What is the added value of more HTA collaboration in Europe?
EUnetHTA JA3 - more than a year later

Wim Goettsch
Director EUnetHTA JA3 Directorate

RedETS (Tenerife), December 4, 2017
Outline

• European collaboration on HTA (in general)
• EUnetHTA
  o Historical perspective EUnetHTA;
  o Objectives for Joint Action 3 (JA3);
  o WP4 Joint assessments;
  o WP5 Additional data collection
    o Early dialogues/scientific advise
    o Post marketauthorisation data collection;
  o WP6 Quality Management;
  o WP7 Implementation.
EU cooperation on HTA

- **Policy and strategic cooperation**
  - Art 15 Directive 2011/24
  - Set up October 2013
  - Multiannual work programme
  - **Permanent**

- **Scientific and technical cooperation**
  - Started in the 1990's – EunetHTA 1 & 2
  - Joint Action 3 – 2016 – 2020

- **Cooperation beyond 2020**
  - Inception Impact Assessment
  - Description of the status quo
  - Options for the future
### EU initiative on HTA

#### Policy options (suggestion EC end 2017)

<table>
<thead>
<tr>
<th>Option 1</th>
<th>Option 2</th>
<th>Option 3</th>
<th>Option 4</th>
<th>Option 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status quo – voluntary cooperation</td>
<td>Long-term voluntary cooperation (beyond 2020)</td>
<td>Cooperation through the collection, sharing and use of common tools and data</td>
<td>Cooperation on production of joint REA (relative effectiveness assessments) reports</td>
<td>Cooperation on production of joint Full HTA reports (REA+ economic)</td>
</tr>
</tbody>
</table>

- **Non-legislative / voluntary**
- **Legislative / voluntary + mandatory**

+ Issues to be addressed

EUnetHTA Historical timeline

EUnetHTA Collaboration

2006 2016

EUnetHTA Project

Joint Action 1 Joint Action 2 Joint Action 3

Inception

Putting into practice Strengthening practical application Turning pilots into standard practice
EUnetHTA JA3 (2016-2020)

Aims to contribute to a sustainable model for the scientific and technical cooperation on Health Technology Assessment (HTA) in Europe

81 partners consisting of national, regional and non-for-profit agencies that produce or contribute to HTA

Project Coordinator:
Dutch National Health Care Institute (ZIN)
Summary of Activities in EUnetHTA JA3

- **WP4 Joint Production**
  - To produce **37** rapid REA on pharmaceutical and **43** on other technologies;
  - To provide a system for topic selection and prioritization, e.g. horizon scanning.

- **WP5 Evidence Generation**
  - To conduct Early Dialogues (joint HTA or parallel/joint with regulators);
  - To link additional data collection to several activities (adaptive pathways, MEA, etc.).

- **WP6 Quality Management**
  - To provide quality management for EUnetHTA joint products;
  - To further develop methodologies and tools for joint work if necessary.

- **WP7 National implementation and impact**
  - To facilitate the reuse and implementation of joint products at the national/local level;
  - To measure the impact of joint work in collaboration with other work packages.

- **WP1 Coordination**
- **WP2 Dissemination**
- **WP3 Evaluation**
HTA in the life cycle of technologies

- Presenting and discussing requirements studies in ED*
- Collecting evidence in development
- Preparing submission files for EMA and HTA
- Rapid REA
- Assessment for market authorization
- Comparative or full HTA / REA
- Additional data collection

*Early dialogue
Objectives WP4 General

- **Production** of Joint and Collaborative Assessments

- **Refine the production processes** of jointly produced assessments based on lessons learned and experiences from JA2 and current Joint Assessments

- **Facilitate the implementation** of Joint Assessments in national/local practice
Joint Assessments

• Centralised Project management by WP4 Co-Leads
• EUnetHTA processes and quality management
• Topic selection and prioritisation process (ongoing)
• Use of submission file
• Use of HTA Core Model and EUnetHTA guidelines
• Broad and standardised stakeholder involvement (mandatory scoping meetings with industry)

Collaborative Assessments

• Decentralised Project management by WP4 Co-Leads and Activity Centre Departments
• EUnetHTA processes and quality management
• Topic selection based on national work program (min. 3 partners interested in collaboration)
• Optional use of submission file
• Use of HTA Core Model and EUnetHTA guidelines
• Optional scoping meetings with industry
Tools & templates

Guidelines provide methodological guidance

- Consideration of other Core Model applications
- Provides working framework through a set of research questions*

Guidelines on Methodological Issues:
- Comparators and comparisons:
  - Criteria for choice of most appropriate comparator(s)
  - Methods of comparison: direct and indirect comparisons
- Outcomes:
  - Clinical endpoints
  - Surrogate endpoints
  - Composite endpoints
  - Health-related quality of life
  - Safety
- Level of evidence:
  - Internal validity
  - Applicability

Assessment template and Project Plan template provide guidance for reporting

* + checklist for ethical, organisational, social and legal issues
WP4 Joint Assessment pharmaceuticals

- **Novartis** - Midostaurin *for the indication of Acute Myeloid Leukaemia* Published: November 2017

- **Bayer** - *Regorafenib (Stivarga©)* indicated as monotherapy for the treatment of adult patients with hepatocellular carcinoma (HCC) who have been previously treated with *sorafenib* Published October 2017

- **Roche** - *Alecensa* as monotherapy is indicated for the first-line treatment of adult patients with ALK+ advanced NSCLC publication: January 2018
EU Regulatory Process

WP4 HTA Process

Stakeholder involvement

<table>
<thead>
<tr>
<th>Timeline (days)</th>
<th>EU Regulatory Process</th>
<th>WP4 HTA Process</th>
<th>Stakeholder involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>EMA Process</td>
<td>Expression of interest from pMAH</td>
<td>Identification of clinical experts and patients</td>
</tr>
<tr>
<td>-180</td>
<td>CHMP opinion</td>
<td>Preparation of draft submission file from pMAH</td>
<td>Review project plan by clinical experts</td>
</tr>
<tr>
<td>-90</td>
<td></td>
<td>Development draft project plan</td>
<td>involvement of patients</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td>Scoping meeting with pMAH</td>
<td>MAH provides evidence file</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Finalization of project plan</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td></td>
<td>Receive final submission file</td>
<td>Review by external experts and fact check by MAH</td>
</tr>
<tr>
<td>75</td>
<td></td>
<td>Co-production of 1st version of REA</td>
<td></td>
</tr>
<tr>
<td>85</td>
<td>Positive decision of EC</td>
<td>2nd version of REA Including editorial review</td>
<td>Local REA’s (e.g. national, regional)</td>
</tr>
<tr>
<td>100</td>
<td>EPAR</td>
<td>Consultation</td>
<td></td>
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</tbody>
</table>
6 Activity Centre Departments

- Face-to-face **training meeting** May 2017
- Training material
- **Support** by LBI HTA

- Project management of Collaborative Assessments
3 published Collaborative Assessments

OTCA01: *Wearable cardioverter-defibrillator* (WCD) therapy in primary and secondary prevention of sudden cardiac arrest in patients at risk – Nov 2016

OTCA02: *Antibacterial-coated sutures* versus non-antibacterial-coated sutures for the prevention of abdominal, superficial and deep, surgical site infection (SSI) – April 2017

OTCA05: *Repetitive transcranial magnetic stimulation* for treatment-resistant major depressive disorder – April 2017
4 ongoing Collaborative Assessments

OTCA03: Screening of fetal aneuploidies whereby non-invasive prenatal test (NIPT) – *due in January 2018*

OTCA04: Added value of using gene-expression signature for adjuvant chemotherapy decisions in early breast cancer (MammaPrint) – *due in January 2018*

OTCA06: Transcatheter aortic valve implantation (TAVI) in patients at intermediate surgical risk – *due end 2017*

OTCA07: Relative effectiveness assessment of Femtosecond laser-assisted cataract surgery (FLACS) compared to standard ultrasound phacoemulsification cataract surgery – *due in May 2018*

No published or ongoing Joint Assessments.
WP5A: Involvement of HTA bodies (HTAB) in Early Dialogues (ED) / Scientific Advice (SA)

• **SA by one single HTAB**
  - Started in 2009
  - NICE, G-BA, AIFA, HAS…
  - HTAB only or in parallel with national regulatory agency

• **SA by multiple HTABs:**
  - Started in 2012: EUnetHTA:
    13 Early Dialogues
  - Dedicated project:
    **SEED Shaping European Early Dialogues:**
    14 HTABs coordinated by HAS.
    11 EDs, 4 in parallel with EMA
  - Enhanced participation and coordination at the HTA level
One process for parallel regulator-HTA
Early Dialogues/Scientific advice:
EUnetHTA actors and process

Session 1: EUnetHTA JA3 progress

EUnetHTA Forum

presented by Hannah Bruehl
Scientific Officer, Federal Joint Committee
WP5A New Process in JA3 - 2 pathways for parallel consultations

Parallel consultation – individual (PCI)
- EMA + voluntary HTABs coordinated by EUnetHTA

Parallel consultation – consolidated (PCC)
- EMA + EUnetHTA EDWP + voluntary HTABs
- EMA / EUnetHTA Parallel Consultation Procedure (+/- EDWP participation according to prioritization)
Process - EUnetHTA EDC
The Early Dialogue Committee (EDC) is constituted for a specific product and the members will fluctuate to a degree for each Consultation.

Individual PC

Consolidated PC

The preferences of the Applicant (indicated in the Letter of Intent) will be taken into account, but participation of those HTABs cannot be guaranteed.

Composition of the EDWP as of Sept. 14th 2017: France (HAS), Germany (G-BA), United Kingdom (NICE), Italy (AIFA with alternate RER), Hungary (NIPN), and a shared seat for The Netherlands/ Belgium (ZIN/ RIZIV-INANMI)
Process - EUnetHTA EDWP selection criteria

• The product should aim to bring added benefit to patients i.e. by:
  • A **new mode of action** for the indication
  • **AND** targeting a **life-threatening or chronically debilitating disease**
  • **AND** responding to **unmet need** (no treatment or only unsatisfactory treatment available)

• ➔ EDs should represent a wide array of topics, therapeutic areas etc.
WP5B: EUnetHTA actions with regard to post-launch evidence generation

Objectives of WP5B

• improving post-launch evidence generation;
• special focus on the use of registries as data source:
  ➢ main activity: PLEG pilots (B1)
  ➢ supporting activity: Standards Tool for Registers in HTA (B2).

Example PLEG pilot: Qualification of registries for a rare disease, cooperation with EMA

• Invitation to participate by EMA’s new sort of Scientific Advice to qualify disease registries

Procedure = EMA Qualification of novel methodologies for drug development:


➢ Outcome: qualification opinion or qualification advice
WP6 – Organisation of work

**6A.1**  
QM Concept Paper  
(fundamental aspects and EUnetHTA specific means of QM for joint work)

**6A.3**  
Processes and Process Flows  
(e.g. for Rapid REA)  
SOPs (incl. Checklists and Templates)  
(e.g. data extraction)

**6A.4**  
Training Activities  
(on how to apply QM measures)

Activity Centre A  
**Quality Management**  
led by IQWiG 🇩🇪

Activity Centre B  
**Sci. Guidance and Tools**  
led by KCE 🇧🇪

**WP6**  
EUnetHTA Companion Guide  
(web-based)

**6A.2**  
QM System

**6B.3**  
HTA Core Model®

**6B.5 - 6B.9**  
Practical Tools  
(existing tools such as POP database and new tools)

**6B.4**  
Handbook

**6B.1**  
Inventory & Planning

**6B.2**  
Methodological Guidelines  
(e.g. on information retrieval)

**6B.4**  
Training Activities  
(on how to use tools and methodology)

**6A.1**  
QM Concept Paper  
(fundamental aspects and EUnetHTA specific means of QM for joint work)

**6A.3**  
Processes and Process Flows  
(e.g. for Rapid REA)  
SOPs (incl. Checklists and Templates)  
(e.g. data extraction)

**6A.4**  
Training Activities  
(on how to apply QM measures)

Activity Centre A  
**Quality Management**  
led by IQWiG 🇩🇪

Activity Centre B  
**Sci. Guidance and Tools**  
led by KCE 🇧🇪

**WP6**  
EUnetHTA Companion Guide  
(web-based)

**6A.2**  
QM System

**6B.3**  
HTA Core Model®

**6B.5 - 6B.9**  
Practical Tools  
(existing tools such as POP database and new tools)

**6B.4**  
Handbook

**6B.1**  
Inventory & Planning

**6B.2**  
Methodological Guidelines  
(e.g. on information retrieval)

**6B.4**  
Training Activities  
(on how to use tools and methodology)
Overview of WP7 activities

• Research and analysis. Analyses of agencies’ HTA processes to identify how within existing processes they could (1) engage in EUnetHTA activities, (2) use jointly produced HTA information and (3) reuse HTA information from other jurisdictions;

• Case studies. In-depth examples to support understanding agency HTA processes, examples of existing cooperation and use of EUnetHTA reports;

• Technical support for model development. Report with commentary on the options for HTA cooperation (options developed by WP1), and potential adjustments that could maximize the likelihood of national implementation;

• Implementation network. Support for agencies to use EUnetHTA products and feed back issues with the pilot model of HTA cooperation and use of EUnetHTA products, through informal feedback and formally though questionnaires, interviews and case studies.
Aim of the implementation network

• The aim of the implementation network is to support increased use of EUnetHTA products by:
  • Providing EUnetHTA with feedback from agencies about the experience of using of EUnetHTA products, so EUnetHTA can ensure their products meet user needs
  • Helping maximise awareness of EUnetHTA products and activities
  • Carrying out implementation activities so that agencies
    • see benefits of HTA cooperation,
    • see how they can use a EUnetHTA product in their work,
    • overcome implementation issues,
    • put in place changes needed to use collaborative HTA in the post 2020 scenario
Implementation leads

- WP7 cannot provide a personalised implementation experience if all activities are centralised
- Work is delegated to and shared between a group of “implementation leads”
Conclusions

• EUnetHTA JA3 has delivered many products since its start in June 2016;

• Joint EUnetHTA products can be used on a national and regional level. Implementation will be a key activity;

• How can RedETS help with the implementation of some of these products nationally and regionally?

• Also training activities on EUnetHTA products, tools and processes may be very crucial; RedETS may assist to initiate training activities on EUnetHTA products as part of their activities?