autorité de Santé (Leader) France 2 RER-ASSR Regione Emilia-Romagna, Agenzia Sanitaria e Sociale Regionale Italy 3 AIFA Italian Medicines Agency Italy 4 AVALIA-T Conselleria de Sanidade de Galicia Spain 5 GB-A Gemeinsamer Bundesausschuss (Federal Joint Committee) Germany 6 GYEMSZI National Institute for Quality and Organizational Development in Healthcare...

SEED (Shaping European Early Dialogues for health technologies) is an international project financed by the European Commission for a duration of 22 months (October 2013 – August 2015).

The SEED Consortium, led by HAS, is composed of 14 European agencies specialized in the field of Health Technology Assessment (HTA).

The aim of the SEED project is to conduct pilots on early dialogues between its member HTA agencies and developers of health products (pharmaceuticals and medical devices) whose products are currently in the development stage. In total, ten early dialogues are planned with an aim to conduct 7 on drugs and 3 on medical devices.
Muti HTA early dialogues: Are they sufficient?
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Two types of collaborative actions: 1

Cooperation on HTA production

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Actions</th>
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<tbody>
<tr>
<td>• Avoid duplication of work</td>
<td>• Joint assessment reports / Core HTA information</td>
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<tr>
<td>• Increase consistency</td>
<td>• Template for companies to submit data</td>
</tr>
<tr>
<td>• Increase transparency</td>
<td>• Methodological guidelines</td>
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## Two types of collaborative actions: 2

### Improvement of quality of data produced in primary research

<table>
<thead>
<tr>
<th>Objectives</th>
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<tbody>
<tr>
<td>• Improvement of the development plans of new technologies</td>
<td>• Early Dialogues</td>
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<tr>
<td>• Improvement of the additional data collection (to reduce uncertainty after initial assessment)</td>
<td>• Disease specific guidelines</td>
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<td></td>
<td>• Definition of common core protocols for additional data collection</td>
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Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval

H-G Eichler¹,², K Oye²,³,⁴, LG Baird², E Abadie⁵, J Brown⁶, CL Drum², J Ferguson⁷, S Garner⁸,⁹, P Honig¹⁰, M Hukkelhoven¹¹, JCW Lim¹², R Lim¹³, MM Lumpkin¹⁴, G Neil¹⁵, B O’Rourke¹⁶, E Pezalla¹⁷, D Shoda¹⁸, V Seyfert-Margolis¹⁴, EV Sigal¹⁹, J Sobotka²⁰, D Tan¹², TF Unger¹⁸ and G Hirsch²

European Medicines Agency,
MIT,
Agence Français de Sécurité Sanitaire des Produits de Santé,
Harvard Medical School,
Novartis Vaccines & Diagnostics,
NICE,
Commonwealth Fund,
AstraZeneca,
Bristol-Myers Squibb,

Singapore Health Sciences Authority,
Health Canada,
FDA
Johnson & Johnson
CADTH
Aetna,
Pfizer,
Friends of Cancer Research, Ohio Northern Univ.
Raabe College of Pharmacy,

Clinical pharmacology & Therapeutics, mars 2012
Current state: 1-step process
Adaptive Licensing: 2-step process
Importance of additional data collection

Key elements for success
- Scientific guidance → relevant evidence
- Funding for data collection and analysis
- Coordination of partners
- Regulatory framework → implementation of actions
Some research projects on the use of observational (« real life ») data

• **IMI Get Real**
  – Objective: to better understand how real-world data can be used to improve the relevance of knowledge generated during development, e.g., through innovation in clinical trial design.
EUnetHTA actions on Additional Evidence Generation

1. Exploring the possibilities for collaboration on AEG
   - literature review,
   - survey among EUnetHTA partners
   - Development of guidelines and pilots (for HTA agencies)

   ✓ Guideline/concept paper on how to best formulate the research question

   ✓ Guideline/concept paper on how to decide on the appropriate trial design

   ✓ Pilot of a common core protocol for AEG (for a technology of common interest)

2. Further development and promotion of the EVIDENT database

3. Cooperation with EMA
EMA EUnetHTA 3-year workplan

Areas of collaboration

– Scientific advice/early dialogue involving regulators and HTAs.
– Scientific and methodological guideline development.
– Post-licensing (post-authorisation) data generation.
– Availability of clinical study data.
– Orphan medicinal products.
– Cooperation in pilot projects.
– Cooperation in specific pilot projects of EUnetHTA JA2.
– Conferences, workshops and seminars/meetings.
EMA-EUnetHTA 3-year Workplan

• Post-licensing (post-authorisation) data generation
  – Regular mutual updates on the developments in this activity area
  – Explore coordinated approaches on post-authorisation data collection, such as possible parallel advice,
  – and explore the possibility of developing or testing methodologies for post-authorisation data collection that are relevant to support regulatory and HTA activities.
  – Develop cooperation EUnetHTA - ENCePP
Collaboration with ENCePP

European Network of Centres of Pharmacoepidemiology and Pharmacovigilance

• ENCePP Working group on HTA (Chair Marlene Sinclair, co-chair François Meyer)

• Mandate (revised -15 Oct 2013):
  – The group will provide a forum of academics and service providers for consultation as appropriate to support the development of guidance by ENCePP, EMA and EUnetHTA
  – The group will explore **capacity building** in the context of the ENCePP Research Resources Database on the conduct of studies that bridge to meet the requirements of medicines regulators and HTA bodies
  – In the long term, the group may lead [...] the development of a **consideration paper** on practice in conducting post authorisation studies that might meet the needs of regulators and HTA bodies
EUnetHTA Conference

WELCOME TO
HTA 2.0 EUROPE -
TEAMING UP FOR VALUE
30-31 October, 2014
Sheraton Roma Hotel and Conference Centre, Rome, Italy

Conference programme
The conference will bring you up-to-date on the latest developments in the interface between science and policy in European healthcare. A year on from the establishment of the HTA Network under Article 15 of the EU Directive on patients' rights in cross-border healthcare, HTA 2.0 Europe will address questions such as:

- What are the key achievements in the European cooperation in HTA that may impact national/regional healthcare systems and meet their needs?
- What is the present-day state of the interface between HTA, research, regulation and health policy making?
- What are the current challenges and opportunities in getting an effective technology to the patients in Europe?

Conference target groups:
- Policy-makers
- Technology assessors and developers
- Researchers (HTA-contributing fields of research)
- Payers
- Providers
- Patients

Facts about EUnetHTA
EUnetHTA was established to create an effective and sustainable network for HTA across Europe – we work together to help developing reliable, timely, transparent and transferable information to contribute to HTAs in European countries.


Conference networking opportunities
During the 2-day conference, you can attend plenaries, panels and round table discussions and ask questions to the EUnetHTA tools and methodologies development teams. You will have many opportunities to learn how collaboration, defragmentation and integrative approaches can lead to improvements in healthcare systems across Europe.

During the reception at the end of the first conference day, you can further expand your networks in an informal atmosphere.

Registration fees (excluding 22% VAT)

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<thead>
<tr>
<th>Type</th>
<th>Early (before August 31)</th>
<th>Regular (after August 31)</th>
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</thead>
<tbody>
<tr>
<td>EUnetHTA Partners &amp; Associates</td>
<td>200€</td>
<td>250€</td>
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<tr>
<td>Governmental/public institutions</td>
<td>200€</td>
<td>300€</td>
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<tr>
<td>Non-profit healthcare/social care providers, students</td>
<td>400€</td>
<td>700€</td>
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Language
The official conference language is English.