Update on Early Dialogues

François Meyer
The French National Authority for Health (HAS)
Background document for Plenary Assembly (May 28-29th, 2015)
Multi HTA early dialogues: Background

- Early dialogue/ Scientific advice at regulatory level since the 1990s
- High Level Pharmaceutical Forum recommendations in 2008: HTA bodies to engage in early dialogues
- ‘Single HTA’ scientific advice possible with some HTA bodies since late 2009
- 2012 : Introduction of Early Dialogues activities in the EUnetHTA JA2 for drugs AND medical devices

JA2 WorkPlan:
- 3 pilots of ED on drugs
- 1 pilot of ED on a medical device
Early engagement in health technology assessment (HTA)

- 3 options to get the HTA advice in Europe
  - National
    - HTA advice from national HTA body
      (HTA alone or with the Regulatory Agency)
  - 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 (no fees)
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.
Multi-HTA advice

Voluntary, not binding, confidential

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
Multi-HTA advice (Cont.)

Main topics

- Population
- Comparator
- Design of the trial (duration, dosing)
- Endpoints
- Statistic analysis (subgroups, stratification)
- Economic data (population, comparator, model, utility values, resource utilisation)
Multi HTA Early Dialogues (1) 2012 - 2013

- 3 pilot Early Dialogues planned (EUnetHTA contract)
- 10 done: 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
  - 10 drugs in various therapeutic fields
- 2 more pilots to be done following budget reallocation
  June 2015 (Orphan Drug) and September 2015 (medical device)
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

– Similar to EUnetHTA (same initial procedure). In addition:
  • inclusion of patient representatives
  • Collaboration with regulators with the conduct of parallel EMA/SEED early dialogues
Brief ED Overview: EUnetHTA & SEED

- 2 preparatory early dialogues
- ED procedure drafted for JA2

- Draft ED procedure in JA1 used for 8 ED pilots
- ED survey conducted after first 6 ED pilots
- Refined ED procedure produced following WP7 FtF meeting (Jan’14) based on discussion (taking into account survey results)

- Revised JA2 EUnetHTA ED procedure used as the basis for SEED
- ED procedure further amended (Nov’14) and progressively introduced with SEED’s 8th ED
- Conducted 9 EDs to date (6 drugs / 3 medical devices)
- 10th ED planned in March; additional 11th ED planned in June

- 1 ED ongoing (medical device in heart disease)
- 2 additional EDs budgeted; to be conducted in June and Sept 2015
SEED Update: changes to procedure and early dialogues conducted
Key Changes SEED ED Procedure

- **Start and end dates**
  - Earlier start date (D-90) \(\rightarrow\) 15 additional days for HTA knowledge of BB
  - Later end date (D+30) \(\rightarrow\) 10 additional days to finalize deliverable

- **D-75: Written List of points for clarification**
  - Done 15 days earlier and by email with HTAs (e-meeting no longer held at this step); final list sent to the company for development of the final BB

- **D-30: List of Key issues to company (E-meeting)**
  - **New step:** concerns only relevant points on product’s development plan; written key issues submitted in writing prior to E-meeting and serves as basis for HTA discussion. A list of Key Issues finalized for company to follow-up in writing prior to FTF or during FTF.

- **D+10 (business days): Final HTA Written answers**
  - Previously considered an internal document; now finalized replacing the validation step of the company meeting minutes; submitted to company
Revised JA2 EUnetHTA ED procedure used as the basis for SEED

<table>
<thead>
<tr>
<th>Date</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-90</td>
<td>BB pre-validation by HAS</td>
</tr>
<tr>
<td>D-75</td>
<td>Draft BB communicated to HTA bodies by HAS</td>
</tr>
<tr>
<td>D-60</td>
<td>Written list of points for clarification (E-meeting)</td>
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<tr>
<td>D-45</td>
<td>Final BB</td>
</tr>
<tr>
<td>D-10</td>
<td>HTA written answers to company’s questions</td>
</tr>
<tr>
<td>D-7</td>
<td>Compiled HTA positions sent to HTAs</td>
</tr>
<tr>
<td>D0</td>
<td>Face-to-Face meeting</td>
</tr>
<tr>
<td>D+10</td>
<td>Company provides draft meeting minutes</td>
</tr>
<tr>
<td>D+20</td>
<td>Review (HTAs) and validation (HAS) of minutes</td>
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</table>
Current SEED ED Procedure

Following several phases of refinement

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<td>D-30</td>
<td>List of <strong>Key issues</strong> to company (E-meeting)</td>
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<tr>
<td>D-15</td>
<td>Company’s answers to key issues</td>
</tr>
<tr>
<td>D-10</td>
<td>Written HTA answers to the coordinator</td>
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<tr>
<td>D0</td>
<td>Face-to-Face meeting</td>
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<tr>
<td>D+10</td>
<td>Final HTA Written answers</td>
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</tbody>
</table>

Refined ED procedure to be used for remaining EUnetHTA EDs
# Early Dialogue Candidates

**Early Dialogues:**
10 completed; 1 ongoing (ED11)
8 drugs, 3 medical devices
7 multi-HTA advice; 4 EMA-multi-HTA advice

<table>
<thead>
<tr>
<th>Company</th>
<th>Indication</th>
<th>Tech</th>
<th>Type of ED</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEED-ED1 Sanofi</td>
<td>relapsed/refractory multiple myeloma</td>
<td>Med</td>
<td>multiHTA only</td>
</tr>
<tr>
<td>SEED-ED2 Caviskills SAS</td>
<td>Solid tumors, at least 2 cm³ in volume, at maximal depth of 10 cm, visible under ultrasound imaging</td>
<td>MD</td>
<td>multiHTA only</td>
</tr>
<tr>
<td>SEED-ED3 TRANSGENE</td>
<td>advanced non-small cell lung cancer</td>
<td>Med</td>
<td>multiHTA only</td>
</tr>
<tr>
<td>SEED ED4 Genzyme</td>
<td>rare disease (orphan drug)</td>
<td>Med</td>
<td>EMA-multiHTA</td>
</tr>
<tr>
<td>SEED-ED5 GSK</td>
<td>Myasthenia Gravis</td>
<td>Med</td>
<td>EMA-multiHTA</td>
</tr>
</tbody>
</table>
## Early Dialogue Candidates

**Early Dialogues:**
- 10 completed; 1 ongoing (ED11)
- 8 drugs, 3 medical devices
- 7 multi-HTA advice; 4 EMA-multi-HTA advice

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<tbody>
<tr>
<td>SEED-ED6 Saint Jude Medical</td>
<td>MD for heart failure patients</td>
<td>MD</td>
<td>multiHTA only</td>
</tr>
<tr>
<td>SEED-ED7 Amgen</td>
<td>oncology (indication not to disclose)</td>
<td>Med</td>
<td>multiHTA only</td>
</tr>
<tr>
<td>SEED-ED8 Sanofi and Regeneron</td>
<td>moderate to severe asthma</td>
<td>Med</td>
<td>multiHTA only</td>
</tr>
<tr>
<td>SEED-ED9 Daxonhit</td>
<td>EHT Dx15 thyroid cancer diagnostic test</td>
<td>MD</td>
<td>multiHTA only</td>
</tr>
<tr>
<td>SEED-ED10 Mesoblast Limited</td>
<td>Treatment of Discogenic back pain (advanced therapy medicinal product)</td>
<td>Med</td>
<td>EMA-multiHTA</td>
</tr>
<tr>
<td>SEED-ED11 Roche</td>
<td>Haemophilia A</td>
<td>Med</td>
<td>EMA-multiHTA</td>
</tr>
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</table>
### Early Dialogue Candidates

<table>
<thead>
<tr>
<th>Potential Products</th>
<th>Requests</th>
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<tbody>
<tr>
<td>8 drugs ; 2 non-drug; 2 medical devices</td>
<td>8 for multi-HTA advice; 2 for EMA-multi-HTA advice</td>
</tr>
<tr>
<td>3 medical devices</td>
<td>5 not accepted and/or company withdrawals</td>
</tr>
</tbody>
</table>

- 3 requests for multi-HTA only; 1 for EMA-multi-HTA
- 3 medical devices; 2 drugs
- Future ED (EUnetHTA JA3)
SEED: Plenary Assembly Input
EUnetHTA consultation on SEED proposal

SEED PROJECT Specifications:
Deliverable 4: recommendations for permanent model for conducting early dialogues (ED)

• Based on the experiences gathered in the 10 ED, a permanent model for ED shall be developed.

• The draft model with clear and tangible recommendations should be presented to a EUnetHTA plenary assembly and to the HTA network.

• The SEED consortium should take comments and suggestions made at these meetings into account and provide subsequently a revised version of the permanent model.

• DG SANCO will organise the HTA network meeting and liaise with the EUnetHTA coordinator for the plenary assembly meeting.
HTA network recommendations on ED

HTA NETWORK REFLECTION PAPER ON “REUSE OF JOINT WORK IN NATIONAL HTA ACTIVITIES”

- Lifecycle approach:

- Recommendations:
  - Maintain and clarify different options to perform ED.
  - Strengthen interactions with regulators and define one single for ED involving HTA bodies and regulators at European level, building on existing experiences.
  - Consider a possible mechanism that could enable feeding the results of the ED into the future development of disease specific guidelines.
  - Explore possible funding and organisational models to make these activities self-sustainable, including the possibility of collecting fees.
Some challenges ahead

- From a EU sponsored model to a self-sustainable model.
- Choice of participating HTA bodies
- Relatives roles of national vs international
- Code of conduct
- Production of disease specific guidelines when necessary
- Adaptive pathways pilots: combines two approaches: Early Dialogues + Additional evidence generation
EFPIA

• Industry particularly welcomes the increased collaboration between the EMA and HTA authorities in the area of scientific advice to facilitate development plans and align evidence requirements both pre- and post-approval.

• Industry considers that a joint process of scientific advice would consist of a coordinated and consistent process involving regulatory and HTA/payer authorities.

• Shared discussions (in one room) involving the company representatives, regulatory and HTA/payer authorities would result in consistent advice documents with the aim of bridging existing gaps, where feasible. However, since the regulatory and HTA/payer authorities’ remits are different, the advice documents might take a different form.
EFPIA - General principles

• Confidentiality: To preserve the competitiveness of the R&D, confidentiality of advice requests and the related submission documents should be guaranteed by all parties.

• Good governance: Adequate governance structure, clear responsibility in HTA authority, funding and project management capabilities need to be available to ensure that the system can deliver consistent output with high quality within a strict timeline.

• Scientific excellence: Sound expertise for the assessment is mandatory to ensure scientific excellence and efficient decision-making.

• Concise process: The timeline for the advice process needs to be no longer than 60 days to fit into the drug development process as companies strive to shorten their development cycles.

• Joint, reliable outcome: the documented advice needs to represent the consistent advice of participating regulatory and HTA authorities to enable the development plan of companies. Any divergences need to be clearly outlined in the documented advice.
EFPIA (Continued)

Pre-notification

• Sponsors need clear guidance and more transparency around any specific requirements from national HTA bodies. The national contact points for questions and submissions must be clearly identified. A compilation of information around the national mandatory consultation processes and any conditions that must be fulfilled and national timelines should be available at a central location.

Pre-validation

• One harmonized guideline for briefing booklet building on Regulatory documents should be developed jointly between Regulators/HTA in consultation with Industry to avoid extensive re-work of existing documents. The booklet should be clear, concise and focus on the essential elements. This will significantly streamline the sponsor resource requirements during the pre-validation phase as well as the assessor’s time required for conducting an assessment.

Discussion meeting

• The list of issues to be discussed at the meeting should be set by the sponsor. Clarification on issues and other questions by agencies should be available to sponsors in advance of the meeting to ensure a good preparation of arguments and background. It is valuable for sponsors to know which party raised which issue.

• The discussion among Regulators, HTA bodies and sponsors should focus on issues of divergent views to ensure best use of available meeting time. Attendance of high-level experts during the discussion.
Eucomed view on Early Dialogue as proposed by EUnetHTA JA2 and the SEED programme

• Eucomed supports timely dialogue on innovative medical devices involving manufacturers and other relevant stakeholders such as MoH, payers, clinicians, and patient organizations, provided that this happens at the right time in the overall life cycle of medical technology, with clear objectives and transparent processes with a concept of partnership in mind.

• Eucomed sees that early dialogue for medical devices, as currently presented by EUnetHTA JA2 and the SEED program does not provide the value that should be expected (based on initial feedback of some participants). Proposed early dialogue aims to bring together HTA agencies from several Member States interested in defining and providing advice on the scientific data to be developed. As countries have very different data requirements, use HTA information in different ways and as the process of HTA is often not linked to decision making, the current implementation has very limited value in its current format.
Eucomed suggests that following facts are considered:

- HTA for medical devices is currently performed in very sporadic manner and in general there is a disconnect between HTA and reimbursement.

- Consequently HTA agencies have limited experience and knowledge of trial design and evidence generation for medical devices. They are very often experts in assessing published evidence and in pharmaceutical evidence-based medicine.

- Currently the possibilities for constructive dialogue with HTA agencies at country level are very diverse, unclear and/or non-existent. Industry is very often receiving contradictory information.

- The term “early” is misleading and it cannot be intended like for pharmaceutical product development; dialogue for medical devices may also happen after CE-Mark. If the dialogue is done pre-market, confidentiality needs to be ensured. This request derives from having weaker intellectual property rights (lack of data exclusivity and only partial patent protection).
Eucomed suggests the following way forward:

• We suggest rephrasing “early dialogue” into “timely & continuous dialogue” as for medical devices regular dialogue throughout the life-cycle of the technology is more appropriate and valuable.

• Timely scientific dialogue will be very valuable if different approaches to evidence generation are explored, and the strengths and weaknesses of each discussed to reach a sensible clinical strategy.

• The link into national decision-making needs to be strong and clear. Ultimately links into the reimbursement pathways at country level need to be visible. Payers and clinicians need to be closely involved in order to make it meaningful for industry. It should translate into reduction of uncertainty about future funding and increase of predictability concerning the acceptability of the evidence.

• It should be agreed that the output from the dialogue has to be achievable. The dialogue should also include discussions on alternatives (i.e. design, control, endpoints, methods, measurements).

• HTA agencies would benefit from real-world experience of the technology, allowing for more profound assessment which is not based on theoretical knowledge of the therapy only. The dialogue could be an opportunity to explore this. In this regard physicians and patients are possible sources of more complete information.

• Dialogue at country level and voluntarily at EU level (several member states) is more appropriate for medical devices due to different market access requirements across different countries and regions.
IVD Manufacturer’s Input
Early Dialogue (SEED)
EDMA would like to share key points to enhance the value of Multi- HTA Early Dialogue (SEED) for the IVD industry

- EDMA thinks that the chance to communicate with HTA agencies at an early stage of the evidence development process would be beneficial for IVD industry provided that:

  - The IVD technology in focus is likely to undergo an HTA pathway.
  - Adequate confidentiality procedures and documents are in place to protect commercially sensitive information provided by manufacturers.
  - The overall aim is to collaborate to construct a Fit-for-Purpose assessment for IVDs, so the HTA process is facilitated and faster decisions regarding adoption, funding & reimbursement of new products are reached by decision makers.
  - An open dialogue is established, allowing a collaborative interaction with all participants, including flexibility to answer different kind of questions (open questions, Fit-for-Purpose comparisons, appropriate and pragmatic study types, etc).
  - Decision makers participate in the process, either actively involved or indirect through proposition of relevant evidence they consider important for decision making on IVDs.
  - The result of EDs at EU level are actionable (acknowledged and accepted by various national/local HTA agencies to facilitate and enhance efficiency of evidence provision in the best interest to patient access)
Patients @ Early Dialogues (HTA/Regulatory)

François Houyez
Treatment Information & Access Director @ EURORDIS
HTAi conference, OSLO, June 2015
EURORDIS role in EMA and in HTA

**European Medicines Agency**

- EURORDIS volunteers members of scientific committees (decision making): COMP(2000) /CAT/PDCO
- Agreement between EMA and EURORDIS for the identification of experts (patients/professionals) for OMP procedures
  - Diseases guidelines
  - Orphan drug designation
  - protocol assistance/scientific advice
  - CHMP consultations
  - product information review...

**HTA**

- Member of EUnetHTA Stakeholders’ Forum (since 2010)
- Experts in EUnetHTA Scientific Advisory Groups
- Represent stakeholders at the HTA Network (EC+MS)
- Volunteers and staff at EUnetHTA trainings
- Agreement with SEED consortium and EMA where EURORDIS helps to identify patients for early dialogue meetings
  - Explain the procedure, their role
  - Prepare for the meeting (briefing doc.)
What needs to be explained to patients in two words

• The objective of an early dialogue is to reduce the risk of inadequate data when products are presented for evaluation in aim of reimbursement by national health insurance.

From SEED consortium project description
When we contact patients for the first time

- Their first questions:
  - Who’s EURORDIS? Why are you contacting me and not HTA experts at the first place?
  - What’s HTA?
  - What’s SEED?
  - What’s EMA?
• briefing book sent by developer to the SEED coordinator (HAS) for pre-validation

• Updated briefing book sent to SEED coordinator (+/- EMA). Briefing Book sent to HTA bodies

• Consolidated list of points for clarification: **Teleconference** developer/coordinator (+/- EMA)

• Responses from developer to SEED (+/- EMA)

• EMA list of issues to developer

• HTA bodies sent draft answers to SEED coordinator. Answers are shared

• **E-meeting** between HTA bodies. Key issues discussed. List of key issues sent to developer.

**Patients come in**

• Early Dialogue **Meeting**. Closed discussion (morning), with developer (afternoon)

• Written answers sent to developer. Developer sends minutes
SEED /EUnetHTA Early Dialogues with patients

- 11 patients / 18 slots (61%)
- 10 patients invited, 28 contacted (36%), 48 organisations, 126 emails (+ phone)
How does it work? Ideally:

<table>
<thead>
<tr>
<th>Day</th>
<th>Action</th>
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<tbody>
<tr>
<td>Day -60</td>
<td>Coordinator announces the meeting to EURORDIS</td>
</tr>
<tr>
<td>Day -59</td>
<td>EURORDIS contacts relevant groups, social media, Summer School or Patients Academy (EUPATI) alumni...</td>
</tr>
<tr>
<td>Day -45</td>
<td>At least 4 patients identified. EURORDIS checks their role, affiliation, disease stage. Telephone brief 30 min EURORDIS sends their contact details to coordinator (+/- EMA)</td>
</tr>
<tr>
<td>Day -40</td>
<td>Declaration of interests &amp; confidentiality (DoICU)</td>
</tr>
<tr>
<td>Day -32</td>
<td>Coordinator’s response on DoICU. 2 patients invited</td>
</tr>
<tr>
<td>Day -20</td>
<td>Travel and accommodation arrangements made</td>
</tr>
<tr>
<td>Day -15</td>
<td>When available, company presentation and list of questions to HTA and regulators are shared with the patients</td>
</tr>
<tr>
<td>Day -7</td>
<td>Conference call to discuss the dossier (2 hours)</td>
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<tr>
<td>Day 0</td>
<td>Face to face meeting</td>
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<tr>
<td>Day 3</td>
<td>Patients fill-in the evaluation</td>
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</table>
Patients comment on **PICO**

### Clinical trial (usually phase III)
- What would you suggest to improve the trial?

### Patients’ population for the target indication
- All stages? Advanced stages? If advanced stages not included, risk of off-label?

### Possible impact of the technology in their life (constrains, efficacy...)
- e.g. implantable devices. Important to select relevant outcome measure

### Diversity of healthcare in Europe
- Usually confirming HTA experts’ information. Impact on the comparator choice

### Regulatory aspects
- Unavoidable, even if not expected

And much more...
Issue (1): timing and proceedings

• For HTA experts:
  – At present (pilot phase) 1 Early Dialogue per month
    • A lot of preparatory work with colleagues
    • 1 conf. call, 1 e-meeting, 1 face to face meeting all day
  – But when 10 early dialogues per month?
    • Full day meeting too long?
    • More conference call and e-meetings
    • Via conference calls or e-meetings, patients likely to feel lost in HTA
Issue (1): timing and proceedings

- HTA experts have 90 days to become familiar with the dossier, and are experienced.

- Patients, even when trained (EUPATI, EUenetHTA training) have no or little knowledge on HTA.
  - And receive the briefing book only 7-10 days ahead of the meeting.

- One day meeting is just enough to start understanding what it is about and to contribute.

- More time would be better.
  - Pre-meeting with the developer or some HTA experts.
  - Or possibility to send comments, remarks, questions that come to their mind the day after.
Issue (3): training and preparation

• EUPATI and other initiatives to train patients on HTA
  – Hundreds of patients trained already

• Yet, in most cases patients invited to SEED/EMA Early Dialogues will not have been trained
  – Training must be ad hoc, few days before the meeting
  – Need for training materials, e-learning, webinars, videos

• Patients may find it intimidating or difficult to express themselves
  – Meeting very “intense”. “Take the floor as soon as you can”
  – Chair could ask for their input more pro-actively
  – Some express a high degree of frustration
    • “not having the opportunity to express my thoughts”
    • or being told “this is not what we expect from you”
Other Issues

- **Invitation to the right patient**
  - The exact stage of the disease not always known when patients are first contacted – varies during the 90 days
  - Difficult to say “sorry but no” to those who said yes already

- **Specific questions for the patients**
  - Prepared by developer and/or coordinator + HTA experts
  - And patients have the possibility to address all issues they think relevant, not just on what “expected to comment on”

- **Patients should receive written answers and/or minutes**

- **A pre-meeting questionnaire on special needs would be useful**

- **Travel and accommodation expenses need to be prepaid**
  - Can represent a third or a half of a person’s monthly income
  - Else authorise reimbursement to the patient’s organisation
Conclusions

Patients highly appreciate having the possibility to participate.

“A learning by doing” phase. A great thank you to SEED/EMA ED coordinators

Difficulties realising the impact of their contribution
### EUnetHTA PA: topics to address in the drafting of the permanent ED model

<table>
<thead>
<tr>
<th>Operational aspects</th>
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<tbody>
<tr>
<td>✅ <strong>Appropriate timing of ED during the development process and possibility of follow-up</strong></td>
</tr>
<tr>
<td>✅ <strong>Selection process for health products</strong></td>
</tr>
<tr>
<td>• Establishment of criteria and selection process for investigational technologies (clear / transparent)</td>
</tr>
<tr>
<td>• Focusing on particular topics (e.g. orphan indications) on a scheduled basis (e.g. yearly)</td>
</tr>
<tr>
<td>✅ <strong>Impact on the organization of HTA bodies / Qualitative and quantitative estimate of manpower</strong></td>
</tr>
<tr>
<td>• Managing ED workload</td>
</tr>
<tr>
<td>✅ <strong>Quality Assurance Process</strong></td>
</tr>
<tr>
<td>• Evaluation of the ED programme in terms of process and outcomes</td>
</tr>
<tr>
<td>✅ <strong>Organizational aspects</strong></td>
</tr>
<tr>
<td>• Establishment of a permanent working group of HTA bodies participating in EDs (along with operational rules and procedures)</td>
</tr>
<tr>
<td>• Establishment of a minimum number of HTA bodies to participate per ED</td>
</tr>
<tr>
<td>• Establishment of dedicated administrative and project management support for EDs</td>
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<tr>
<td>• Means of introducing new, inexperienced HTA bodies to the ED process</td>
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</table>
Scientific and Technical aspects
- Technical credibility and quality of advice from HTA partners
- Minimum information/evidence requirements for qualification for EDs
- Reporting divergent HTA positions
- Relation of multi-Early Dialogue and EMA/HTA Scientific Advice
- Collaborating on evidence reviews during preparation for ED and ensuring production of an appropriate scientific advice document
- CE marked or non CE marked medical devices

Financial aspects
- **Possible sources of funding**
  - Establishment of a fee-for-service joint HTA advice (processes/management/funding/leadership) including expenses related to travel and translations
  - Establishment of fees in the case of EMA and multi-HTA advice
  - Funding from industry
  - Resourcing of HTA agencies to take part in EU-HTA advice, including subcontractors/external professionals with HTA-expertise

Legal aspects
- Ensure an appropriate legal status for EDs at the European level (single HTA vs. multi-HTA)
- Establishment of a template contract
...continued

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<thead>
<tr>
<th>Strategic aspects</th>
<th>Benefits and risks of ED activities for HTA bodies</th>
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<tbody>
<tr>
<td></td>
<td>• Sharing of ED outputs (when/how) to enhance return of ED for HTA at large</td>
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<tr>
<td></td>
<td>• Relations with regulators</td>
</tr>
<tr>
<td></td>
<td>• EMA-HTA parallel advice service vs. EU-HTA advice – collaboration or separate offers</td>
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<tr>
<td></td>
<td>• Value of the ED if regulators (EMA or national agencies) are present</td>
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<td><strong>Medical devices</strong></td>
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<td>• EDs in medical devices: continuation of pilots</td>
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<td>• Relations with regulators of medical device</td>
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<thead>
<tr>
<th>Managing conflicts of interest</th>
<th>Declaration of interest and confidentiality agreement: EUnetHTA documentation usage and/or adaptation to the ED process</th>
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<tr>
<td></td>
<td>• Sharing final HTA written answers with non-participating HTA bodies</td>
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<td>• Keeping policy making independent from science making</td>
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