HTA Expert meeting

Current experience and developments in HTA of medical technology[1] in Europe

8 May 2014, 10:00- 17:00, Rue Joseph II, 40 – 1000 Brussels

SUMMARY OF DISCUSSIONS

Agenda

9:30 – 10:00	**Registration and Coffee**
10:00 – 10:15	**Welcome and Introduction:** Prof Finn Børlum Kristensen for EUnetHTA and industry
10:15 – 12:30	**Co-Moderators:** Prof Finn Børlum Kristensen for EUnetHTA and Eucomed for industry
10:15 – 11:30	**HTA for medical technologies: For different medical technologies, where does HTA fit in the care pathway in Europe?**
11:30 – 12:30	**WP7 SG3 Methodological Guideline on Medical Devices. The current guideline development process in EUnetHTA and guideline structure**
12:30 – 13:15	**LUNCH**
13:15 – 15:00	**Co-Moderators:** Prof Finn Børlum Kristensen for EUnetHTA and EDMA for industry
13:15-15:00	**EUnetHTA WP4 and WP5 Strand B: Discussion on challenges and current processes**
	WP4 and WP5 Strand B experience
15:00 – 15:15	**Coffee break**
15:00 – 16:45	**Co-Moderators:** Prof Finn Børlum Kristensen for EUnetHTA and COCIR for industry
15:15 – 16:15	**WP7 SG1 Early Dialogues: Initial exchange of views and identification of the issues**
16:15 – 16:45	**WP7 SG4:** Template development for medical devices
16:45 – 17:00	**Wrap up, Conclusions and Next Steps**

1. Welcome and Introduction

[1] Medical Technology = Medical Devices, In-vitro Diagnostics, Medical Imaging and Health ICT

Yves Verboven (Eucomed, EDMA) welcomed the participants, highlighting the purpose of the meeting as part of a continuous dialogue between the HTA agencies and the medical technology[2] industry.
Finn Borlum Kristensen (EUnetHTA) emphasized the importance of interaction with the Stakeholder Forum members and the role of the meeting as an important step in further exploring how to best proceed with HTAs performed on medical technologies. FBK briefly presented EUnetHTA (Appendix 1, FBK slides).
Sophie Cros (Abbott Vascular) stressed the dialogue aspect of the meeting and expressed an appreciation for the opportunity to engage face-to-face and explain the considerations to be taken when assessing medical device technology.

2. First session

4 presentations given by industry representatives

- Pharma vs. Medical Technology Models - Adrian Griffin (Johnson & Johnson) (Appendix 2, AG slides]
- Examples of the role of HTA in the healthcare pathway for MEDICAL DEVICES - Pascale Brasseur (Medtronic)(Appendix 3, PB presentation)
- Role of HTA in HealthCare Pathways for IVD - Seong Chen (Roche Diagnostics) (Appendix 4, SC presentation)
- Examples of the role of HTA in the healthcare pathway for medical technology Medical Imaging & Health ICT - Werner Van den Eynde (GEHC) (Appendix 5, WvdE presentation)

Key comments and discussion points:

- The HTA of medical technologies, and the EUnetHTA activities around medical technologies may include different aspects than the HTA of pharmaceuticals"[3].
- Diversity of medical technology and high prevalence of Small and Medium Enterprises (SMEs).
- Significant differences in reimbursement pathways for different types of medical technologies are specific to each country. Furthermore, the variation between countries in the way any particular MedTech gets to market is more diverse than for any given drug. For specific technologies HTA is performed at multiple points in time requested by multiple agencies for different purposes. HTA is not part of market access in many countries and may have a different role requiring an approach that is fit for purpose. This is an important consideration when developing processes and methodology of HTA for medical technologies and for possible cooperation between HTA agencies. Any collaborative approach needs to ensure it is considering the final local use, to be 'fit-for-purpose'.
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- Heterogeneity of pathways for reimbursement & funding of medical technologies as well as systems that are rarely designed to incentivize value or incentivize manufacturers to develop the evidence were indicated as important context to consider in optimizing the value of European HTA cooperations.
- When it comes to the broad family of medical technologies, Intellectual property rules are fundamentally different from those applied to pharmaceuticals which adds to the complexity of the context
- The link between funding & reimbursement and national/regional HTA is missing in a majority of Member States for medical technologies. In many instances it is not the stand-alone product that is reimbursed.Reimbursement is granted to a procedure and includes the relevant devices as accessories or implants.This creates decision points and financial streams and the need for an HTA that are very different than those in the pharmaceutical pathways.
- Innovation in medical technology often comes more directly from clinicians' insights and needs; they also inform further iterative improvement of medical technologies. Improvements are based on the use of medical technologies in practice, and this contributes to challenges associated with developing systematic evidence, including taking into consideration the learning curve for medical technologies, in order to assess technology and establish their true incremental value.
- Early dialogues are potentially useful in informing the process of evidence generation and can reinforce attempts to align study design and strengthen evidence expectations during the phases of investigation and evaluation in

[2] Henceforth the term "medical technology" is understood as medical devices, in-vitro diagnostics, medical imaging and health ICT.
[3] The purpose of HTA is to inform decision-making, and meet the needs of the decision-makers. Assessment methods and practices need to fit the technologies to be assessed, specific to the decision to inform.

line with needs of decision makers. Early dialogues need to be fit for purpose and could be useful for additional evidence generation. They may also be useful for advising on additional evidence generation after the technology is introduced in healthcare. It will be helpful to clarify the position of the medical technology industry in relation to early dialogues, specifically how European cooperation and coordination can be helpful.

- For HTAs to be considered as “fit-for-purpose” they need to be clearly connected to and inform a decision.
- Development of medical technologies is a more dynamic process than of pharmaceuticals, which in addition to the different market access pathways available, impacts on the way HTA of medical technologies should be performed (i.e. same standards of HTA applied through methodology that reflects these differences, timing of HTA, frequency, etc.).
- HTA is not a tool that solely exists for the purpose of informing market access or as a “route” to get reimbursement, rather it is a means to assess evidence of clinical effectiveness, clinical utility and as well as additional domains (cost and economic considerations, organizational, social, ethical,….) to assess the value and appropriate use of technology. Focus on the scientific nature of HTA would be helpful as well as understanding what kind of evidence needs to be collected and how (including why and when). It is key to find effective ways for HTA agencies and the medical technology industry to establish a dialogue and partnership to improve the HTA process.
- Communication with and involvement of healthcare professionals and patients receiving or using the medical technology is important for an informed HTA process.
- The arguments provided by the medical technology industry calling for differentiation between the HTA of medical technologies and of pharmaceuticals when applying general HTA methodological standards have been understood. This includes not only the specific methodological and practical challenges with generating evidence but also factors such as continuous improvement in technology and outcome through increased use/experience in real world practice. Additionally, there is an understanding that HTA of medical technologies is used to inform decision makers at different points in time of coverage / adoption into practice (not at time of market entry) and that the specific purpose that HTA serves depends on the needs of decision-makers in the member states, which nevertheless often overlap. In that context, special attention should be paid to the type of evidence that makes sense for instance in the case of in vitro diagnostics (IVD), and to the care pathways in which those products are used. The cooperation between the HTA agencies needs to reflect this in their joint activities and services offered. EUnetHTA acknowledges these as important factors for their activities and already works along these lines to support national work.

3. Second session

WP7 SG3: Methodological Guidelines on Medical Devices. The current guideline development process in EUnetHTA and guidelines structure – Jörg Lauterberg (IQWIG) (Appendix 6)

Key comments and discussion points:

- Proposed approach of a face to face dialogue, collecting expertise at time of scoping of any medical technology-related guidelines is considered valuable i.e. improving a dialogue and understanding between the HTA community and medical technology industry
- Concretely, review the possibility to update time plan; consider having a face-to-face workshop at some stage of the guideline development, possibly instead of a written SAG consultation at the end of the project, Step 6 in the process (April-May 2015). EUnetHTA Secretariat to explore this possibility.
- Consulting physicians/professional societies/ industry statistical-clinical experts and potentially patients would be helpful in bringing useful insights to the methodological issues of assessing medical technologies.
- SAG could be involved in Step 2 of the guideline elaboration process (see slide # 20).
- Indication of usefulness of early dialogues as a means of identifying appropriate evidence collection to be mentioned in the guidelines.

- Emphasis on the importance of ensuring that experts in the assessment of specific types of medical technology are involved in the work.
- There are outstanding issues as to how to get innovation to the patient, but this is more of a task for the HTA Network as the strategic and policy arm of the European cooperation on HTA.
- The discussions regarding the types of assessment and evidence generation are a tasks of WP7 SG1 and 2 (evidence generation).
- It would be helpful to have EUnetHTA guidelines on areas specific to medical devices (learning curve, iterative improvement of technology, type of evidence to be considered in addition to RCTs).
- Guidelines should be more than a compilation of available guidelines, they should be synthetic and address differences between existing guidelines.
- It is important to tailor the content (or at least sufficiently explain the concepts and terminology) to the potential audiences of the guideline text to ensure outreach and understanding by a broader group, while still respecting the choice of the primary target group (i.e. the health technology assessors).
- It was agreed that the project team will consider circulating the concept draft to the WP7 SAG for comments (Step 2 of the process) in July[4]. A final decision on this should be communicated to the SAG as soon as possible in order for them to be able to provide input on time.

4. Third session

EUnetHTA WP4 (Core HTAs) and WP5 Strand B (rapid REA of non-pharmaceutical technologies): Discussion on challenges and current processes - Marina Cerbo (AGE NA.S) (Appendix 7) and Anna Nachtnebel (LBI-HTA)(Appendix 8) WP4 and WP5 Strand B experience - Sebastian Gaiser (St. Jude Medical) (Appendix 9)

Key comments and discussion points:

- Identifying relevant stakeholders for each of the pilots is crucial, making the issue of sufficient timing ever more important.
- Mutually ensuring appropriate handling of confidentiality is of utmost importance; EUnetHTA recently (April 2014) further strengthened procedural aspects of appropriate confidentiality management in JA2.
- One of the main objectives of the pilots is to improve the process of joint assessment – expressed appreciation of the lessons learned that are now informing current adjustments of the process for upcoming pilots. Critical to have a clear process of further use and to avoid duplication of work to be done to satisfy both joint HTA activities and local HTA requests *(The benefit of joint assessment versus individual for different stakeholders should be assessed in terms of quality, timely assessment, …).*
- The medical technology industry associations, registration D-bases, and professional associations and individual companies, can be sources of information on CE-marked products as is the clinical trials registration system (eg clinicaltrials.gov) to obtain information on available products and data/ongoing studies for a certain therapy/procedure/device being assessed
- Rapid assessment of technologies early after products become available and while effectiveness data collection is still ongoing might be of limited value and it could be a challenge to cover all products as some of the latest innovations and break-through technologies come from small companies. Incentives for those companies developing evidence are currently not in place during a Class assessment which compiles all evidence. This is a topic for further consideration.It was explained by WP5 Strand B that topics for pilot assessments are selected by searching the EUnetHTA POP database for topics of interest to several countries, and/or by exploring which countries share an interest in an assessment of a particular topic. The aim is that the countries, from which the authors and co-authors of the joint assessment, and possibly the reviewers come, are committed to using the pilot assessments in the production of a respective national report. This means that the final audiences of the joint

[4] The designated first author is commencing the work in mid of June. Please note that the concept paper has to be revised by the draft group and the responsible EUnetHTA WP 7 subgroup first, before it can be send to the SAG.

assessments are the decision making agencies of the countries from which the authors and co authors (and possibly the reviewers) come.

- Physicians and hospitals need to be involved in the pilot assessments. These may have a lot of implications for hospital management and budgets. Physician experience is a key source of information.
- Early dialogues on planned assessments were identified as a useful form to inform HTA expectations and improve appropriate preparedness of the medical technology companies to produce needed evidence and define appropriate time point for assessment allowing ensuring latest trial data.
- HTA education targeting medical technology industry and physicians is needed – education must be tailored appropriately; standardisation of HTA education in Europe is needed
- Pragmatic engagement between HTA doers and those working on registries or any post-market entry evidence collection could be helpful.
- Piloting of European HTA joint work and its implementation has been a “bottom-up” process, whereby HTA agencies in Europe looked into the ways of working together in the health technology assessors’ community. As these efforts became known by e.g. those responsible for market access within companies more attention and feedback from this environment has arisen. This has forced all of the affected parties to start adapting to the needs of HTA production in a period of field testing joint HTA work and tools.
- EUnetHTA works in a formal context of an EU joint action mechanism, which as a tool does not offer a lot of flexibility and does not allow much responsiveness to the changes that e.g. the external environment requires of EUnetHTA. This is a real challenge that needs to be understood also by all stakeholder groups.
- The HTA Network is responsible for identifying the priorities and needs for assessment of health technologies in general by looking at individual European healthcare systems. EUnetHTA JA2 will be developing recommendations for sustainable mechanisms of European cooperation on HTA and will look to an appropriate degree into the issues of priorities relevant to the remit and scope of work performed by the scientific and technical level of the European cooperation on HTA.
- Industry is willing to provide information and responses to requests on an ad hoc basis, but this may still leave a gap as not all companies (in particular SMEs) belong to European trade associations. Also restrictions within companies might apply at times of releasing trial results. A direct contact with the company can inform when release of data might be expected.

5. Fourth session

WP7 SG1 Early Dialogues: Initial exchange of views and identification of the issues - Francois Meyer (HAS) (Appendix 10)

Key comments and discussion points:

- The point at which early dialogue would be requested by a medical technology company is rather open and depends on the company; however, from WP leader perspective it should be conducted before any trials or evidence collection to inform HTA on a given technology.
- Presence of CE-mark should not serve as restricting criteria for choosing a technology for early dialogue.
- In case of fewer places available for early dialogues within the framework of EUnetHTA or SEED, the choice will be made based on, for example, diversity and availability of expertise to provide sound advice on the technology in question.
- Specific advice on a certain technology is completely confidential and data is anonymised, i.e. it’s not possible to back tract to individual patient identities.
- Concern was expressed by medical technology industry about the possibility of a negative indirect influence by a recommendation of early dialogue pilots in situations where the advice do not actually have any role in the market access decision making in a specific country (i.e. what is the incentive for involvement?)
- Early dialogues in the SEED framework is an opportunity to test and improve the model to check whether it makes sense, and to see how to continue with the early dialogue activity at the European level in the long run.

- The Medical Devices industry does not currently see a value of a joint early dialogue in its current format compared to work with individual countries where there is a specific need at time of market entry. A diagnostic company started with engagement but retracted due to complexity and the perceived value of the process
- Adjustment of the (early) dialogue concept with medical technology companies to define evidence needs will be explored. The incentives for those that develop the evidence should be considered as should the background for choosing a technology.

6. Fifth session

WP7 SG4: Template development for medical devices: Zoe Garrett (NICE) (Appendix 11)

Key comments and discussion points:

- The draft submission template was developed based on the evidence requirements provided by all national agencies that have standardised evidence requirements and it also arranges the evidence requirements in line with the HTA Core Model® structure.
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- The draft submission template is to be piloted in WP5 Strand B. Feedback from manufacturers participating in pilots based on the template will be collected via a questionnaire, while a wider consultation on the template will be done after piloting has been completed (beginning 2015).
- The purpose of the template is to reflect the evidence requirements of national agencies involved in the reimbursement of medical devices. Through piloting in WP5 Strand B there will also be an understanding of which aspects of the template in terms of data requirements and questions are also appropriate and relevant at a European level where there is collaboration between national agencies.
- Participation in the European cooperation on HTA is voluntary and HTA organisations from several countries have been actively involved in the template development. One of these agencies will also be piloting the template for their national processes.
- The structure of the draft submission template is flexible and modular in terms of which parts of the template can be used by agencies from different countries.
- Industry noted the objectives of a common template, and the principle that a common approach would be developed to provide efficiencies to all parties. Industry made a comment that it would be more difficult to develop a suitable common template and delivered efficiencies for MedTech industry due to the variety of access routes (as highlighted in the morning session), the device-specific reimbursement pathways, and the lack of clarity on who the 'end user' would be. For example, with pharmaceuticals, one key use of the common template is for use in the pilot rapid relative effectiveness reviews, whereas this is not an objective with the non-drug pilots (WP5B), as industry does not make a formal submission in those pilots, beyond responding to the scoping document. Therefore, if a template is not for use at an 'EU' level, the objective of the template must therefore be at a 'national' level. However, given the diversity in objectives of national reviews in the MedTech space, (timing, perspective, decision being informed), a common template will likelyneed to be a summation of all national requirements which would only serve to increase information 'ask' from each member state, without due consideration for its local need.[5]

[5] *EUnetHTA clarification on the purpose and nature of the submission template for medical devices:* Access routes for medical technologies into clinical practice may vary between technologies and countries, but this would not affect the scientific assessment of the relative effectiveness of a medical technology. The scientific assessment process and decision-making based on HTA results are two interconnected but distinct from each other processes.
The 'end users' of the submission template are the national/regional HTA bodies that receive evidence from manufacturers as part of the re-imbursement process. In many countries this is the case. If a submission template covers all individual national evidence requirements, it can be used at national levels, and forms an ideal basis for joint assessments.
The use of the draft submission templates in the Joint Action 2 pilots is part of the development and validation of the submission templates, not its ultimate purpose, and some of the WP5 stream B pilots involve manufacturer submissions.

7. Conclusions - Consideration

- Successful meeting, face-to-face set-up appreciated as a platform for effective communication and continuing dialogue, other stakeholder groups (eg, patients, providers) probably need to be given more opportunity to be heard which can further enrich the discussion.
- The framework in which EUnetHTA has to operate is better understood.
- Important to engage early, preferably through face-to-face meetings, with end-users of medical technologies and with industry, other stakeholders and experts to develop methodological guidelines and perform appropriate HTAs.
- Better understanding of a relationship between EUnetHTA and HTA Network, with the latter taking care, in the future, of strategic priorities on a European level for HTA and EUnetHTA having the responsibility to be the scientific and technical arm of European collaboration in HTA.
- Helpful to discuss concrete examples of what is being done by EUnetHTA in their joint work to understand challenges faced by assessors and needs of industry to have activities that are fit-for-purpose informing decision points on market access.
- Appreciation of the willingness to engage in open and constructive dialogue on both sides.
- Diversity of the medical device industry and medical technologies plays a role in conducting an HTA since HTA plays a different role in market access in various countries. There are opportunities to learn from and through rapid HTA pilots the challenges and opportunities to define the appropriate time points to perform assessment and identify complementary evidence development. Opportunities of engaging in early dialogues need to be explored. Eg. to restrict to agencies that require data at time of market entry or to reconsider the best time in market access to discuss data collection possibly leading to a process of a more dynamic model of HTA for medical devices and evidence development.
- Relevance of HTA for decision-makers is important for both sides.
- Need for continuing internal discussions in companies on value of HTA and internal discussion amongst HTA assessors how to ensure a joint initiatives bring added value and can provide value to companies that engage. A frequent dialogue will be a good basis to further enter into an effective partnership.

8. Concrete actions :

a. WP7 SG3: Methodological Guidelines on Medical Devices. The current guideline development process in EUnetHTA and guidelines structure
    - EUnetHTA to explore an opportunity to have a face-to-face interaction between the medical technology and EUnetHTA experts at one point in the development of the methodological guideline on medical devices
    - Discuss with industry how they could facilitate this face-to-face interaction

b. Medical technology associations to provide assistance, whenever possible, to joint assessment teams in EUnetHTA with identifying medical technology companies whose products correspond to a technology selected for pilot assessment in EUnetHTA

c. Explore possibility for general cooperation at early stage of the process with WP leaders

d. WP7 SG1: Early Dialogue
    - Explore possibility to set up dialogue between WP7 SG1 and Medical technology industry to discuss framework and process of “Early Dialogue” for medical technologies.

e. Explore possibility to set-up face-to-face Expert meetings with industry on yearly basis

List of participants

EUnetHTA secretariat and WP leaders or co-leaders

1. Finn Børlum Kristensen, EUnetHTA Secretariat / DHMA, Denmark
2. Julia Chamova, EUnetHTA Secretariat /DHMA, Denmark
3. Marina Cerbo, WP4: Agenas, Italy
4. Antonio Migliore, WP4: Agenas, Italy
5. Luciana Ballini WP4: ASSR, Italy
6. Sarah Kleijnen, WP5: ZiN (CVZ), Netherlands
7. Claudia Wild, WP5: LBI-HTA, Austria
8. Anna Nachtnebel, WP5: LBI-HTA, Austria
9. Julia Mayer, WP5: LBI-HTA, Austria
10. Francois Meyer, WP7 SG1: HAS, France
11. Jörg Lauterberg, WP7 SG3: IQWIG, Germany
12. Elisabeth George, WP7 SG4: NICE, UK
13. Zoe Garrett, WP7 SG4: NICE, UK

European Commission

14. Flora Giorgio, European Commission

COCIR, EDMA, and Eucomed

15. Nicole Denjoy, COCIR
16. Yves Verboven, Eucomed & EDMA
17. Pascale Brasseur, Medtronic
18. Soeng Chen, Roche Diagnostics
19. Sophie Cros, Abbott Vascular
20. Sebastian Gaiser, St Jude Medical
21. Adrian Griffin, Johnson & Johnson
22. Bernd Hofmann, Siemens
23. Anne Postulka, Cepheid
24. Torsten Strunz Mckendry, Roche Diagnostics
25. Werner Van den Eynde, GEHC
26. Geoffrey Wilson, GEHC
27. Lisa da Deppo, Boston Scientific

OBSERVERS

Stakeholder Forum Groups

1. Nicola Bedlington, EPF
2. Edith Frenoy, EFPIA
3. Magda Kalata, EDMA
4. Marie-Astrid Libert, COCIR
5. Miranda Moussa, AESGP
6. Irina Odnoletkova, AIM
7. Zuzana Pisano, Eucomed

Appendix 1:

Welcome and Introduction: Presentation by Professor Finn Børlum Kristensen, EUnetHTA Secretariat Director

HTA Expert meeting

Current experience and developments in HTA of medical technology in Europe

8 May 2014

Agenda I

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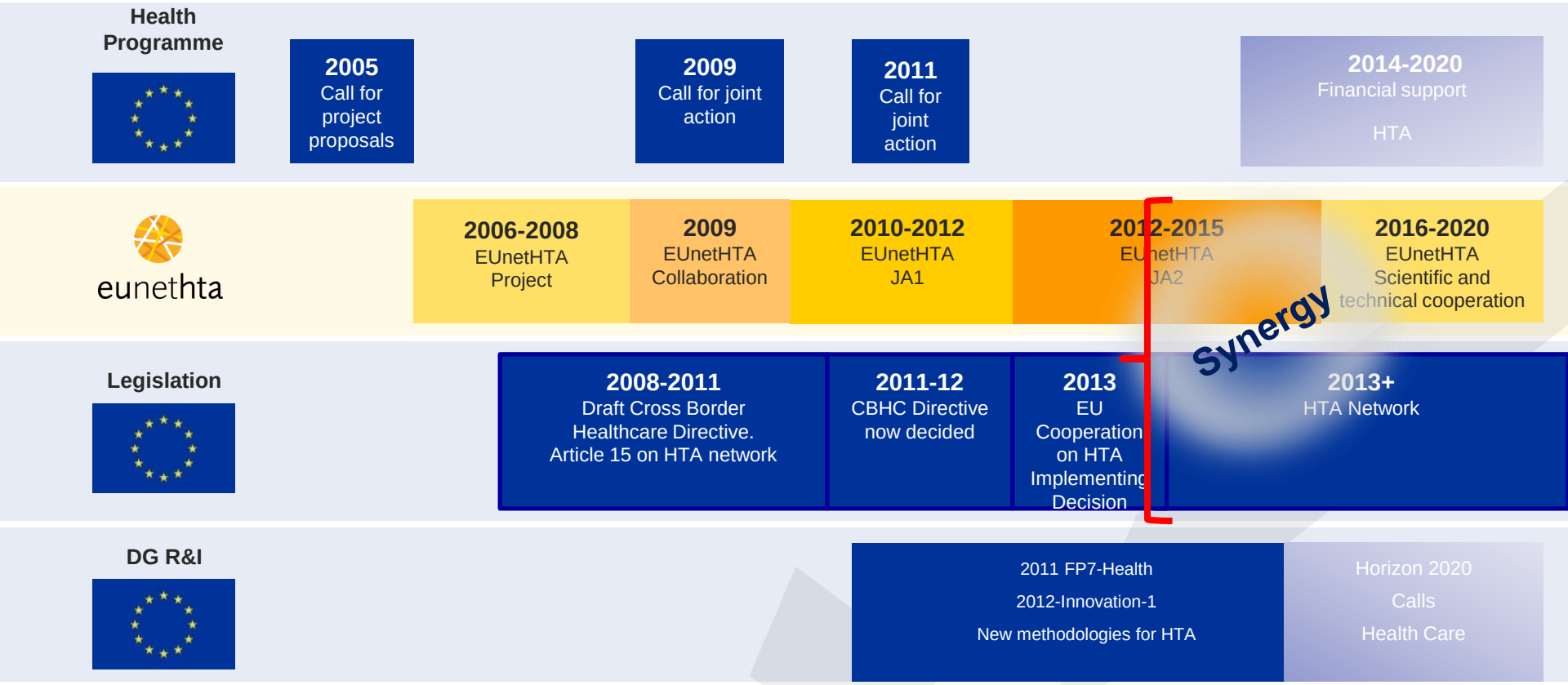
12:30 – 13:15	**Lunch**

Agenda II

13:15 – 15:00	**EUnetHTA WP4 and WP5 Strand B: Discussion on challenges and current processes and experience**
15:00 – 15:15	**Coffee break**
15:15 – 16:15	**WP7 SG4: Template development for medical devices**
16:15 – 16:45	**WP7 SG1 Early Dialogues: Initial exchange of views and identification of the issues**
16:45 – 17:00	**Wrap up, Conclusions and Next Steps**

The timeline of reaching a sustainable and permanent HTA network in Europe

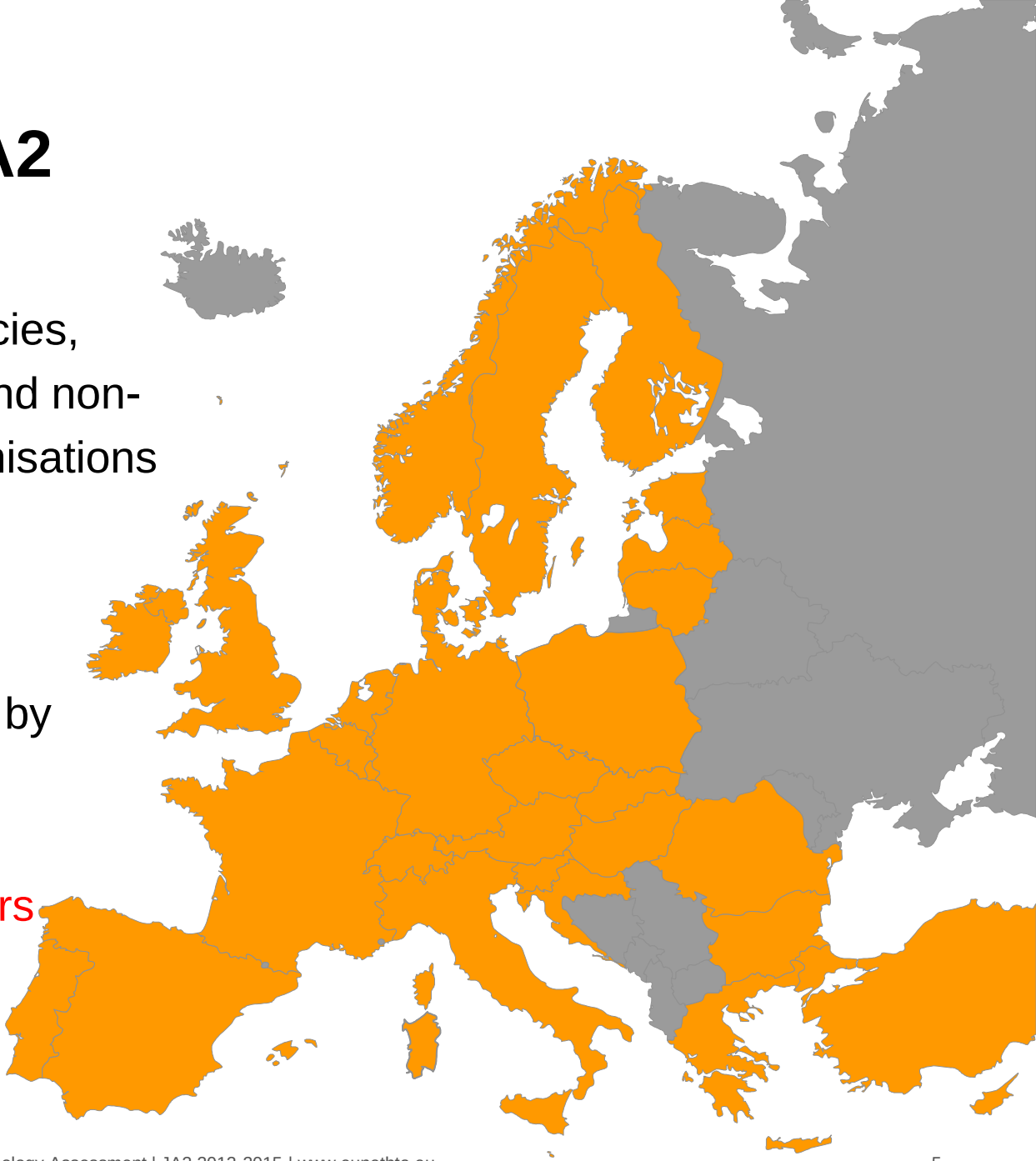


Participants JA2

National, regional agencies, universities, hospitals and non-for-profit research organisations

38 Associated Partner organisations and a Coordinator designated by Member States

31 Collaborating Partners contribute in kind



Definition of Health Technology

Health technology is the application of scientific knowledge in health care and prevention

Examples of Health Technology

- Diagnostic and treatment methods
- Medical equipment
- Pharmaceuticals
- Rehabilitation and prevention methods
- Organisational and support systems within which health care is provided

The Domains of the HTA Core Model®

EUnetHTA Joint Action 2 has received funding from the European Union, in the framework of the Health Programme

Conference, October 2014

Under the patronage of the Italian Ministry of Health

Conference website: www.eunethta2014.it

Appendix 2:

Pharma vs. Medical Technology Models: Presentation by Adrian Griffin (Johnson & Johnson)





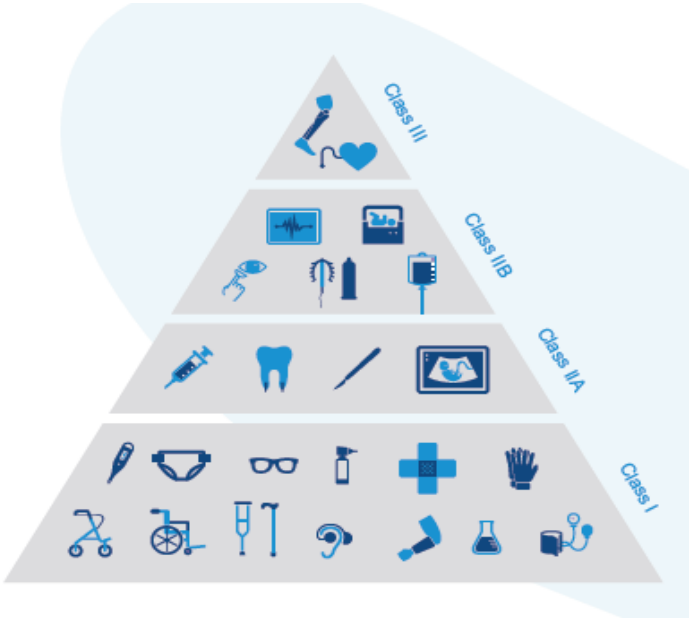

Pharma vs. Medical Technology Models

Adrian Griffin, 8 May 2014

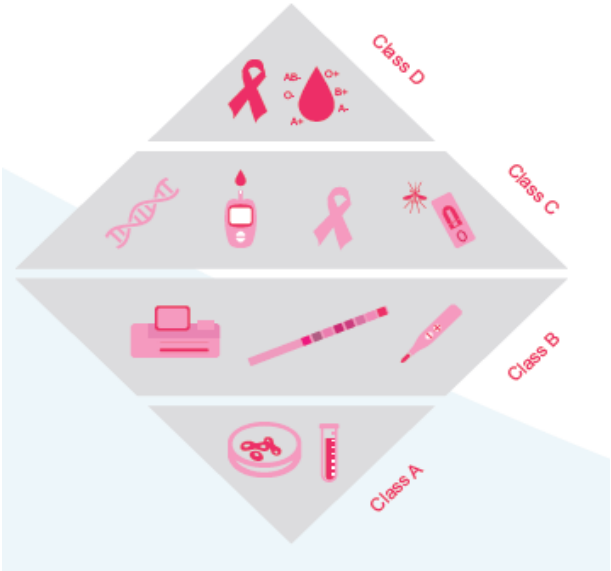
Terminology

Medical Technology = Medical Devices (Eucomed), In-vitro Diagnostics (EDMA), Medical Imaging and Health ICT (COCIR)

Medical Devices, Imaging and Health ICT



In-vitro Diagnostics



COCIR

edma
DIAGNOSTICS FOR HEALTH

Eucomed
Medical Technology

HTA: A Tool to Inform Decision-Making

So understanding the decision-point informs appropriate HTA

Assessment

Evidence

Scientific

HTA is a multidisciplinary scientific approach to assess the evidence to help policymakers make funding and coverage decision.

Appraisal

Policy-making

Data from HTA will be one factor in appraisal process to inform pricing and reimbursement decision.

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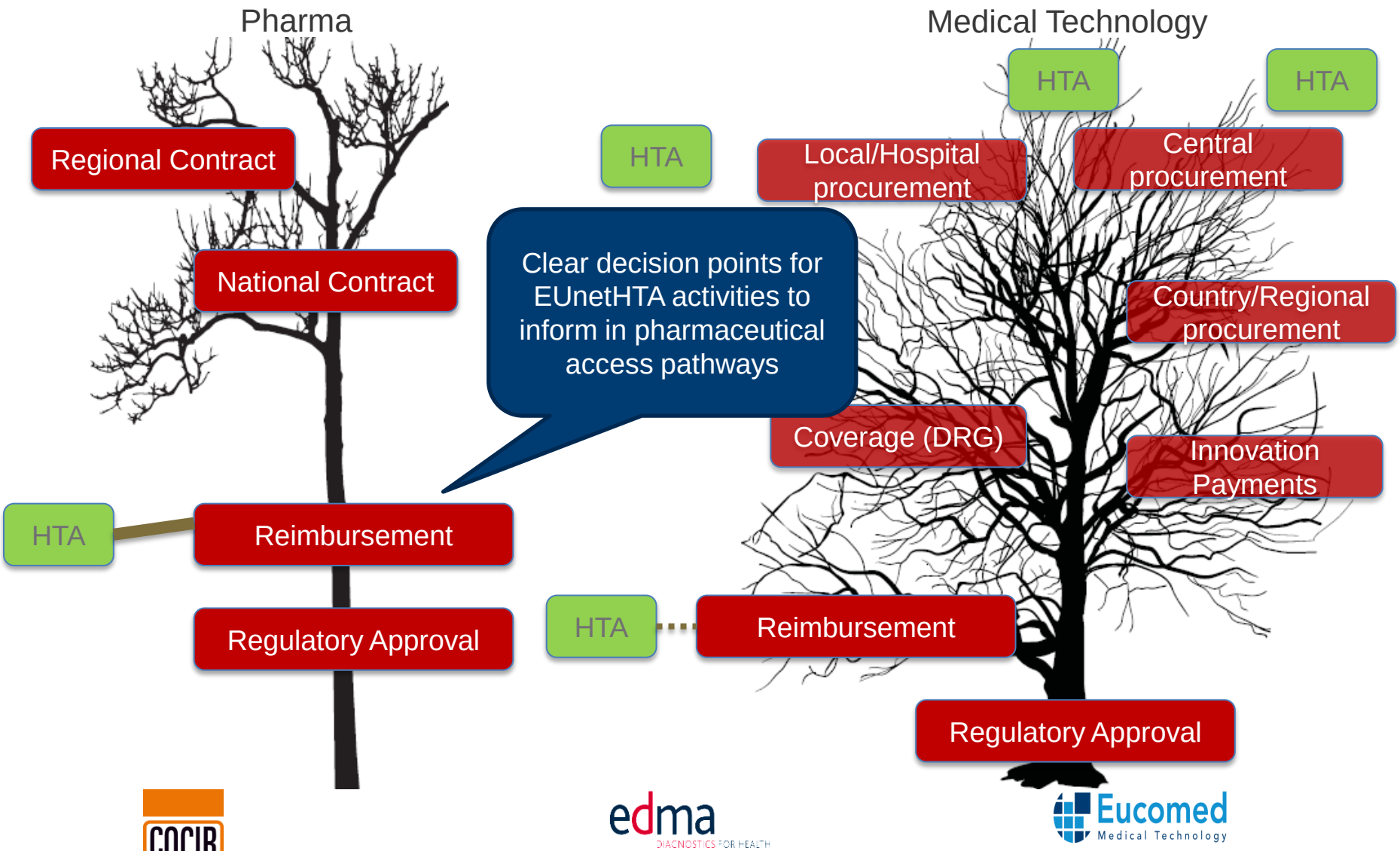
Eucomed Medical Technology

Where HTA Informs the Route to Market



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Medical Technology

Relative merits of Existing EUnetHTA Pilots

Across Pharmaceuticals and Medical Technologies

Sector	Rapid Relative Effectiveness Assessments	Early Dialogues
Pharmaceuticals	HTA is routine activity to access market Collaboration could reduce duplication Clear value in exploring	HTA is routine access procedure Therefore HTA Evidence routinely required
Medical Technologies	HTA is not a routine activity to access market Reimbursement often by procedure & Procurement (funding) often local What would 'collaboration' inform?	HTA is not a routine process to Funding & Reimbursement Early dialogues with few exceptions do not inform an access point

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Eucomed Medical Technology

The Potential Value of EUnetHTA Work Programmes

	Pharma	Medical Devices	IVD's	Medical Imaging & Health ICT
Core HTA			?	?
Rapid REA			?	?
Early Dialogue			?	?

Clear decision points for EUnetHTA activities to inform in pharmaceutical access pathways

The existing EUnetHTA activities do not 'map' to consistent decision points for Medical Technologies access pathways

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Eucomed Medical Technology

Discussion Questions on Rapid REA

- Strategically – HTA is beginning to be used more broadly in Medical Technologies

- Tactically – The access pathways are DIFFERENT from pharmaceuticals, so do they require a different process?
  - Where can European Collaborative HTA add value?
    - Is it ‘rapid’ or ‘robust’?
    - Single technology or class?
    - When is the right time to do HTA for medical technology?
  - Markets that review both are beginning to recognise pathways are different
    - UK, Canada

COCIR

edma DIAGNOSTICS FOR HEALTH

Eucomed Medical Technology

Discussion Questions on Early Dialogues

- Strategically – Is there a role in the ‘access pathway’
  - Does relevance vary by type of technology?
    - Medical device category, diagnostics etc.?
  - Does the role of collaborative HTA need to be addressed before scope of early dialogue?

- Tactically - Lack of capacity where there is existing demand
  - Pharmaceuticals

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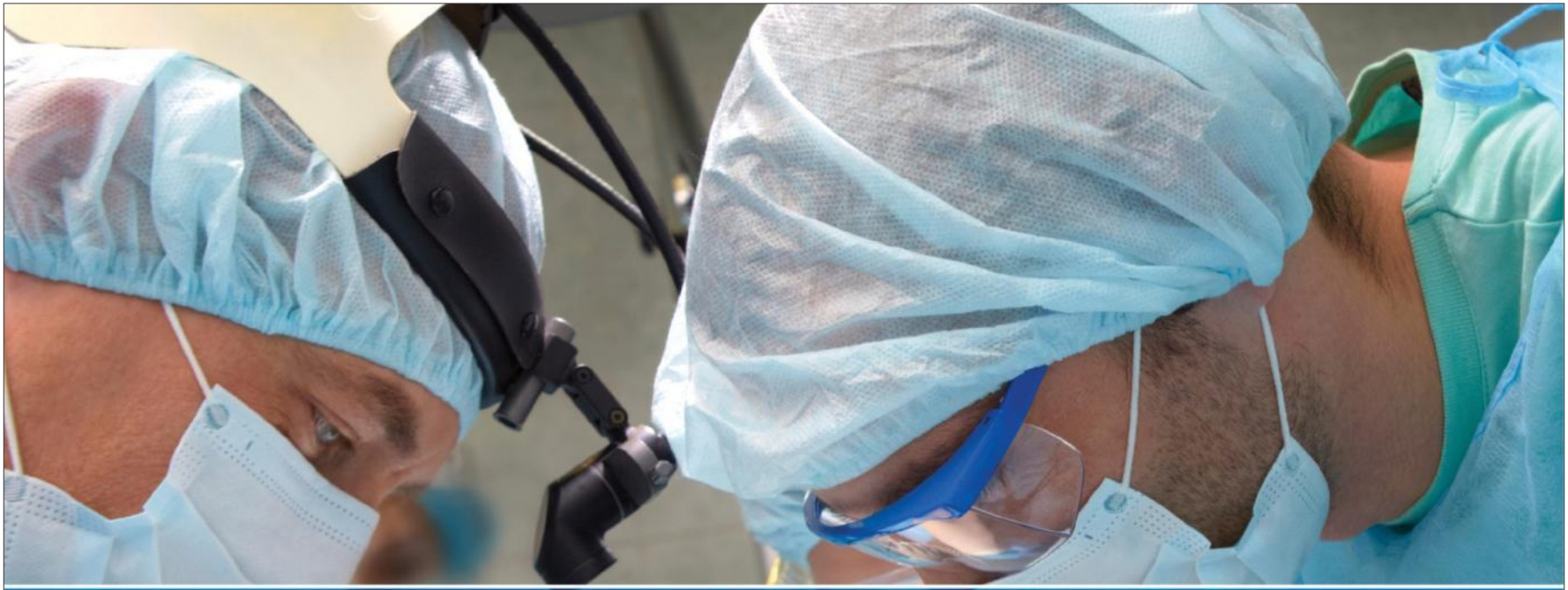
Eucomed
Medical Technology

Appendix 3:

Examples of the role of HTA in the healthcare pathway for MEDICAL DEVICES: Presentation by Pascale Brasseur (Medtronic)

Eucomed
Medical Technology

www.eucomed.org

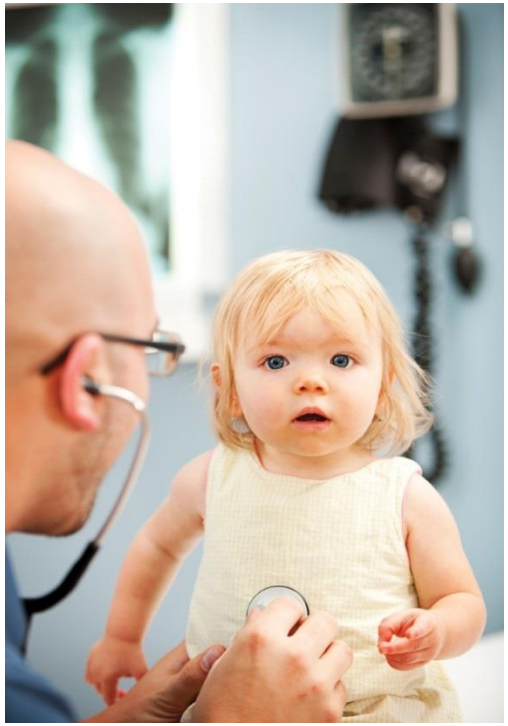


Examples of the role of HTA in the healthcare pathway for MEDICAL DEVICES

Pascale Brasseur, 8 May 2014

Eucomed

- Eucomed represents the medical technology industry in Europe. Our mission is to make modern, innovative and reliable medical devices available to more people.
- Based in Brussels, Belgium
- 28 staff
- Members:
  - 67 direct corporate members
  - 25 national associations
  - 6 associate national associations
  - 3 corporate associate member



Medical technology industry in the EU

- About **25,000** medical technology companies in Europe → **95%** SMEs
- **> 500,000** products available in about 10,000 generic groups
- **€100,000** billion rough market size in Europe, **30%** of the global market
- Nearly **575,000** employee in Europe
- Product lifecycle of only **18-24 months** (10,000 patent applications filled in 2012)

67 corporate members

Differences in approach around Europe for Medical Devices

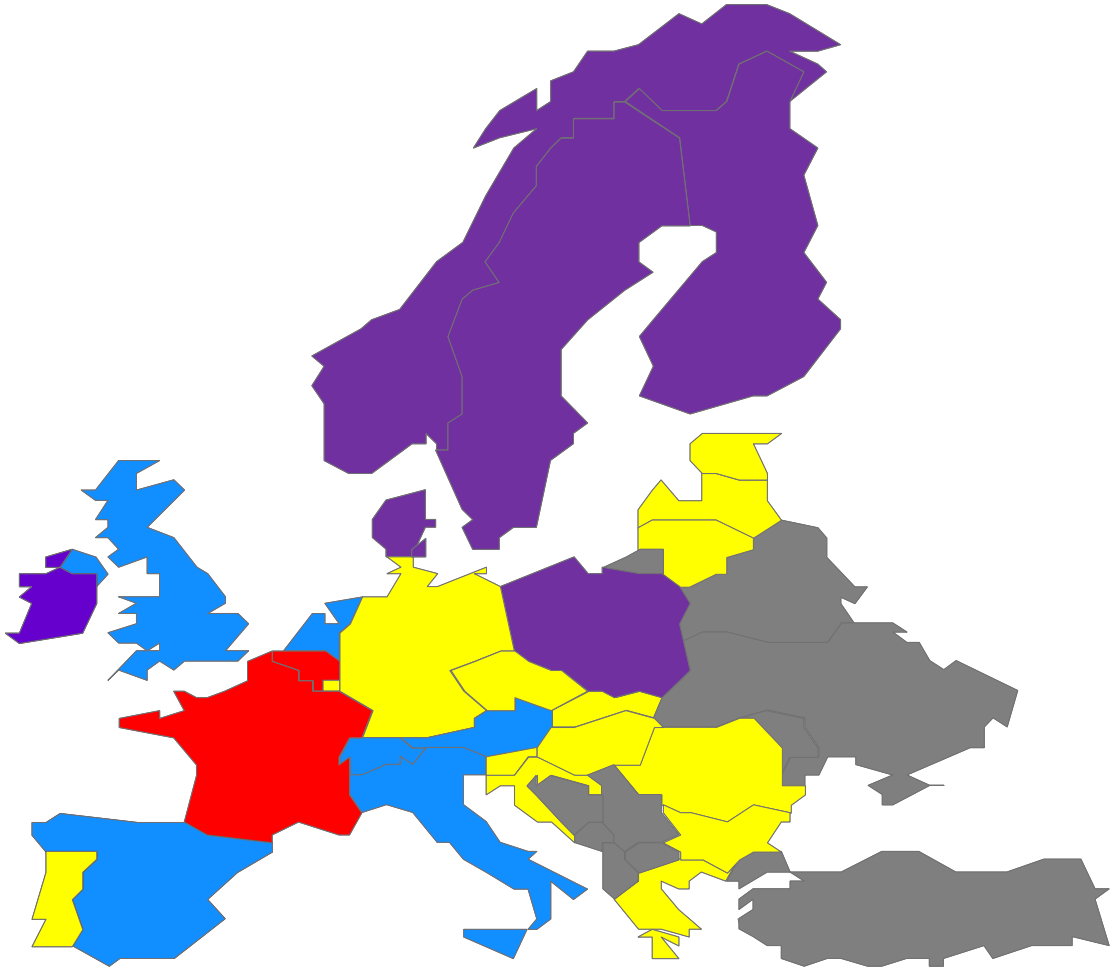
Formal HTA process
Clear link to reimbursement
Impact on diffusion

Formal HTA process
No clear link to reimbursement
Impact on diffusion

Some kind of a HTA process
No clear link to reimbursement
No impact on diffusion

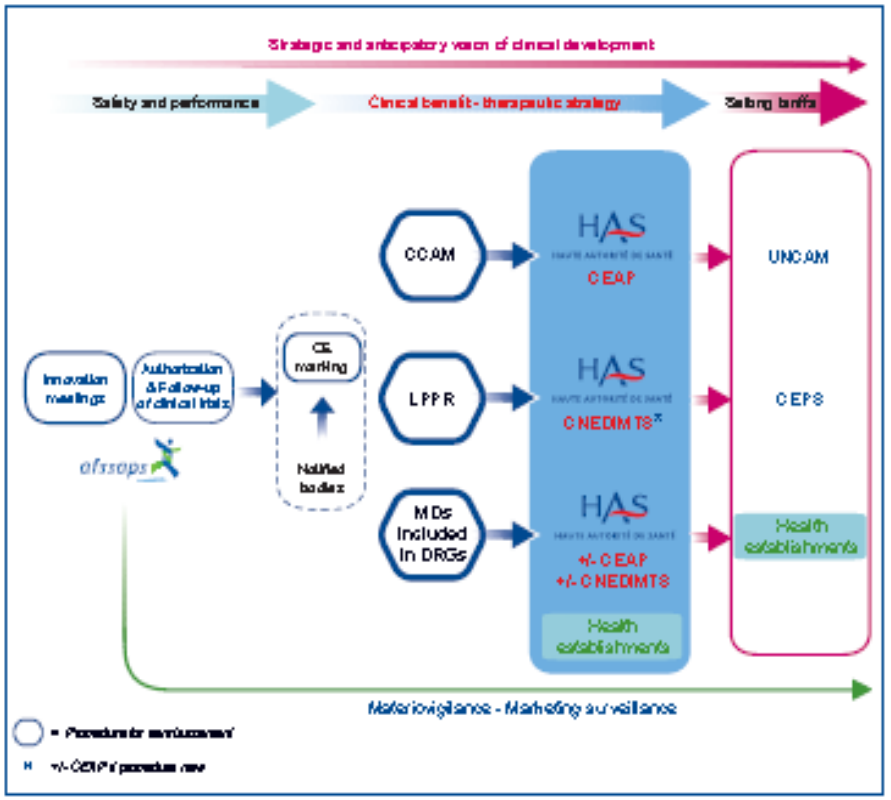
Very sporadic or no HTA

No information



HTA in France

- 1 national HTA body - HAS
- Expenditure on certain MDs is integrated into hospital services (DRG in health establishments).
- Manufacturers can ask for inclusion in the LPPR (list of products and services reimbursed on top of DRG).
- Inscription under generic or brand name
- Limit of 5 years for listing of generic descriptions, then review through HTA.
- Inscription as brand name for product which is innovative in nature or when use of the product requires specific monitoring
- HTA performed on brand names informs pricing and reimbursement . It is based on evaluation of actual benefit of each indication (clinical benefit in the current system)
- No actual benefit means no reimbursement



A Few Figures – CNEDIMTS in 2012

Le service évaluation des dispositifs a enregistré 182 demandes

Demande	Nombre de dossiers
Première inscription	78
Renouvellement d'inscription	50
Modification des conditions d'inscription	45
Autre demande (radiation, modification administrative)	9
TOTAL	**182**

La commission a examiné 142 demandes

Demande	Nombre de dossiers
Première inscription	63
Renouvellement d'inscription	35
Modification des conditions d'inscription	41
Autre demande (radiation, modification administrative)	3
TOTAL	**142**

La CNEDiMTS a rendu 153 avis en réponse à des demandes déposées par les entreprises

Demande	Nombre de dossiers
Première inscription	80
Renouvellement d'inscription	30
Modification des conditions d'inscription	39
Autre demande (radiation, modification administrative)	4
TOTAL	**153**

Les spécialités des dispositifs médicaux implantables sont rapportées dans le tableau ci-dessous

	n	%
Cardiologie	17	39
Gynécologie	1	2
Neurologie	3	7
Ophtalmologie	1	2
ORL	8	19
Orthopédie	2	5
Vasculaire	11	25

Source: Annual Report CNEDIMTS 2012

How Technologies Evaluated through HTA in France Obtain Market Access in Other Countries

Examples

- Cardiovascular: TAVI
- Spine: Lumbar disc replacement

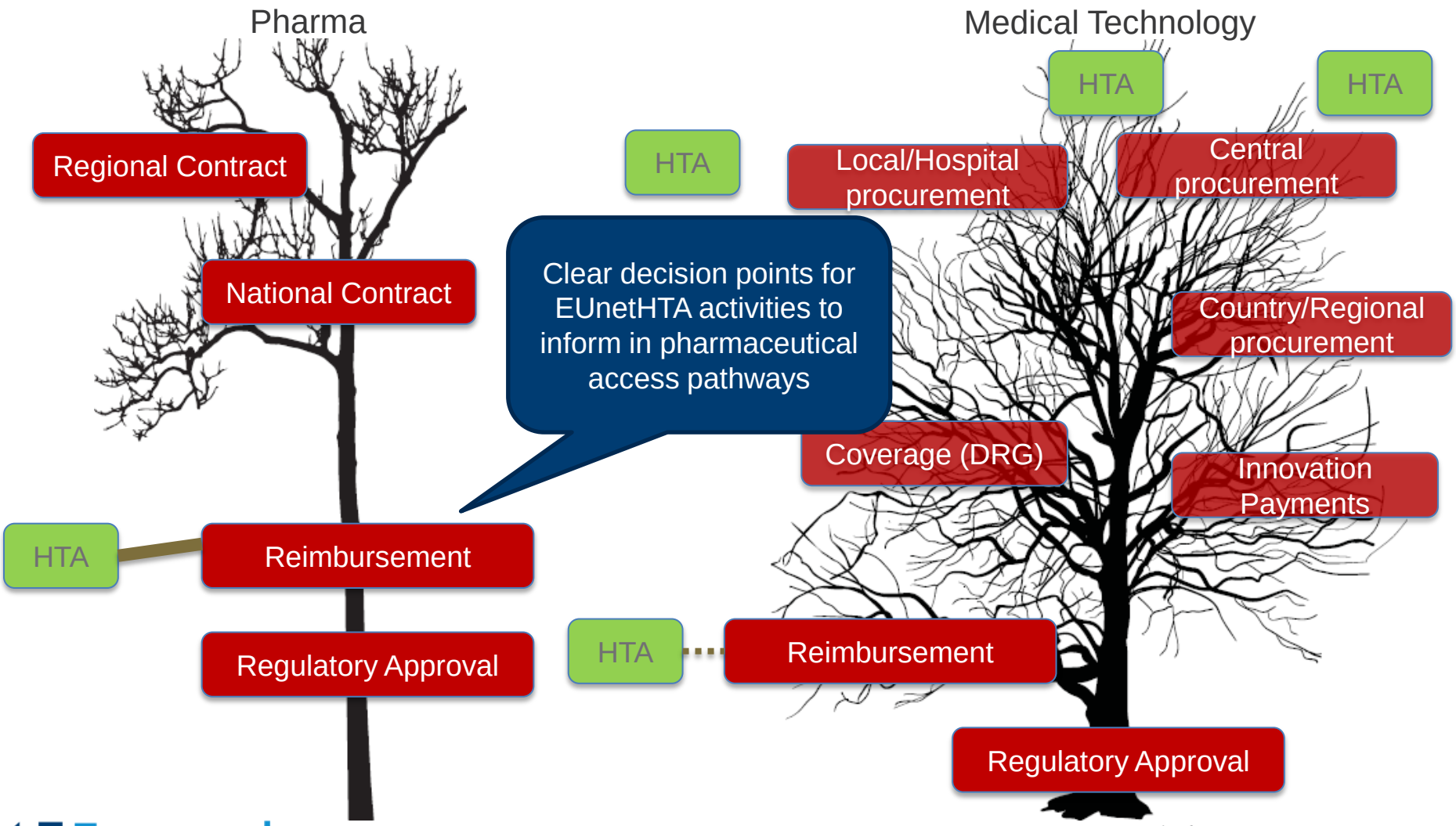
  Vertebroplasty
- Cochlear implants
- Parenteral nutrition at home
- Wound dressings

HTA Agencies that assessed TAVI

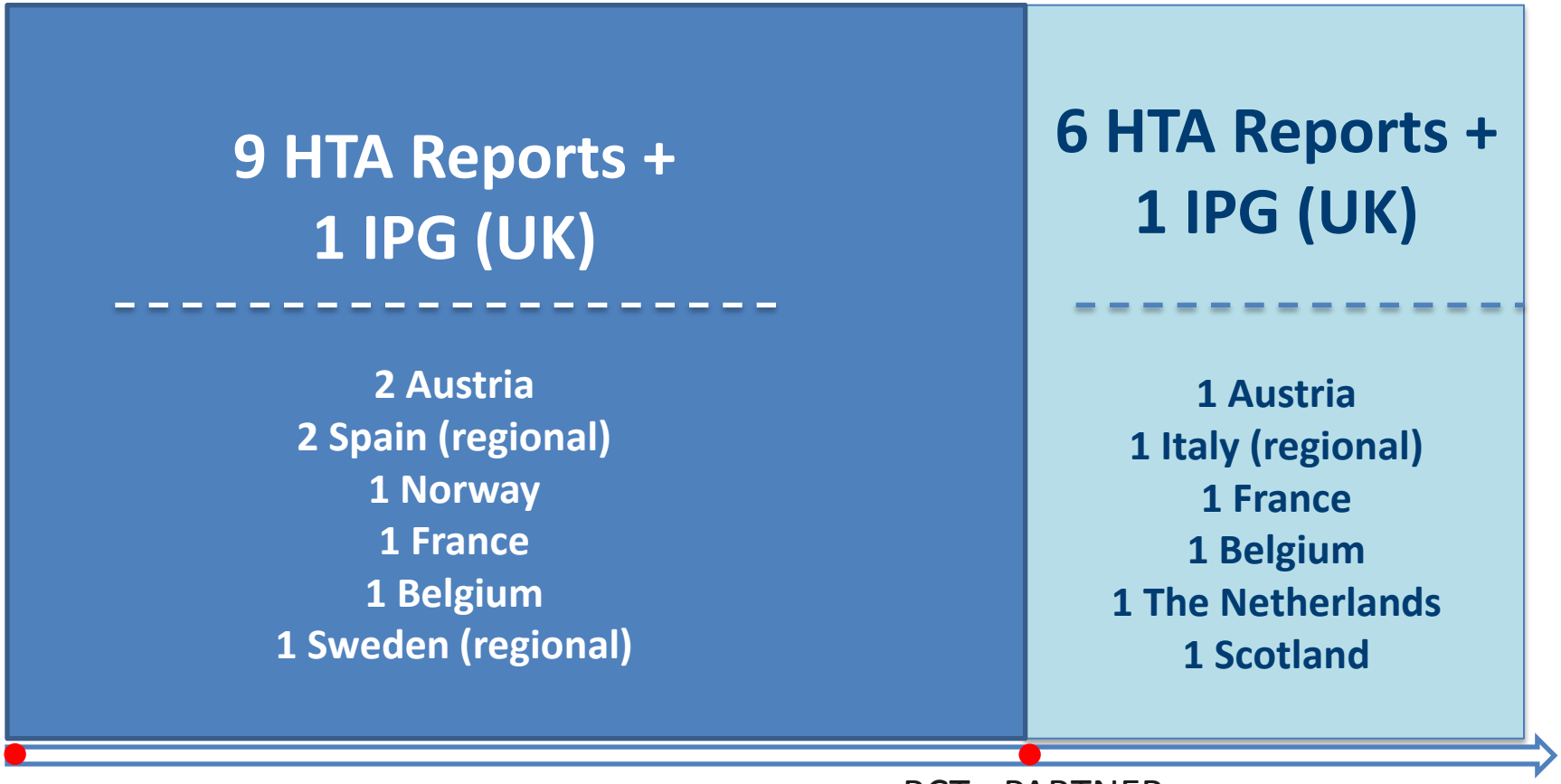
Country	Health Technology Assesment Agency
France	HAS: Haute Autorité de santé
Belgium	KCE: Centre fédéral d'expertise des soins de santé
Spain (Regional HTAs)	AVALIA-T, UETS
Austria	LBI: Ludwig Botzmann Institute for HTA
The Netherlands	CVZ
Norway	Norwegian Knowledge Centre for Health Services (Nasjonalt kunnskapssenter for helsetjenesten), MEDNYTT
Italy (Regional HTAs)	Commissione Tecnica per il Repertorio Unico Regionale (Veneto) dei Dispositivi Medici (CTRDM)
Scotland	Quality Improvement Scotland (NHS QIS)
Sweden	Gothenburg: The Regional Health Technology Assessment Centre (HTA-centrum).

UK: NICE National Institute for Health and Clinical Excellence: *The Interventional Procedure Guidance process considers only efficacy and safety. It does not assess cost effectiveness. No funding flow is linked to positive IP Guidance.*

Where HTA Informs the Route to Market



How many HTA reports on TAVI?



A Few Observations

- The majority of HTA's performed BEFORE publication of the PARTNER RCT (November 2010) were rapid reviews or systematic reviews – with >70% having a negative recommendation.

- 75% of HTA's published AFTER the PARTNER RCT (November 2010) resulted in positive yet restricted recommendation for TAVI.

- CEA's analyses (comparative) are part of only very few HTAs

Key Topics in TAVI HTA Recommendations

- Patients classification and stratification
- Superiority versus standard therapy in terms of
  - Efficacy (mortality and QoL)
  - Direct costs (hospital, device, drugs, blood products) and indirect costs (convalescence)
- Cost-effectiveness
- Inclusion into local registry
- Setting of the procedure: availability of cardiac surgery and a cardiology department
- Center implant performance for: # PCI, heart valve and TAVI

Sustainability

Value for money

Safety

Lumbar discs

Country	Health Technology Assesment Agency
France	HAS - 2007 Intravertebral lumbar disc replacement
Scotland	Quality Improvement Scotland (NHS QIS) – 2011 What is the evidence base for the use of orthopaedic spinal surgery for mechanical low back pain or degenerative spondylolisthesis?
Austria	LBI – 2010 Artificial disc replacement
Spain (Regional)	AETSA (Andalusia) - 2009 Appropriateness criteria for vertebral arthrodesis
Belgium	KCE – 2006 Rapid assessment of emerging spine technologies: intervertebral disc replacement and vertebro/balloon kyphoplasty
UK	NICE – 2004 Prosthetic intervertebral disc replacement
Norway	NOKC – 2002 Treatment of lumbar disc herniation

Vertebroplasty

Country	Health Technology Assesment Agency
UK	NICE – 2013 Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for the treatment of osteoporotic vertebral fractures:
Sweden	SBU – 2011 and 2007 Percutaneous vertebroplasty and balloon kyphoplasty in treating painful osteoporotic vertebral compression fractures
Austria	LBI – 2010 and 2008 Kyphoplasty and vertebroplasty for osteoporotic vertebral compression fracturesA
Denmark	DACETHA – 2010 and 2004 Percutaneous vertebroplasty as a treatment for osteoporotic vertebral fractures
Belgium	KCE – 2006 Rapid assessment of emerging spine technologies: intervertebral disc replacement and vertebro/balloon kyphoplasty

Cochlear Implants

Country	Health Technology Assesment Agency
France	HAS - 2012 CEDIT - 2002
UK	NICE - 2009
Belgium	KCE - 2008
Spain (Regional HTAs)	CAHIAQ - formerly CAHTA - 2006 AETSA - 2002 OSTEBA - 2000
Sweden	SBU - 2003
Joint Nordic-British project	DACEHTA, FinOHTA, SBU, SMM (now NOKC), MRC - 2001

Parenteral nutrition at home

Country	Health Technology Assessment Agency
France	HAS – 2014, 2012 and 2008 Brand evaluations : • 1 in 2013 • 4 in 2012 • 1 in 2011 • 6 in 2010
UK	NICE – 2006 Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition

Wound dressings

Country	Health Technology Assessment Agency
France	HAS - 2010 and 2008 Brand evaluations : • 7 in 2013 • 9 in 2012 • 7 in 2011 • 2 in 2010
Scotland	Quality Improvement Scotland (NHS QIS) 2013 Are silver dressings clinically effective and cost effective for the healing of infected wounds and the prevention of wound infection relative to other types of dressings
Sweden	SBU – 2011 Slow-healing wounds in the elderly
Denmark	DACETHA- 2011 Wound treatment in the patient's own home by collaboration between hospital and home care
Sweden	SBU - 2010 Silver-releasing dressings in treating chronic wounds

A few observations

- Different timings to perform HTA
- Rapid HTA vs full HTAs – repetition of HTA
- Brand specific and generic assessments in France

Appendix 4:

Role of HTA in HealthCare Pathways for IVD: Presentation by Seong Chen (Roche Diagnostics)

Role of HTA in HealthCare Pathways for IVD

8 May 2013

edma
DIAGNOSTICS FOR HEALTH

About in vitro diagnostics (IVDs)

IVDs are non-invasive tests performed on biological samples (for example blood, urine or tissues) to diagnose or exclude a disease.

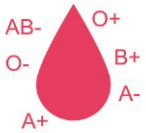
IVD tests are performed on samples.
Samples include blood, urine, stool, sweat and saliva.

IVD tests help
- *Diagnose*
- *Monitor*
- *Screen*
- *Risk assessment*
- *Treatment selection*

Commonly known IVDs

Blood glucose monitor

Pregnancy test



Blood type identification test

Breast cancer screening

EDMA represents the interests of the IVD industry active in Europe

The Association

- Founded in 1979
- 20 members of staff in Brussels
- A recognized healthcare stakeholder at EU level

Our Members

- 23 national associations
- 44 major companies engaged in the research, development, manufacture or distribution of IVDs

Our Mission

- To raise awareness of the importance, usefulness and added value of IVDs in healthcare
- Contribute to the development of legislative and regulatory framework that will shape the IVD industry's future.
- Provide technical, regulatory and market research information to our members.

edma

DIAGNOSTICS FOR HEALTH

44 Corporate Members

22 National Associations
Reaching out to 500 companies

The In Vitro Diagnostics Industry in Europe

Facts & Figures

€11 billion

IVD Market Size

3,000 companies

75,000 people employed

40,000

IVD Products

11% *of employees are dedicated to R&D*

95% *of the industry is SME-based.*

What is the difference between IVDs and medical devices?

- **IVDs never come into direct contact with a person.** They provide information on a sample from a person

- **IVDs do not treat patients.** The role of IVDs is to provide information that enables making of healthcare decisions by HCPs and patients

What is the difference between IVDs and pharmaceuticals?

- **IVDs are tests used on samples taken from a human body to determine status of health** unlike pharmaceuticals, which aim to treat or manage a condition or disease

- **IVDs do not treat patients.** The role of IVDs is to provide information that enables making of healthcare decisions by HCPs and patients

- **An IVD has no physical contact with the body** unlike medicines, which are designed to be absorbed into the body and act systematically

- **For IVDs, innovation results primarily from clinicians' insights**, rather than laboratory exploration. For drugs, R&D takes place to identify a specific compound or molecule, and it takes several years for a new drug to enter the product pipeline

Heterogeneity in Europe

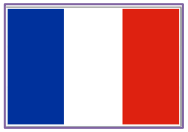
- " Europe presents specific inter- and intra-national heterogeneity in pathway in terms of **IVD Market access and reimbursement.**
  - Transparency and difference in time to access
  - Inconsistent decision-making criteria
  - Local decision making
  - Access funding LDT versus IVD
  - In-Patient vs Out-Patient
  - Systems rarely designed to incentivize value
  - Occasionally complete lack of associated funding

Example: HTA for Rx & CDx (from IVD)

Rx: National HTA , AMNOG appraisal by G-BA/IQWiG
CDx: Laboratory working group (AG Labor)/Competence center for laboratory related issues (COC/L) and medical review board of SHI (MDS)

Regional HTA (England, Scotland, Wales & Northern Ireland)

NICE: CDx/Rx integrated in technology appraisal of drug or diagnostics assessment program (DAP)



National HTA: HAS, separate evaluation
Rx: Transparency Committee
CDx: CNEDiMTS

Rx: National HTA by AIFA (level of innovation)
CDx: No dedicated program. Regional HTAs or locally

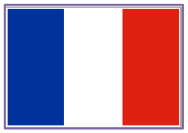
Rx: National HTA

CDx: No dedicated program. Regional HTAs or locally.

Reimbursement decision for CDx mostly not related to HTA

Approved prescription drugs are reimbursed by SHI
CDx: Reimbursement if CDx required otherwise evaluation committee

Rx: Positive NICE guidance → mandatory funding by NHS
CDx: contentious. No NICE guidance: decision by local budget holders



Ministry of Health based on TC/CNEDiMTS recommendation
INCa provides and funds CDx in oncology

Rx: mandatory for important innovations

CDx: No common pathway, in practice generic codes or local/regional decision

Rx: central decision
CDx: Typically no reimbursement

HTA & Market Access
Specific to IVD Application & Country

Diagnostics Application	France	Germany		UK
		Outpatient	Inpatient	
Diagnosis	No formal HTA HAS in review *(unless cancer INCa)*	AG Labor review *(unless existing EBM/ GÖA code)*	No formal HTA required, depending on care setting	No formal HTA required
Screening	HTA type assess HAS review *(unless cancer, then INCa involvement)*	AG Labor review in all cases for reimbursement	AG Labor review in all cases	No formal HTA required
Predictive / Treatment Selection	HAS review *(unless cancer, then INCa involvement)/ HTA will be conducted in parallel with companion drug*	AG Labor review *(unless existing EBM/ GÖA code/ HTA may be conducted in parallel with companion drug*	No formal HTA required, depending on care setting/ *HTA may be conducted in parallel with companion drug*	Formal HTA occurs in context of NICE drug review – requires RCT
Prognosis	No formal HTA required	AG Labor review *(unless existing EBM/ GÖA code)*	No formal HTA required	No formal HTA required
Monitoring	In function application	AG Labor review *(unless existing EBM/ GÖA code)*	No formal HTA required	No formal HTA required

Specific Challenges - HTA

- Variability among EU HTA bodies is more pronounced in the case of IVDs, with the potential for profound implications for both patient access and innovation in this rapidly evolving sector

- One key limitation is that HTA bodies have not considered or aligned study design and strength of evidence expectations with the evidence questions most important to test evaluation*.

*Faulker et al. Value in Health 2012 (8),

HTA - IVD

IVD Position on HTA:

Application of technology assessment needs to be

“fit-for-purpose”

to ensure that an assessment is initiated only when the results will inform a decision point.

Appendix 5:

Examples of the role of HTA in the healthcare pathway for medical technology Medical Imaging & Health ICT: Presentation by Werner Van den Eynde (GEHC)

COCIR

Sustainable Competence in Advancing Healthcare

HTA expert meeting

Thursday 8 May 2014, Brussels

Examples of the role of HTA in the healthcare pathway for medical technology

Medical Imaging & Health ICT

Werner Van den Eynde

COCIR HTA Task Force Chair

What does COCIR do?

COCIR is a non-profit trade association, founded in 1959 and having offices in Brussels and China, representing the medical technology industry in Europe

COCIR covers 3 key industry sectors:

- Medical Imaging
- Electromedical
- Health ICT

Our Industry leads in state-of-art advanced technology and provides **integrated solutions** covering the complete care cycle

COCIR promotes the use of advanced medical and ICT technology – in Europe and beyond - towards seamless care delivery and shared knowledge to build a better world with improved access to affordable, quality and safe healthcare

→ Towards integrated care

COCIR Member Companies

COCIR National Trade Associations Members

AGORIA
no future without technology

Belgium

AXrEM

UK

bvitg

Germany

federación española
de empresas de
fenin TECNOLOGÍA SANITARIA

Spain

FHI MEDICAL TECHNOLOGY

Netherlands

FiHTA

Finland

Holland HealthTech

Netherlands

snitem
créer les instruments du progrès médical

France

SPECTARIS
Deutscher Industrieverband für optische, medizinische und mechatronische Technologien e.V.

Germany

SWEDISH Medtech

Sweden

TIP GÖR DER

Turkey

ZVEI:

Germany

Innovation in Medical Technology

Diagnostics

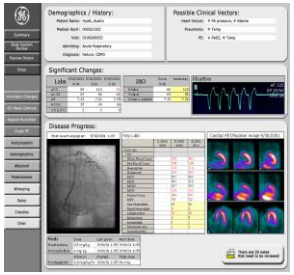
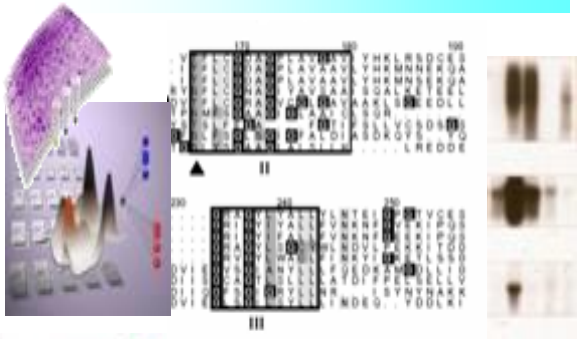
- *Faster, accurate imaging*
- *Molecular imaging*
- *Miniaturisation/portability*
- *Point of Care diagnostics*
- *Therapy selection/monitor*

Biotech & Genomics

- *Targeted therapy*
- *Proteomics/DNA*
- *Biomarkers*
- *Rapid screening tools*
- *Vaccine development*

IT & bioengineering

- *eHealth/Telemedicine*
- *Mobile solutions*
- *BioSensors*
- *Computer Aided Diagnostics*
- *Patient monitoring*

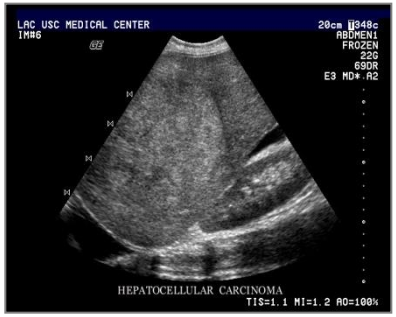





Medical Imaging Evolution

‘80s Mainstream

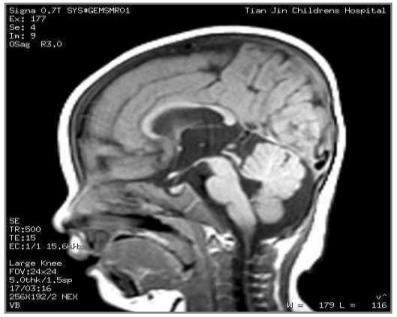
X-Ray-based Anatomical Imaging: XR, CT

Ultrasound



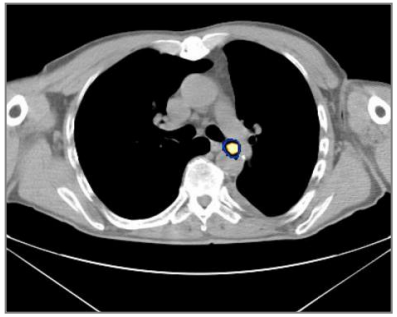
‘90s Mainstream

- CT, MR, US Anatomical Imaging
- Digital Xray



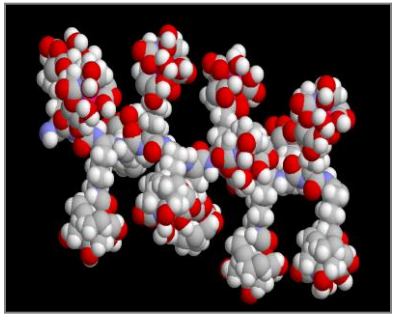
‘00s Mainstream

Anatomical Positioning (Registration) of Functional Imaging: PET/CT, MR



Next Mainstream

Molecular Imaging
+
Molecular Therapeutics
+
Molecular Diagnostics



Emerging

MR Anatomical Imaging (Tissue Visualization)

Emerging

Functional Imaging MR, PET

MR Spectroscopy (Characterization)

Emerging

Anatomical Registration of Molecular Imaging

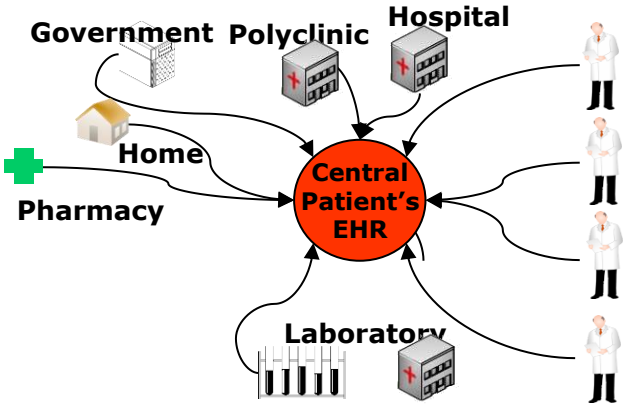
Molecular Therapeutics, Diagnostics & DI

Emerging

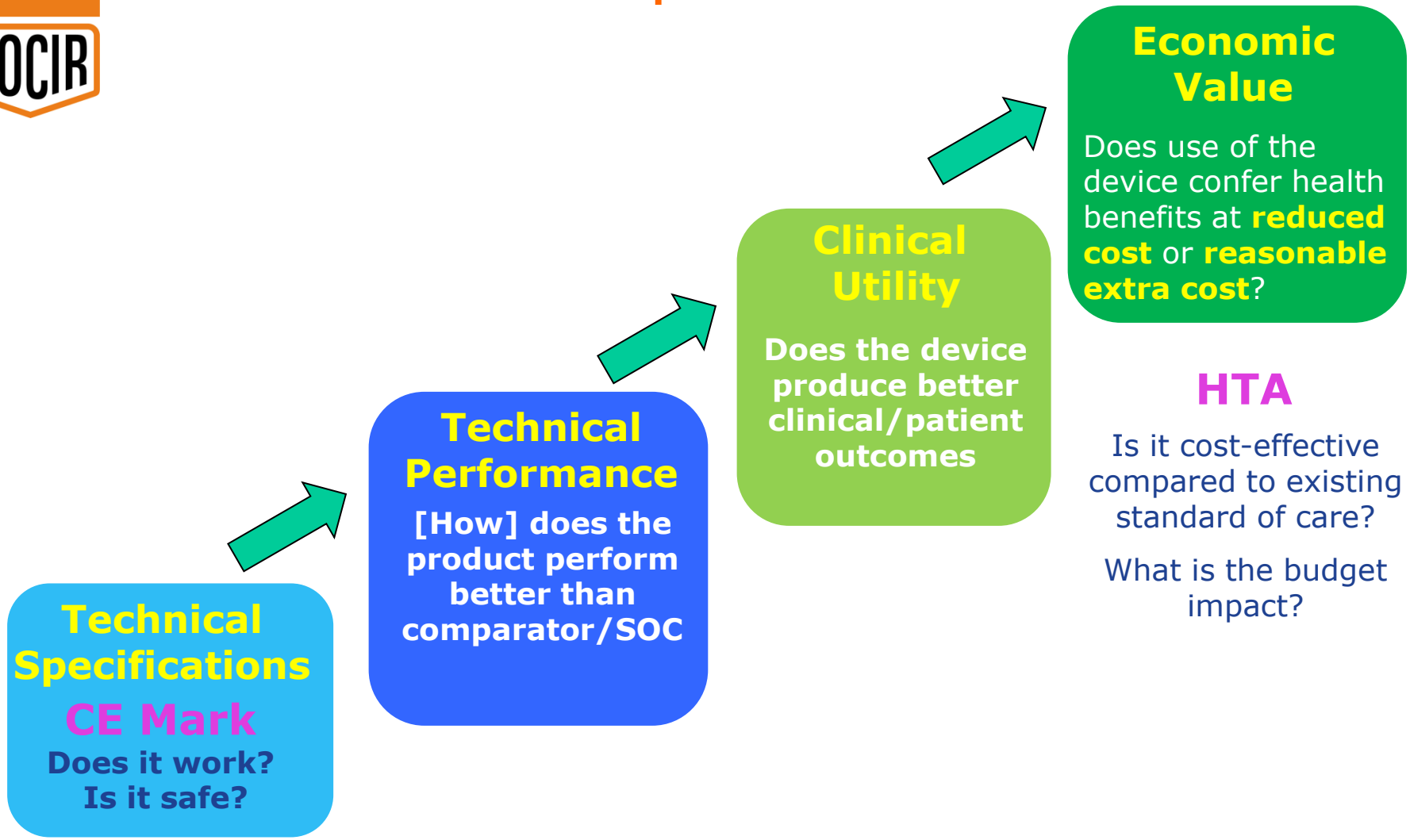
Image-guided Gene Therapy

eHealth supports the delivery of a more efficient and higher quality care

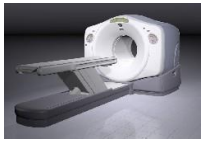
- Health ICT and eHealth →proven high clinical and societal value
- Telehealth →linking patients with care providers
- IT infrastructure →ensure that systems derive maximal value from medical technology (Cloud computing)
- IT connectivity through IHE (Integrating the Healthcare Enterprise) →improving quality and reducing cost
- More investment in eHealth →best-practice clinical pathways / patient's mobility throughout Europe



Evidence Requirements



Medical Imaging & Health ICT play crucial roles at all stages of cancer management



Predisposition

Screening

Diagnosis

Staging

Therapy Selection

Therapy Evaluation

Detection of Residual Disease

Diagnosis of Recurrence

Cancer Disease Management Track

Genomics
BRCA 1,2
Risk Profiling

Mammography
Ultrasound
MR

Proteomics

Microarray

CT
MR
PET/CT
Nuclear Med

PET/CT
Functional
marker

Optical
Functional
Marker

Microarray
PACS
Electronic Health Record
Medication Management

CTMRI
Radiation Treatment

F-Angiogenesis
PET

Mammography
In-vitro test

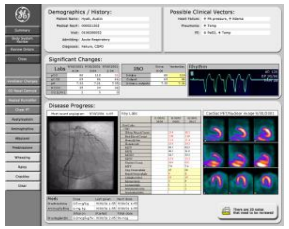
PET/CT
New markers

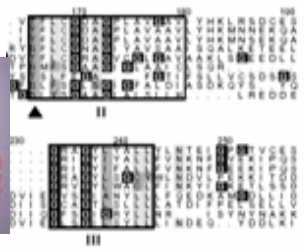
Exist Today

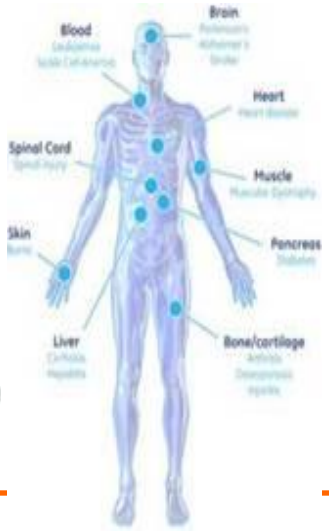
Emerging Research and Technologies

Medical Imaging & Health ICT are different…

- Inform decisions at many stages during care pathway
- Often no outcome (clinical, economic) *per se* – rather enablers of better outcomes for patients, providers and society
- Imaging devices have multiple applications e.g. CT scanner
- Health gains are often operator dependant and disruptional
- Health ICT enables quicker, more reliable decisions – integrating patient data producing a composite analysis of the patient status (e.g. during surgery)
- Efficiency enablers – Healthcare Professionals spend more time with patients
- Traditional Randomised Controlled Trials often inappropriate to capture the full value




…and have different business models

- Different scale of product: e.g. DaTSCAN peak sales $10's of millions, blockbuster drug $billion, 100x more
  - implication: much less to invest

- Limited or non-existent IP – impact of outcomes often shared by manufacturers
  - implication: disincentive to invest heavily in evidence generation

- Medical imaging is not reimbursed by product or often even not by technology but by procedure [despite lack of comparative data]
  - implication: disincentive to invest heavily in evidence generation if other manufacturers can benefit

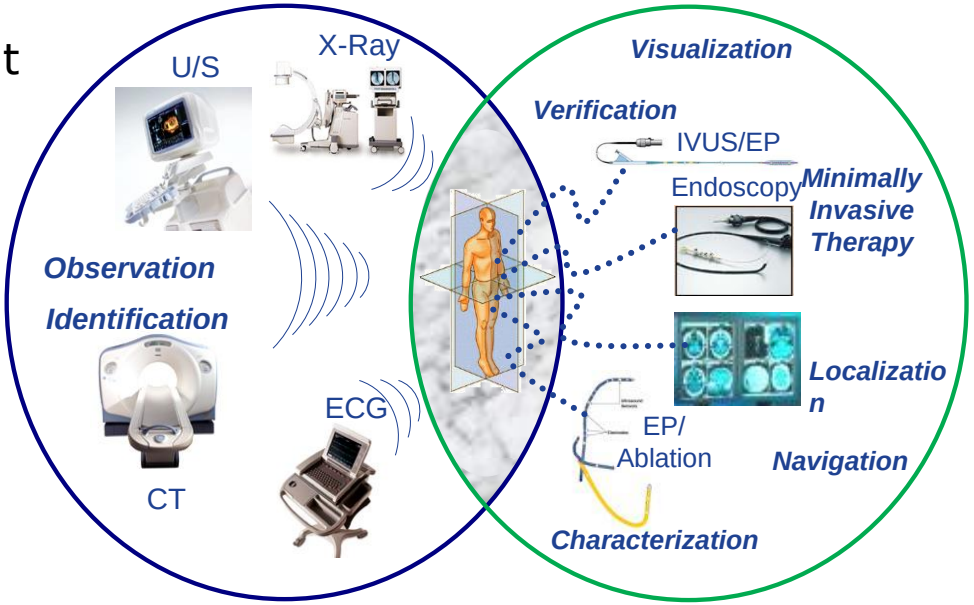
These commercial considerations deter significant up-front investment in expensive studies. Nevertheless innovative Medical Imaging & Health ICT products offer significant benefits to patients, providers and payers

Randomised Controlled Trials often not feasible… Model & extrapolate what can be measured

- Medical Imaging can provide important information across the entire care pathway

  - predisposition, disease stratification, early diagnosis, treatment monitoring, relapse or recurrence

- Often not feasible for technical, ethical & practical reasons to generate evidence demonstrating superiority of a new imaging modality versus usual care – across the whole disease pathway



- Not all outcomes are clinical and it is difficult to measure non-clinical benefits in RCTs

- Need to consider more practical methods of data collection to quantify & qualify the full value of Medical Imaging and Health ICT products

Patients may be denied access to valuable new diagnostics/technologies if these differences are not respected

Not only technologies need to be assessed but the entire process

- **Other elements should be considered besides clinical effectiveness:**
  - Quality
  - Access
  - Patient experience
  - Organisational considerations
  - Ethical considerations

- **Examples of other models recognised for health ICT:**
  - MAST (Model for Assessment of Telemedicine applications): a multi-disciplinary method used to assess telemedicine in Renewing Health project. Although designed for telemedicine innovations, it can be applied to a wide range of eHealth services.
  - PDSA (Plan, Do, Study, Act): a quality improvement method which uses an iterative approach to improve the performance of a process (enabled by technology) until it produces the required outputs.

The aim of these new approaches is to deliver measurable and sustainable improvements

HTA methodology that is fit for purpose:

- Pragmatic + accepts different types of evidence
- Streamlined process - faster assessment & early uptake
- Recognizes broad scope of benefits and evidence
- Implementation support for healthcare providers

What we expect for the future:

- Appropriate methodologies for our specific sector
- Clarification on EUnetHTA pilots and industry participation
- Better understanding on interactions between EUnetHTA, AdoptHTA and other initiatives (MedtecHTA, etc)
- Better understanding on links between European HTA activities and national HTA activities

Appendix 6:

WP7 SG3: Methodological Guidelines on Medical Devices. The current guideline development process in EUnetHTA and guidelines structure: Presentation by Jörg Lauterberg (IQWIG)

EUnetHTA

European network for
Health Technology Assessment

WP7 – SG3: Methodological Guideline on Medical Devices

Jörg Lauterberg – SG3-Coordinator – IQWiG / GERMANY

Agenda

1. **Methododological guideline development in EUnetHTA – Introduction**
2. **Special aspects: Main guideline target group, guideline format, revised elaboration process, internal coordination**
3. **Guideline on Medical Devices**
4. **Questions of the guideline draft group**

1. **Methododological guideline development in EUnetHTA – Introduction**
2. **Special aspects: Main guideline target group, guideline format, revised elaboration process, internal coordination**
3. **Guideline on Medical Devices**
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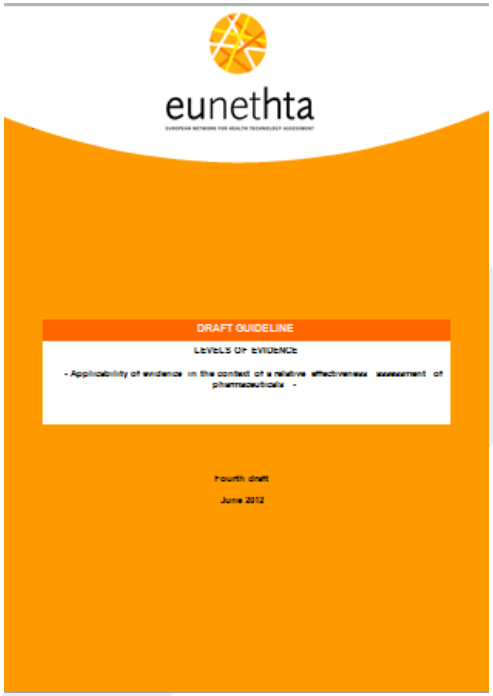
Methodological guideline development

- Agreement on basic methodological standards and their application in projects and pilots is part of the EUnetHTA collaboration in Joint Action 1 (2010-2012) and in Joint Action 2 (2012-2015)
- JA 2 methodological work in WP7:
  - SG1: early dialogues, disease specific guidelines
  - SG2: additional evidence generation
  - SG3: methodological guidelines
  - SG4: manufacturer´s submission file template
- Methodological guidelines especially necessary for joint HTA work, e.g. Relative Effectiveness Assessments (REA) based on EUnetHTA´s Core Model®
- Guideline character: Non-binding recommendations for national HTA
- Purpose: To help and provide guidance to HTA assessors of EUnetHTA organisations

Existing guidelines (JA1 – WP 5) for rapid REAs of pharmaceuticals

1. Applicability
2. Internal validity (of randomised controlled trials)
3. Criteria for the choice of the most appropriate comparator(s)
4. Direct and indirect comparisons
5. Clinical endpoints
6. Composite endpoints
7. Health-related quality of life and utility measures
8. Safety
9. Surrogate endpoints



Link to the guidelines:
http://www.eunethta.eu/eunethta-guidelines

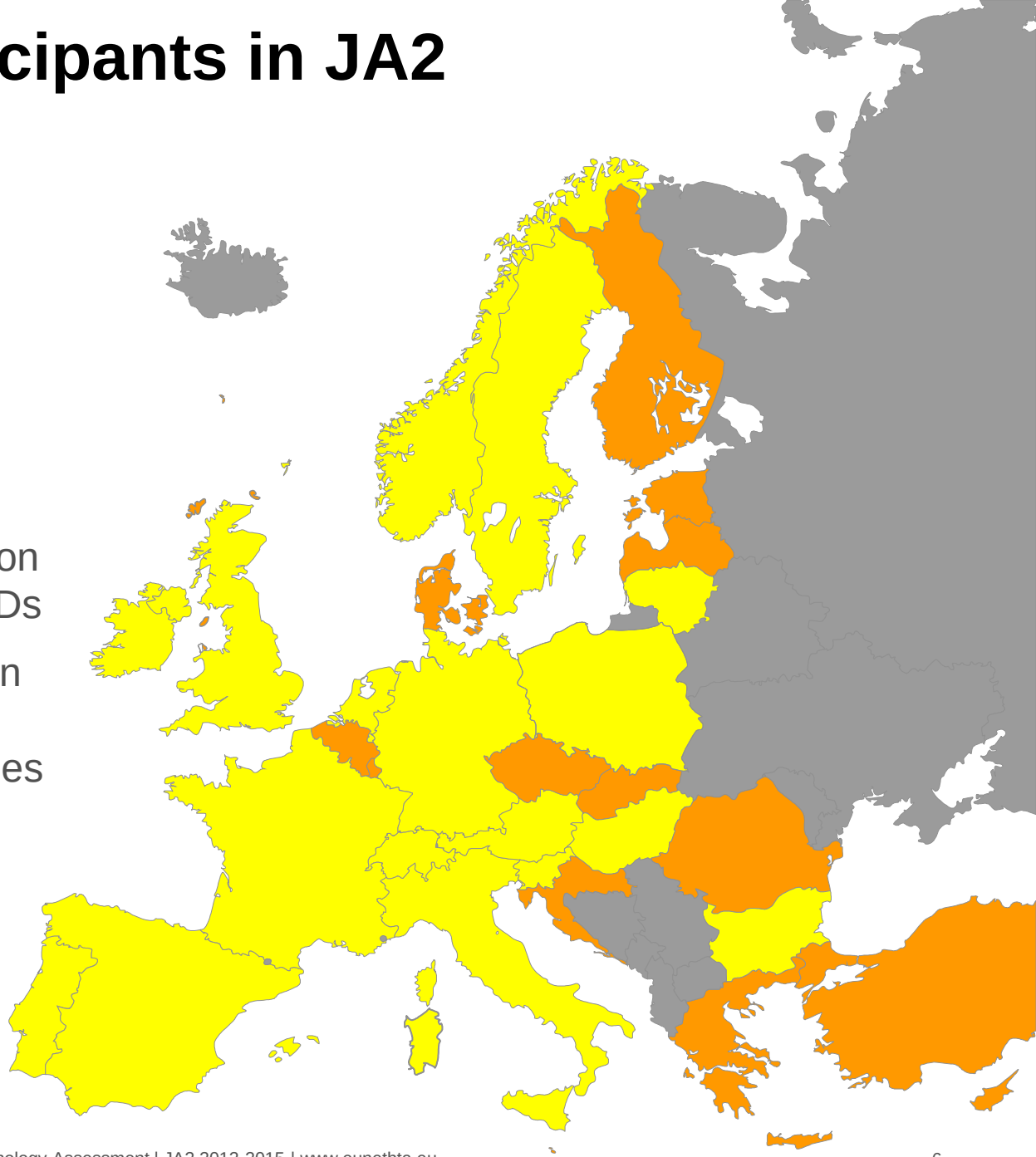
WP7 – SG3 participants in JA2

(yellow)

N = 22 organisations

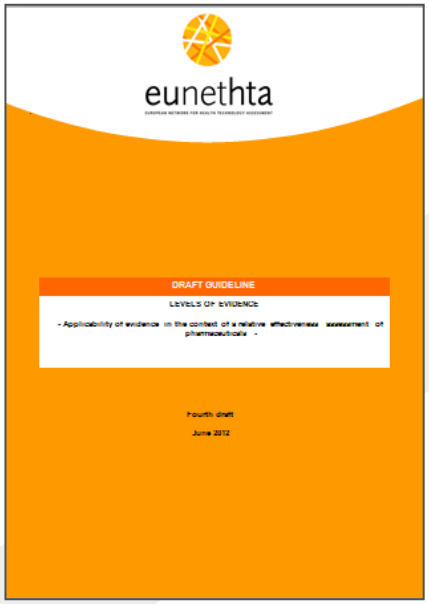
Tasks:

1. Elaboration of new guidelines
2. Revision of the JA1 guidelines incl. adaptation to the assessment of MDs
3. Final process description for elaboration and maintenance of guidelines

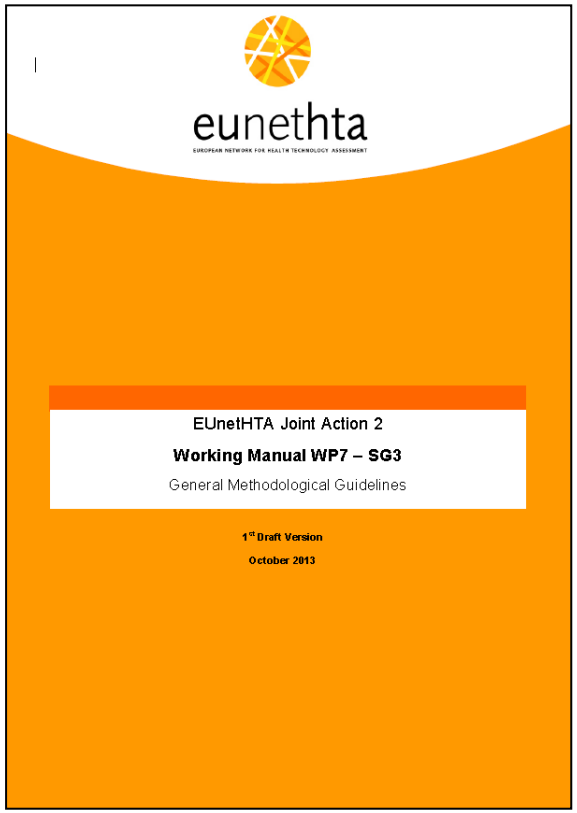


Guideline topics in JA2 – All technologies

Topic	First author
1. Elaboration period 2013 - 2014	
1. Internal validity of non-randomised studies (NRS) on interventions	IQWiG
2. Meta-analysis of diagnostic test accuracy studies	HIQA
3. Economic evaluations	SBU
2. Elaboration period 2014 - 2015	
4. Medical Devices	UMIT
5. Personalised Medicine	OSTEBA
6. Information retrieval in study registries and bibliographic databases	IQWiG



SG3 - Working Manual
(internal document)



JA2 deliverable:

Description of the future methodological guideline elaboration process in EUnetHTA

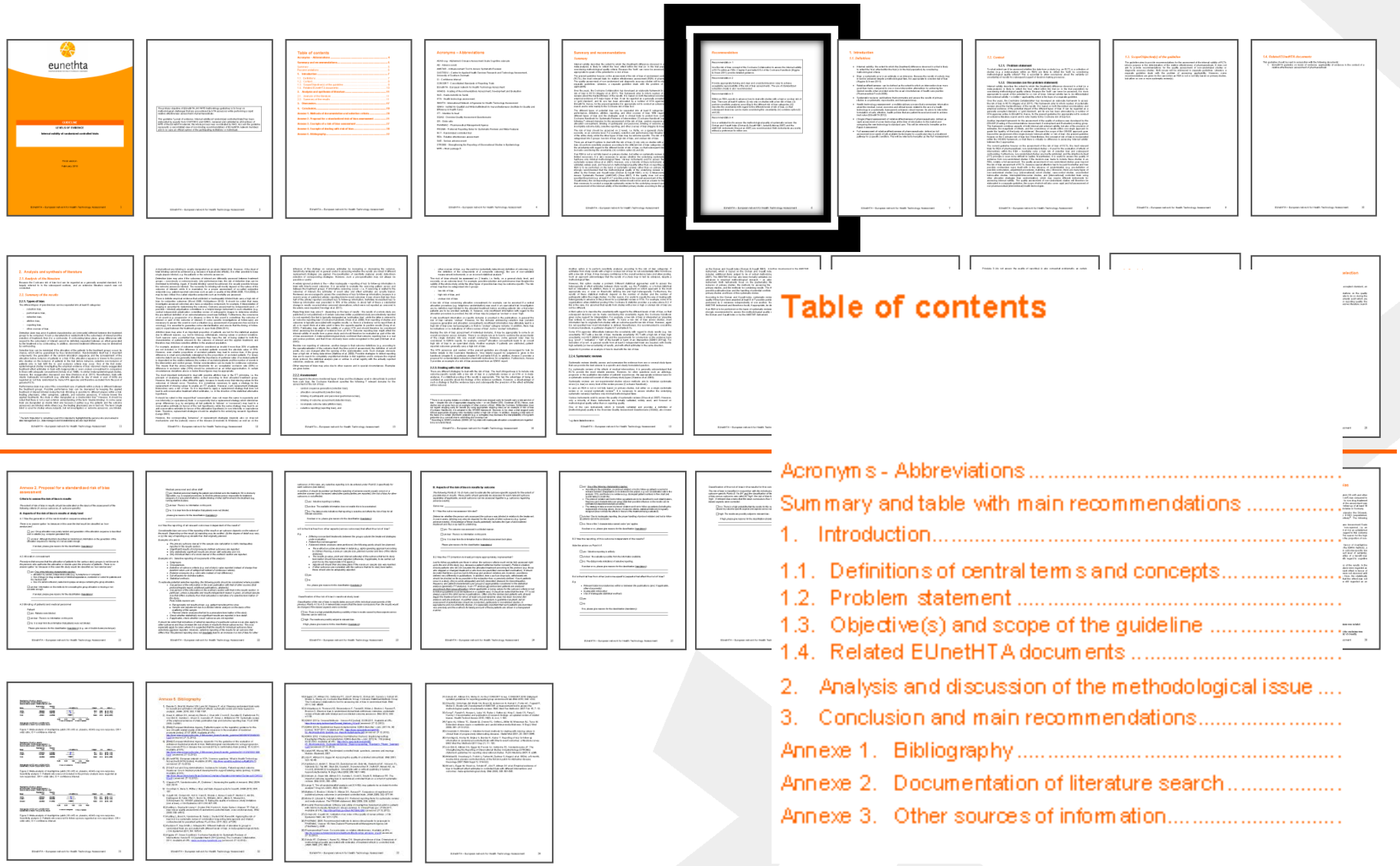
1. **Methododological guideline development in EUnetHTA – Introduction**
2. **Special aspects: Main guideline target group, guideline format, revised elaboration process, internal coordination**
3. **Guideline on Medical Devices**
4. **Questions of the guideline draft group**

EUnetHTA guidelines´ target groups

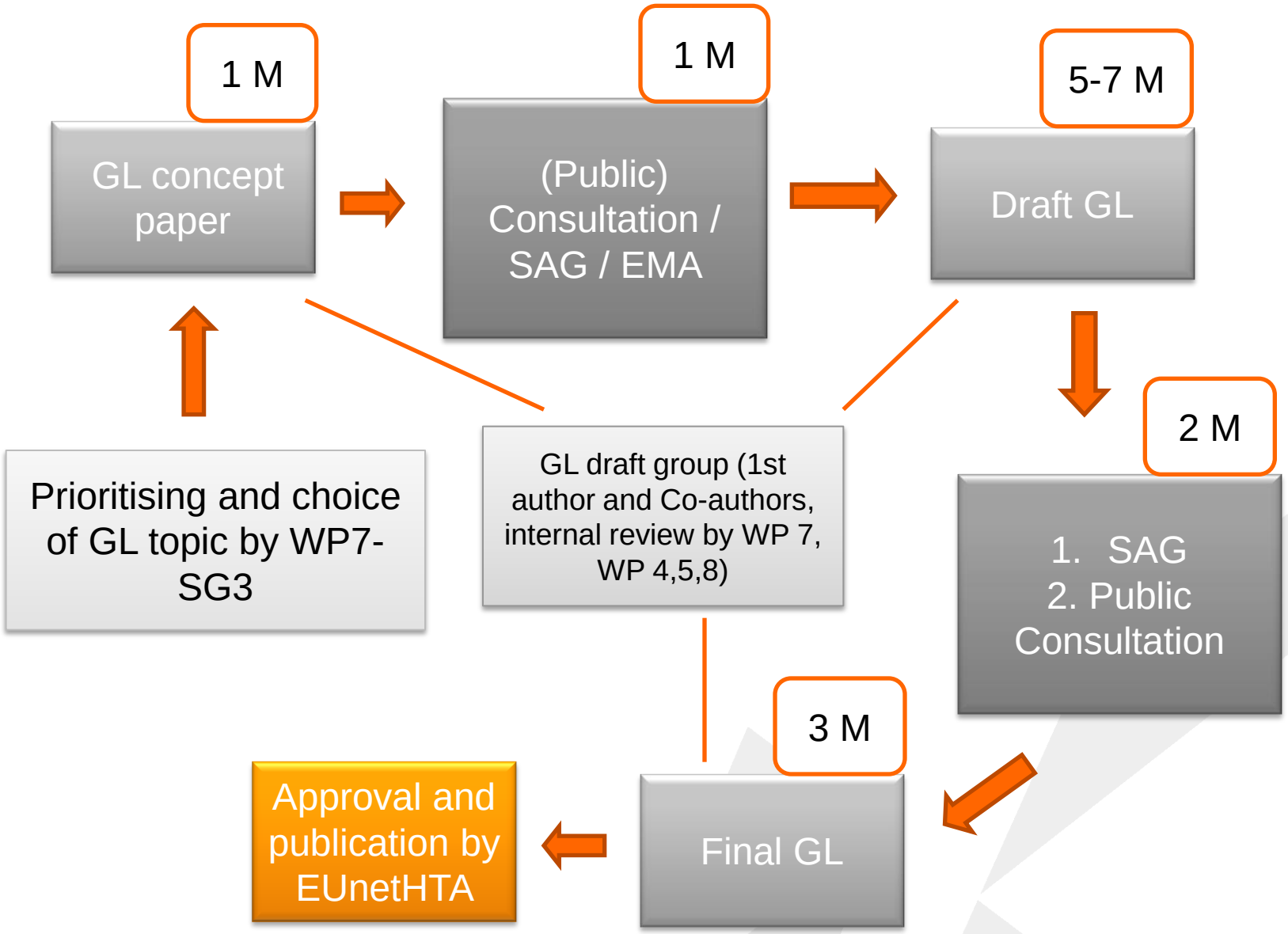
- **Main target group**: HT-Assessors in the EunetHTA member organisations
- Purpose: Guidance to cope with the methodological challenges encountered by HT-Assessors while performing relative effectiveness assessments of pharmaceutical, medical devices and other health technologies

- **Secondary target groups**: decision makers, researchers, industry, other stakeholders
- Purpose: Information on what is deemed
  - good quality of study design and conduct,
  - less biased, reliable and applicable evidence,
  - good reporting and synthesis of evidence,
  - and good practice of statistical data analysis in the context of HTA

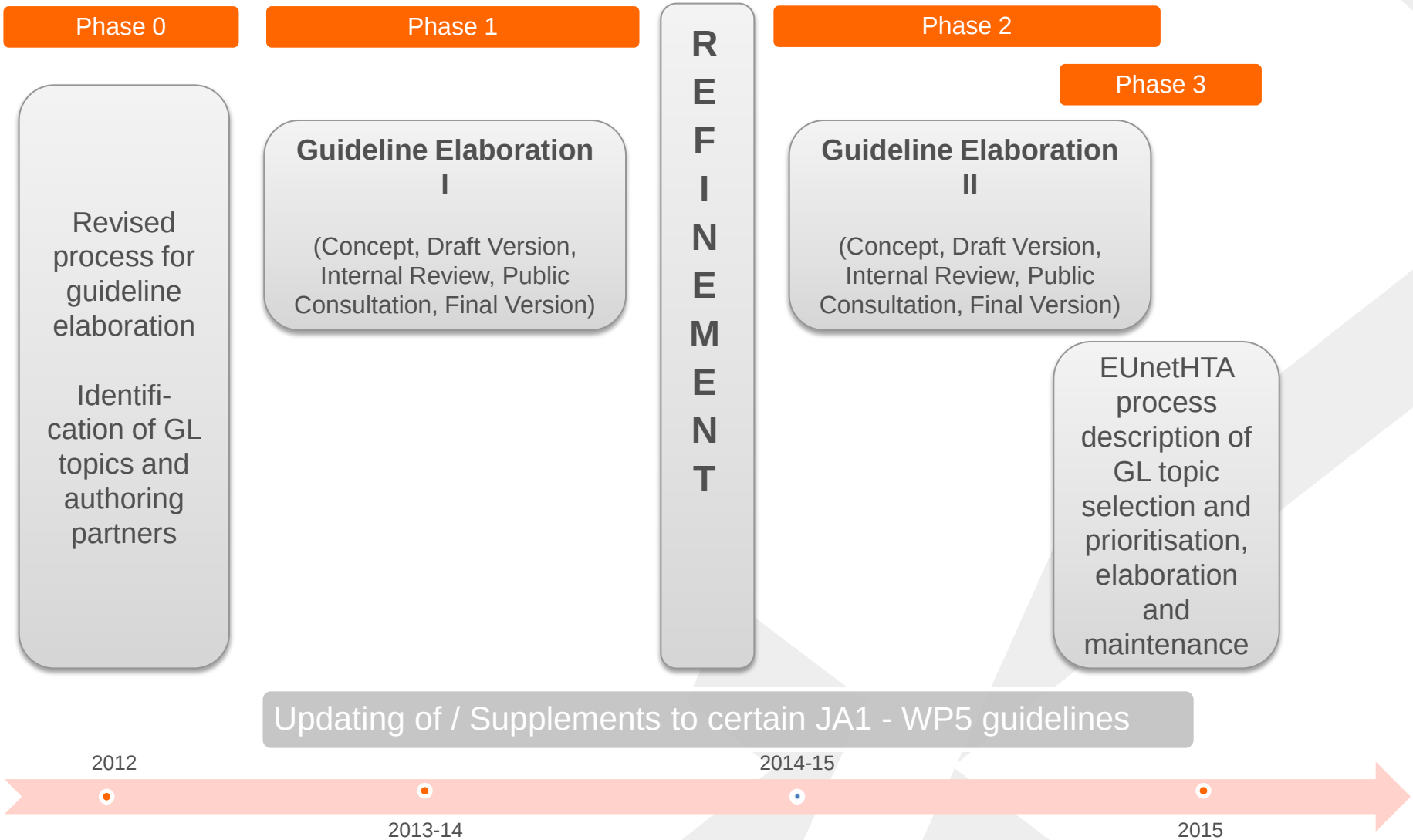
EUnetHTA Methodological Guidelines



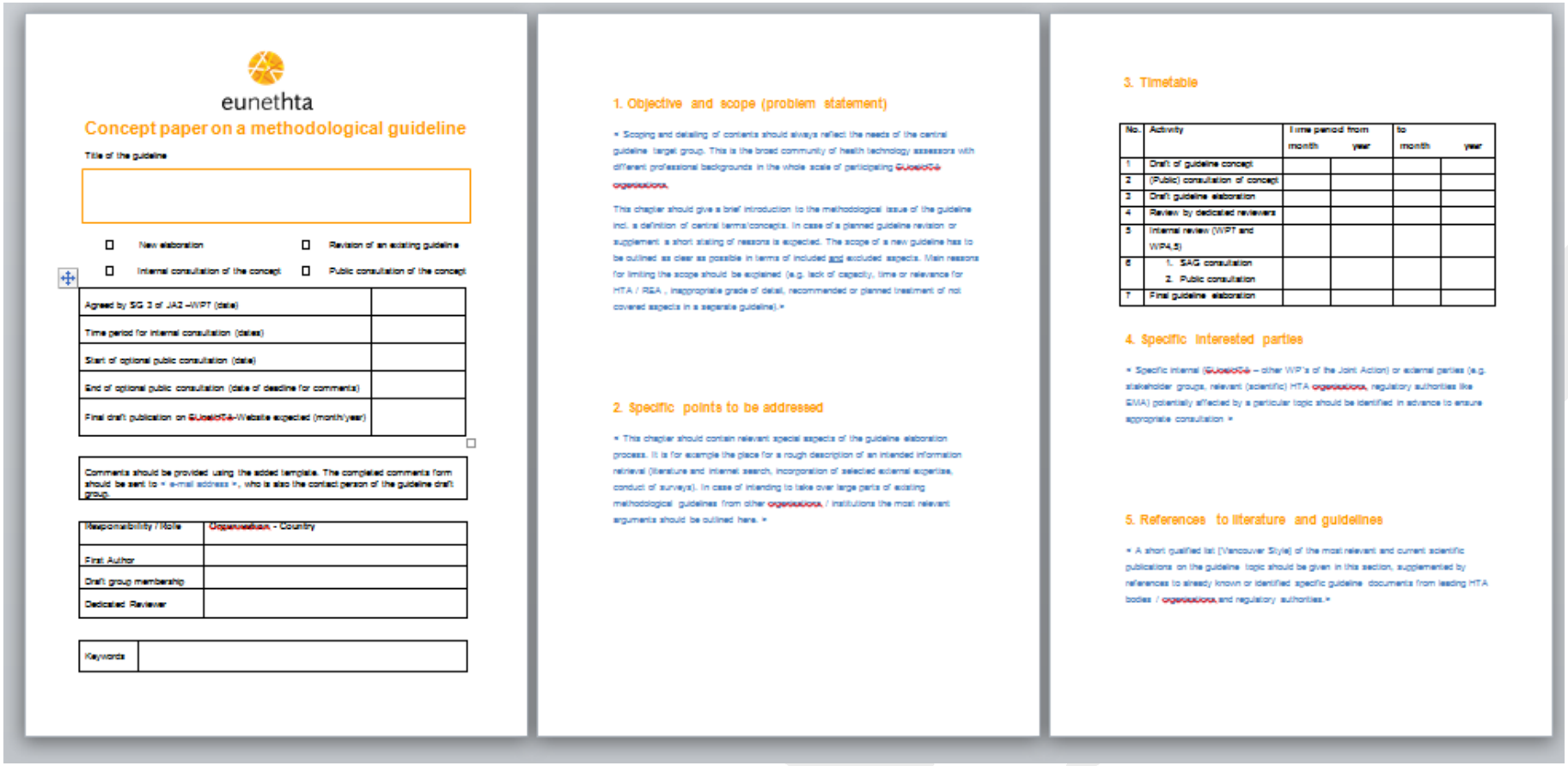
Revised elaboration process for EUnetHTA´s methodological guidelines (JA2)



JA 2 – WP7 – SG3 - Working process



Guideline concept (template)



eunethta

Concept paper on a methodological guideline

Title of the guideline

☐ New elaboration ☐ Revision of an existing guideline

☐ Internal consultation of the concept ☐ Public consultation of the concept

Agreed by SG 3 of JA2 –WP7 (date)	
Time period for internal consultation (dates)	
Start of optional public consultation (date)	
End of optional public consultation (date of deadline for comments)	
Final draft publication on ~~EUnetHTA~~-Website expected (month/year)	

Comments should be provided using the added template. The completed comments form should be sent to < e-mail address >, who is also the contact person of the guideline draft group.

Responsibility / Role	~~Organisation~~ - Country
First Author	
Draft group membership	
Dedicated Reviewer	

Keywords	

1. Objective and scope (problem statement)

< Scoping and detailing of contents should always reflect the needs of the central guideline target group. This is the broad community of health technology assessors with different professional backgrounds in the whole scale of participating ~~EUnetHTA~~ ~~organisations~~.

This chapter should give a brief introduction to the methodological issue of the guideline incl. a definition of central terms/concepts. In case of a planned guideline revision or supplement a short stating of reasons is expected. The scope of a new guideline has to be outlined as clear as possible in terms of included and excluded aspects. Main reasons for limiting the scope should be explained (e.g. lack of capacity, time or relevance for HTA / R&A , inappropriate grade of detail, recommended or planned treatment of not covered aspects in a separate guideline).>

2. Specific points to be addressed

< This chapter should contain relevant special aspects of the guideline elaboration process. It is for example the place for a rough description of an intended information retrieval (literature and internet search, incorporation of selected external expertise, conduct of surveys). In case of intending to take over large parts of existing methodological guidelines from other ~~organisations~~ / institutions the most relevant arguments should be outlined here. >

3. Timetable

No.	Activity	Time period from month	year	to month	year
1	Draft of guideline concept				
2	(Public) consultation of concept				
3	Draft guideline elaboration				
4	Review by dedicated reviewers				
5	Internal review (WP7 and WP4,5)				
6	1. SAG consultation 2. Public consultation				
7	Final guideline elaboration				

4. Specific interested parties

< Specific internal (~~EUnetHTA~~ – other WP's of the Joint Action) or external parties (e.g. stakeholder groups, relevant (scientific) HTA ~~organisations~~, regulatory authorities like EMA) potentially affected by a particular topic should be identified in advance to ensure appropriate consultation >

5. References to literature and guidelines

< A short qualified list (Vancouver Style) of the most relevant and current scientific publications on the guideline topic should be given in this section, supplemented by references to already known or identified specific guideline documents from leading HTA bodies / ~~organisations~~ and regulatory authorities.>

Coordination of SG3 activities (IQWiG – HAS)

- Coordination of the general process and six guideline teams
- Coordination between work package 7 and WP4, WP5, and WP8 (and EUnetHTA secretariat – WP1)
- Cross-linking to existing or EUnetHTA methods documents under development

1. Methododological guideline development in EUnetHTA – Introduction
2. Special aspects: Main guideline target group, guideline format, revised elaboration process, internal coordination
3. **Guideline on Medical Devices**
4. Questions of the guideline draft group

GL-TEAM „Medical Devices “

First author	Draft group members	Dedicated Reviewer
UMIT - AT	OSTEBA – ES G-BA – DE IQWiG – DE	IER – SL VASPVT – LT CVZ – NL HAS – FR

Features of the GL “Medical Devices” I

(draft group proposals, not final)

- **Main target group: Recommendations for those in EUnetHTA who evaluate studies to produce (Core model) HTA reports, or evaluate manufacturer´s submission files on medical devices**
- **Intention: Focus on HTA principles and methods which are specific for MD and refer to already existing standard methods for issues similar to those for other technologies (Referencing to standard HTA methods literature and existing EUnetHTA guidelines)**
- **Emphasis on differences in HTA of MDs concerning**
  - **user dependency / learning curves**
  - **dynamic, incremental technology development**
  - **Focus: therapeutic MDs**

Features of the GL “Medical Devices” II

(draft group proposals, not final)

- **No detailed recommendations on a hierarchy of evidence requirements, despite general principle of ascending level of required evidence with MD class and associated possible risks of patient harm**
- **Information basis (Cooperation with FP7 project MedtecHTA): literature search for WP 3 comparative effectiveness methods with focus on “implantables”, whenever possible, generalisation of derived recommendations to other MDs**
- **Referencing to reporting recommendations for study authors and appraisal tools (risk of bias)**
- **Referencing to manufacturer´s submission file template (SG4)**

Time plan (preliminary)

No.	Activity	Time period from month	year	to month	year
1	Draft of guideline concept	05	2014	05	2014
2	(Public) consultation of concept	06	2014	06	2014
3	Draft guideline elaboration	07	2014	01	2015
4	Review by dedicated reviewers	02	2015	02	2015
5	Internal review (WP7 and WP4,5)	03	2015	03	2015
6	1. SAG consultation 2. Public consultation	04	2015	05	2015
7	Final guideline elaboration	06	2015	09	2015

1. Methododological guideline development in EUnetHTA – Introduction
2. Special aspects: Main guideline target group, guideline format, revised elaboration process, internal coordination
3. Guideline on Medical Devices
4. Questions of the guideline draft group

Questions

1. What does the MD industry think about issues to be considered in the evaluation of Medical Devices?

2. How would the industry determine which MDs belong to the same class?

3. How should incremental development of the same device be dealt with in a HTA setting?

4. What are the preferred methods to take learning curves into account?

Thank you

Appendix 7:

EUnetHTA WP4 (Core HTAs) and WP5 Strand B (rapid REA of non-pharmaceutical technologies): Discussion on challenges and current processes: Presentation by Marina Cerbo (AGE NA.S)

HTA Expert meeting

Current experience and developments in HTA of medical technology in Europe

EUnetHTA WP4: Discussion on challenges and current processes

Brussels
May 8th 2014

Marina Cerbo
Agenas - Italy

WP 4 Lead Partner

agenas AGENZIA NAZIONALE PER I SERVIZI SANITARI REGIONALI

29 partners

from 18 countries

Objectives

Title	Description
Test the capacity of national HTA bodies to produce structured core HTA information (full core HTAs) together and apply it in national context (including collection of data on costs and overall efficiency of the production in the network).	A number of core HTAs and core HTA information based on the core model structure will be produced. The assessments produced will be used for local (i.e. national, regional) reports to inform decision-making. Data will be collected on costs and overall efficiency.
Implement, pilot and further develop models and tools as well as production processes to support collaborative production of core HTA information with reinforced secretariat and coordination function	To provide guidance and testing in identifying and organising collaborations between partners for setting up a specific collaboration (e.g. around an assessment topic).Coordinating function of various activity clusters and overall partnership coordination will be further developed and streamlined.

Deliverables	Deadline
1st Core HTA	M14 *(Nov 2013)*
2nd Core HTA	M23 *(Aug 2014)*
3rd Core HTA	M34 *(Jul 2015)*
Additional deliverables	
Methodological standards and procedures (MSP) for collaboration	M15 *(Dec 2013)*
20 national reports piloted	M36 *(Sep 2015)*

National reporting piloting

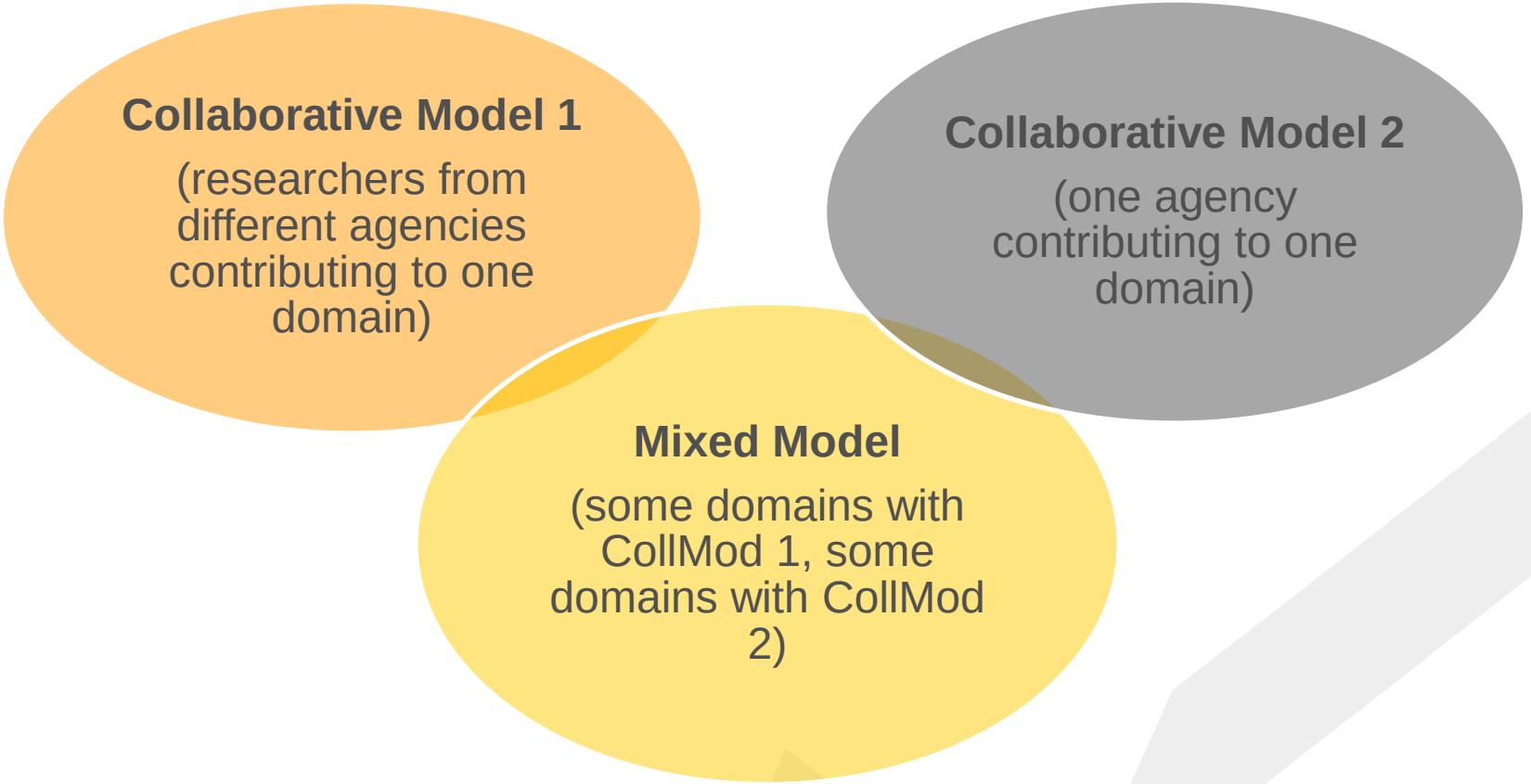
Partners are engaged in :

- producing both core HTA information and local information on prioritized topics, for national reporting.
- producing both core HTA information and local information on topics of interest for national reporting
- integrating core HTA information already available into national reports.

All the national pilots initiatives are notified to LP and monitored

Partners involved in national production gather also data for the evaluation work-package.

Collaborative models for the Core HTA reports production



- **Primary Investigator,** to coordinate the work and interact with Coordinator of the Project (Agenas)
- **Investigators,** to develop the work and interact with PI
- **Reviewers,** to review the document produced by each domain team

Collaborative models for the Core HTA reports production - examples

Coll Mod 1

- JA 1 Core HTA on **Prognostic Tests for Breast Cancer Recurrence**
- JA 2 Core HTA on **Use of Intravenous immunoglobulins for Alzeheimer's disease including Mild Cognitive Impairment**

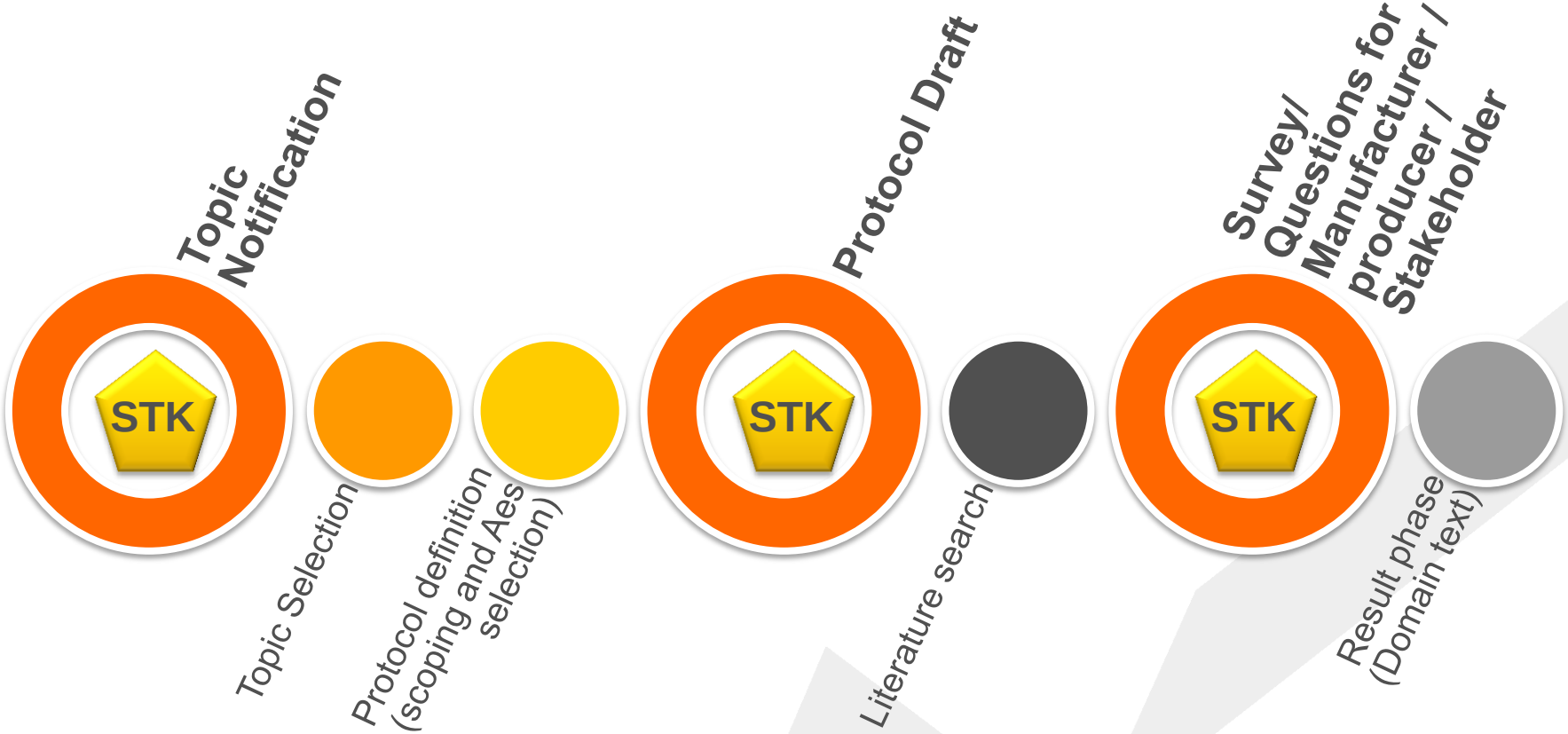
Coll Mod 2

- JA1 Core HTA on **Abdominal Aorta Aneurysm Screening**

Mixed Coll Mod

- JA2 Core HTA on **Fecal Immunochemical Test (FIT) versus guaiac-based fecal occult blood test (FOBT) for colorectal cancer screening**

Production phases for Core HTA – part 1



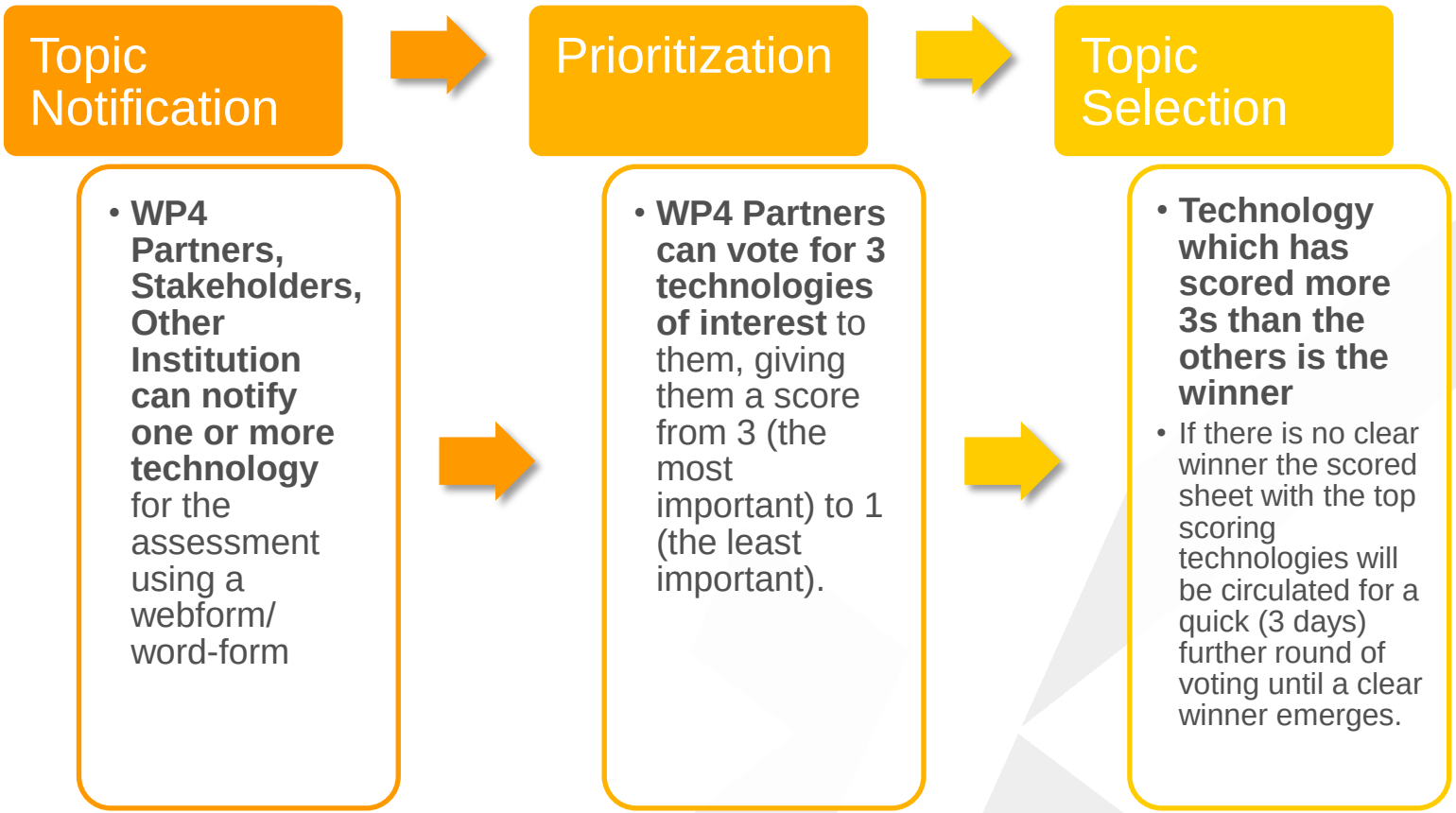
STK: Stakeholders

Topic Selection procedure

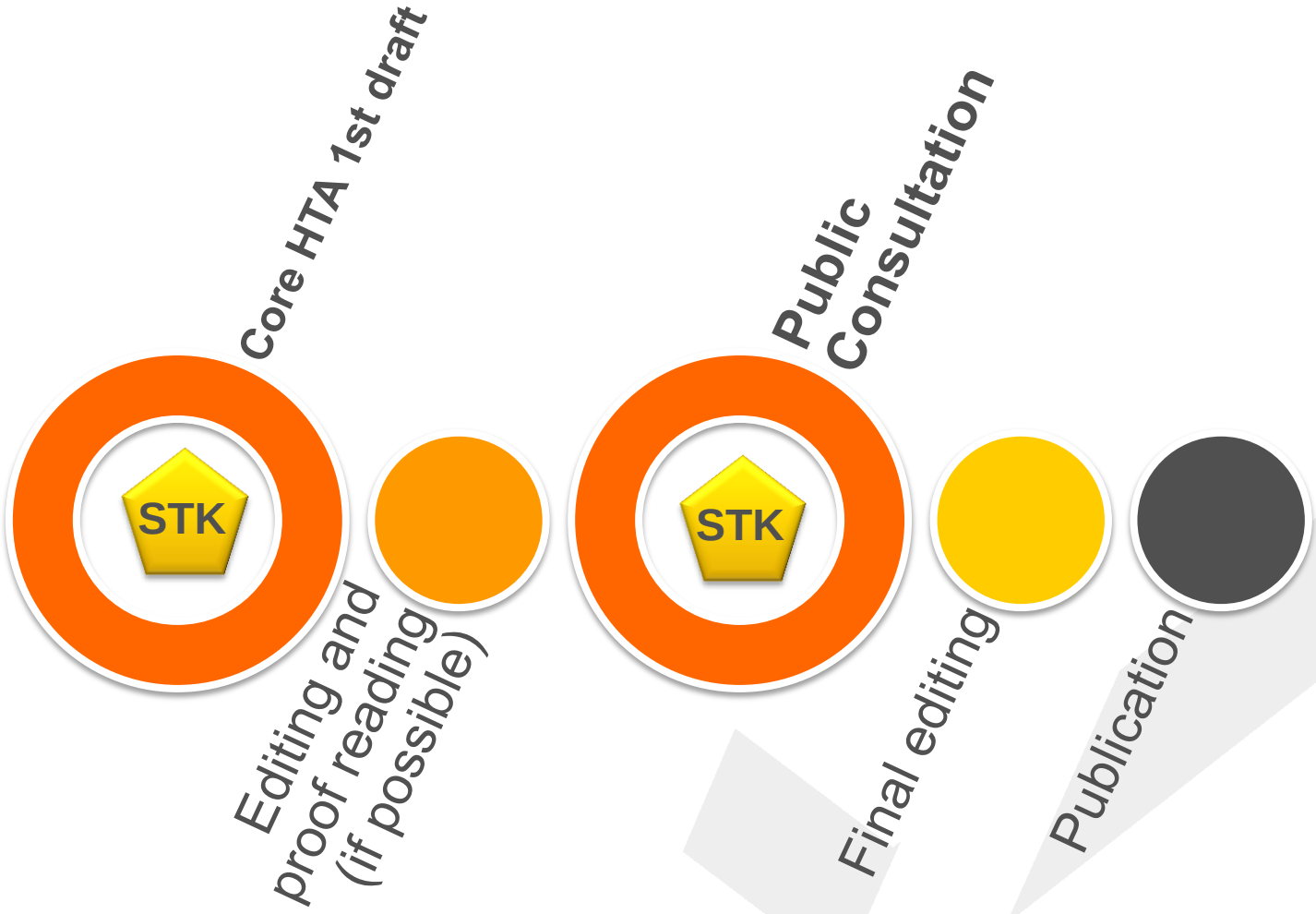
Who?

…a topic selection call will be made and feedback collected from WP4 partners, Stakeholders and other interested institution (DG Sanco), considering also results from the POP database.

(taken from WP4 3-year Work Plan)

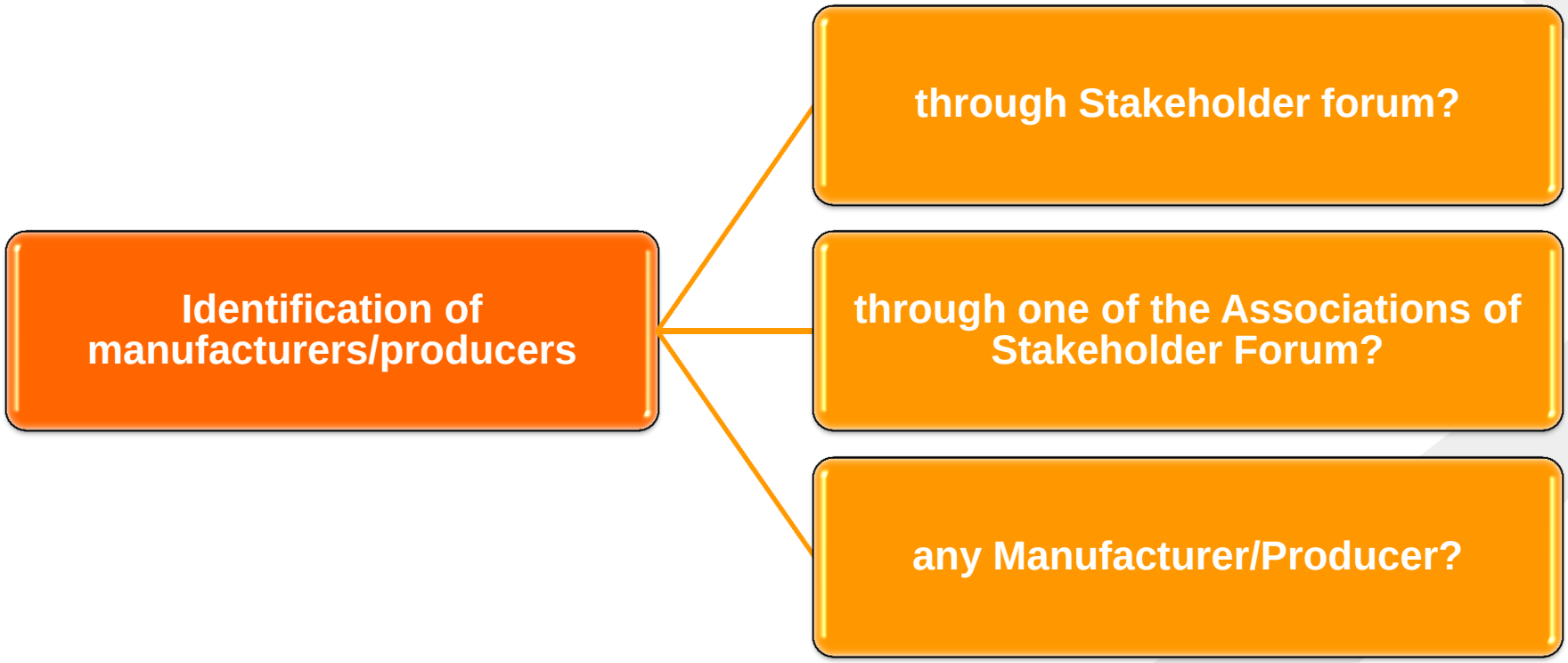


Production phases for Core HTA – part 2



STK: Stakeholders

Producer / Manufacturers involvement: issues



Criticality

- Low response rate

Thank you

For your attention

Appendix 8:

WP5 – Strand B Rapid Assessments of other health technologies such as medical devices, surgical interventions or diagnostics: Current processes and challenges: Presentation by Anna Nachtnebel (LBI-HTA)

WP5 – Strand B

Rapid Assessments of other health technologies such as medical devices, surgical interventions or diagnostics

Current processes and challenges

Brussels, 8 May 2014

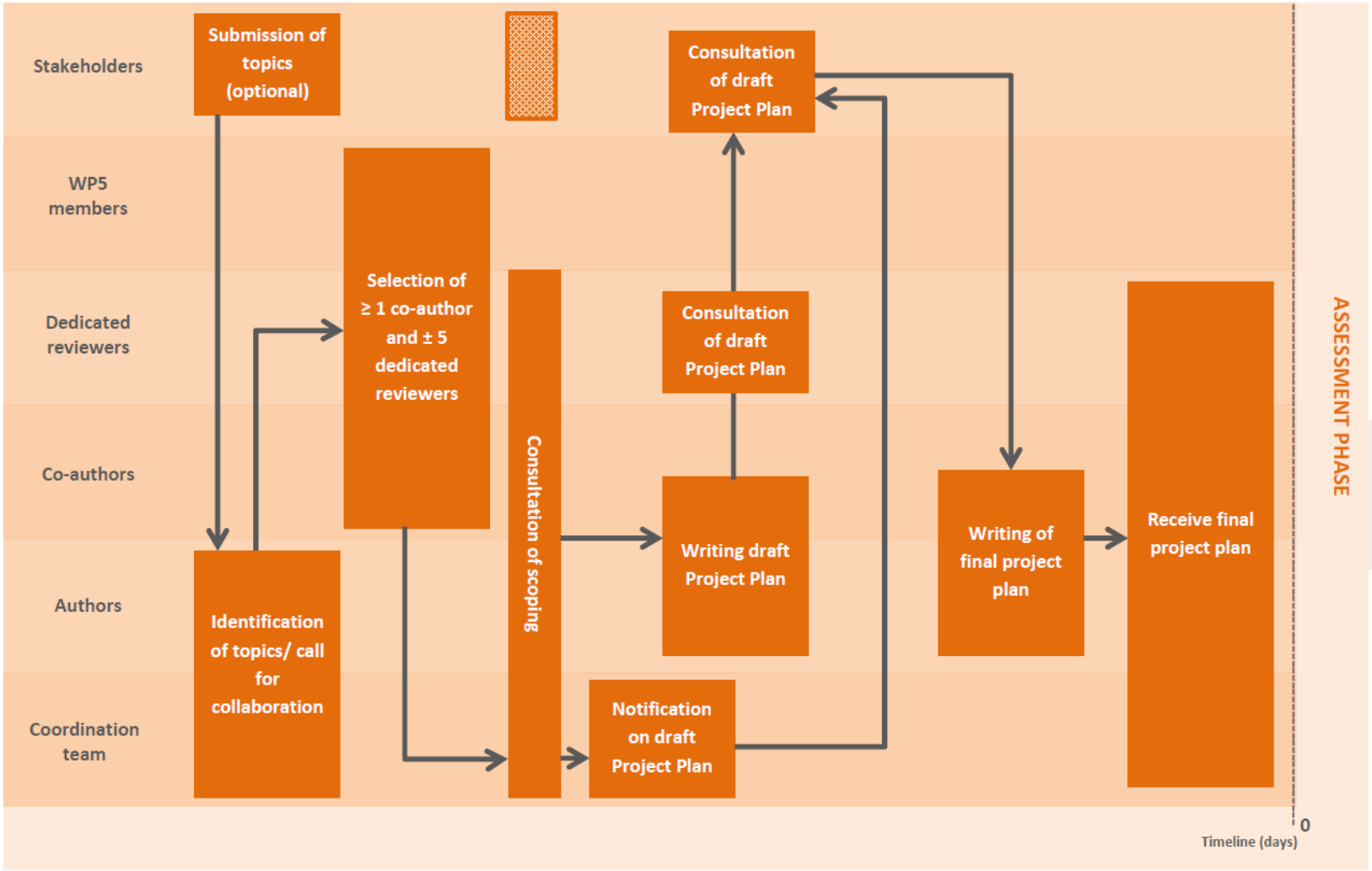
Ludwig Boltzmann Institute for Health Technology Assessment, Austria

Overview

- **Output**: ≥4 joint pilot rapid assessments, >2 national/local reports per pilot rapid assessment, adaptation of HTA Core Model for rapid REA to medical devices

- **Methods:** HTA Core Model for Rapid Relative Effectiveness of Pharmaceuticals but also relevant assessment elements from other HTA Core Models (e.g. screening, interventions), Guidelines

Processes: Scoping phase



Processes: Scoping phase

Topic selection:

1. **Call for collaboration**: authoring agency selects relevant topic(s) out of its own work programme, other members express their interest in acting as co-authors or dedicated reviewers

   Selection criteria:

   - Relevance for authors (reimbursement decision, request by stakeholders)
   - CE mark

2. **POP database**: overlaps in topics listed at POP

Processes: Scoping phase

Pilot team:

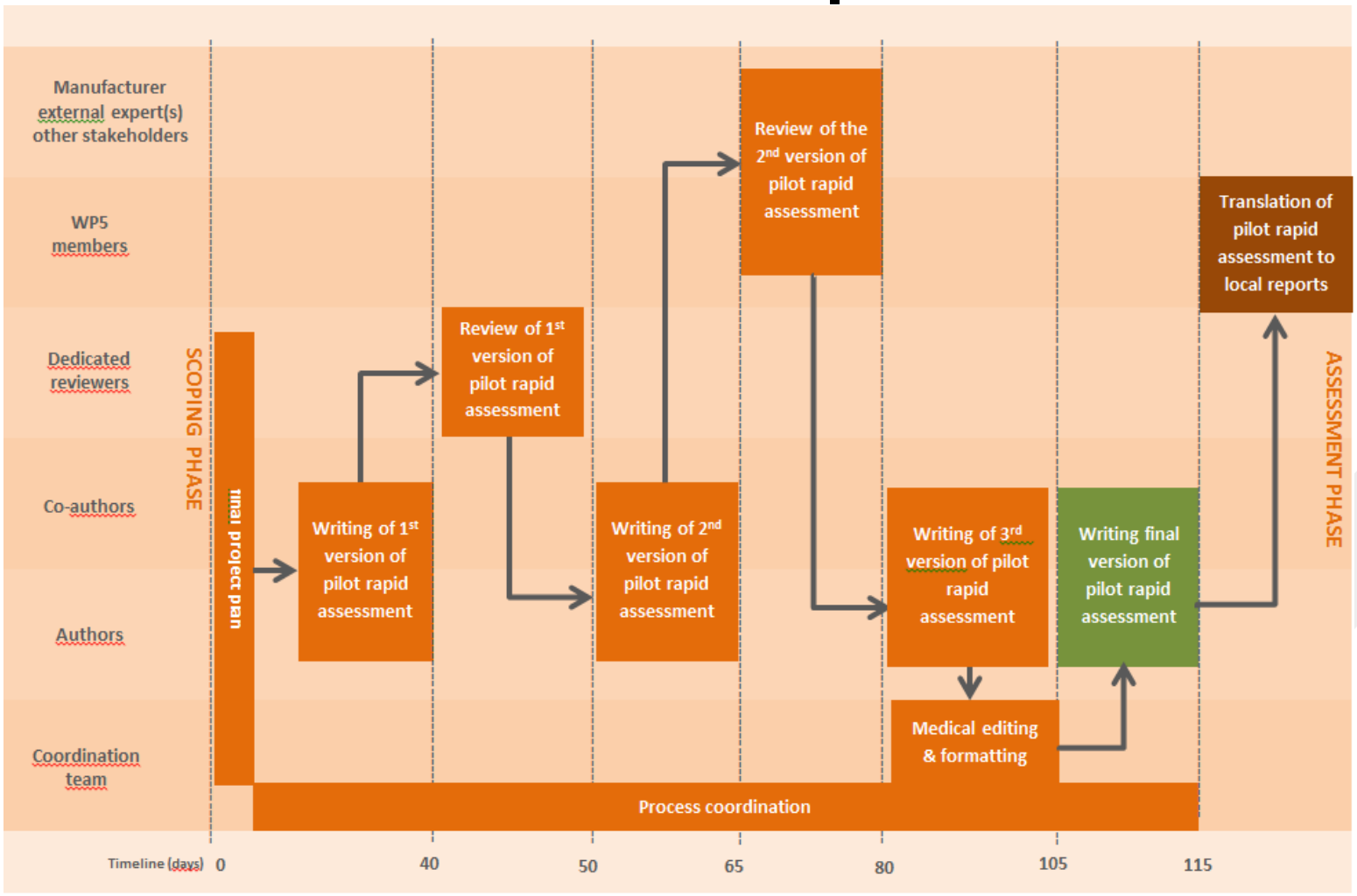
- first author(s) (from 1 authoring organisation or institution)
- co-author(s) (from ≥1 co-authoring organisation or institution)
- a pool of dedicated reviewers (from 2 – 5 reviewing organisations or institutions)
- at least 2 external reviewer(s)
- coordination team (LBI-HTA)

Consultation of draft project plan:

- With co-authors and dedicated reviewers
- Public consultation including Strand B members, manufacturers, SAG/SF

Final Project Plan: PICO(S), Project approach and method, (literature search, quality assessment tools, evidence table), Selection of assessment elements, Checklist for potential ethical, organisational, social and legal aspects, Timetable

Processes: Assessment phase



Processes: Assessment phase

Internal review of the 1st draft:

- Dedicated reviewers

External review of the confidential 2nd draft:

- ≥2 External clinical experts
- Manufacturer(s)
- Strand B members
- Patient representatives

Medical Editing of the 3rd draft

Challenges & adaptations

Topic selection:

→ indication-specific, not technology-specific

→ authors provide a rationale for topic selection

→ CE mark as selection criterion

→ planned: at least 2 topics will be proposed – selection based on expressions of interest by Strand B members

Identification of all relevant technologies and manufacturers:

→ CE mark: how to ensure that all relevant devices were identified?

→ we approach Strand B members, the SAG/SF and identified manufacturers (competing products) during scoping phase

Challenges & adaptations

Selection of external medical experts:

→ a minimum of 2 external clinical experts are involved in the process:

selection by authoring agency, request to European Medical Associations/members of guideline panels, SAG

→ experts are asked to disclose any potential conflict of interest (definition of COI regarding funding of studies etc.)

→ patient representatives: SAG

Timelines:

→ short timelines to review, especially the 2nd draft assessment

→ extension of timelines, but still rapid assessment (~ 6 months)

Challenges & adaptations

Manufacturer involvement:

1. Communication

→ generic e-mail addresses: sometimes the only option

→ identify contact persons at an early stage, reminders

→ should be both-sided, give and take‘ (information on evidence, on-going trials, changes in service provision,..)

2. Confidentiality

→ problems during RDN assessment regarding the circulation of the confidential 2nd version of the assessment; confidential evidence

→ no additional confidentiality agreements will be signed by EUnetHTA members

→ submitted evidence should be eligible for publication

Challenges & adaptations

3. Scoping Meetings

→ challenge: how to make sure all relevant manufacturers are identified in due time?

→ one meeting for all relevant manufacturers?

→ Potential ways forward:

- Learn from Strand A experiences
- Discussion points include available evidence, ongoing trials, relevant outcomes,..; submission file template as a basis?

Thank you

Any questions?

Conference, October 2014

Under the patronage of the Italian Ministry of Health

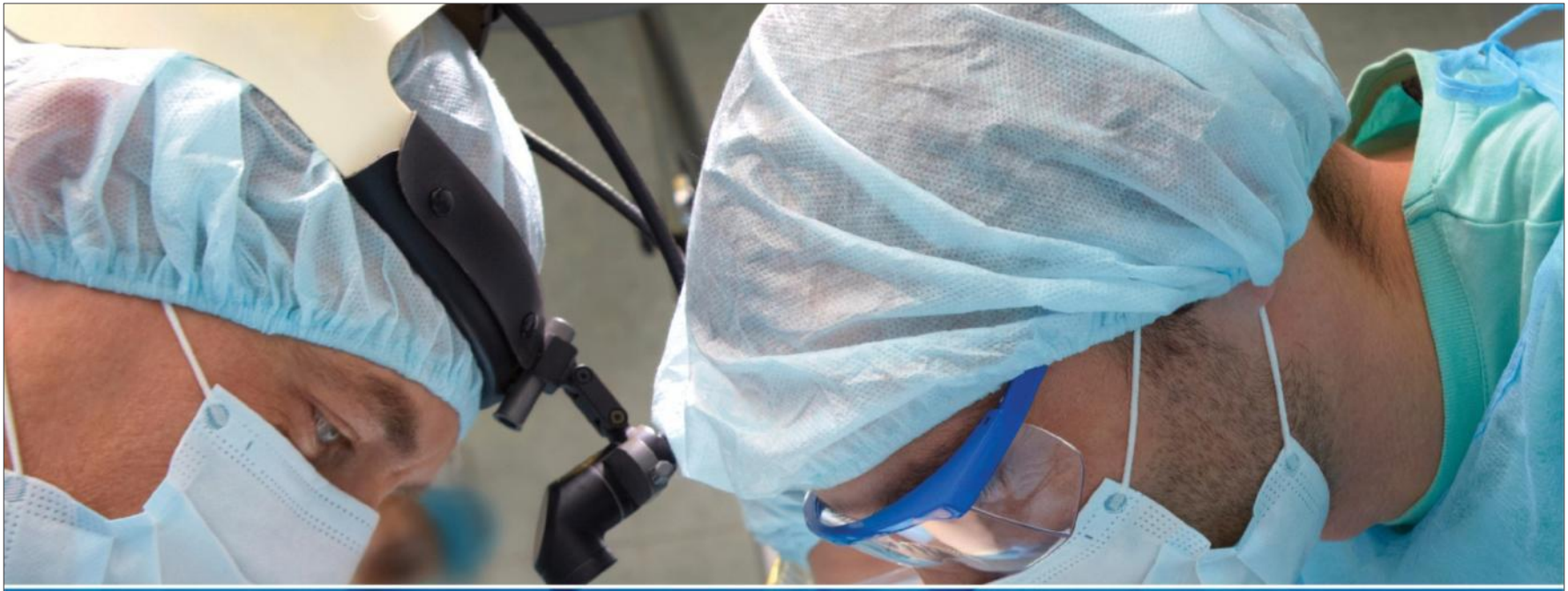
Conference website: **www.eunethta2014.it**

Appendix 9:

WP4 and WP5 Strand B experience: Presentation by Sebastian Gaiser (St. Jude Medical)

Eucomed
Medical Technology

www.eucomed.org



EUnetHTA WP5 Strand B: Discussion on challenges and current processes

Sebastian Gaiser, St Jude Medical (8 May 2014)

Looking back

- What is your view on the Rapid REA on Renal Denervation?

- What is your learning?

Looking back: Selection of Ren-D

- Why was Ren-D selected?
- Who needed this HTA at this time?
- Was there any urgency?

Looking back: Communication

- Why was only one Manufacturer approached by EUnetHTA at the beginning?

- Why was no Ren-D user (clinical expert) in the field of Hypertension and Renal Denervation approached by EUnetHTA?

Looking back: Timing

- The Ren-D EUnetHTA HTA was published on **December 19th 2013**

- On **January 9th 2014** one Manufacturer announced: „U.S. Renal Denervation Pivotal Trial Fails to Meet Primary Efficacy Endpoint While Meeting Primary Safety Endpoint”

Looking ahead – Communication

- Is there a need for a Kick-Off Meeting with Users (clinical experts) and Industry to discuss the Therapy and its evidence before conducting an HTA?

- Is there a need to actually see the therapy being applied?

Looking ahead – Role of Registries

- What role can registries / registry data play in Medtech Assessments?
- What shall we do when there is dominantly Registry Data available for a Medtech diagnostic or device?
- And what shall we do if this real life data shows good Outcome but no RCT exists?

Looking ahead – HTA Education

- Who needs to be educated in the future? (Physicians?, Industry?)

- Do we need a standardization of HTA Education in Europe?

Looking ahead – Trust

- How can we establish a trustful relationship between EUnetHTA and Industry to improve the process of Rapid Assessments?

Appendix 10:

WP7 SG1 Early Dialogues: Initial exchange of views and identification of the issues: Presentation by Francois Meyer (HAS)

Early Dialogues
EUnetHTA WP7 / SG1

HTA Expert Meeting on ***Current experience and developments in HTA of Medical Technology in Europe***
Brussels, Belgium (May 8th, 2014)

François Meyer MD
HAS, Work Package 7 Leader

European context

- European Union supporting/financing cooperation projects in the field of health technology assessment (HTA)
- Formation of a network of European HTA agencies to drive common action under the Directive on Patient's Rights in Cross border Healthcare[1]
- Pharmaceutical Forum of 2005-2008[2] established by the EC declared that "…anticipation of clinical data collection prior to the granting of marketing authorisations would facilitate and accelerate the HTA process…"

(1) http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:088:0045:0065:en:PDF

(2) http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/pharmaforum_final_conclusions_brochure_en.pdf

Purpose of Early Dialogues

- *'Key limitation: Uncertainties regarding clinical and economic evidence requirements' 'HTA bodies have not considered or aligned study design and strength of evidence expectations.."*
- Provide prospective and timely dialogues between health technology assessors and healthcare products developers during the development phase of medicinal products and medical devices
- Reduce the risk of production of data that would be inadequate to support the company's future reimbursement request
- Dialogue between HTA bodies to clarify and probably reduce differences in evidence requirements → work towards a greater alignment overall.

Early engagement in health technology assessment (HTA): available options

Single-HTA: HTA advice from one national HTA body

Multi-HTA: Cooperative advice from EU national HTA bodies

- Projects sponsored by European Commission
  - EUnetHTA early dialogues (2012-2013)
  - SEED project (2014-2015)
- Drugs: parallel EMA-HTA procedure

Principles of EUnetHTA Multi-HTA advice

- Voluntary activity of HTA bodies
- Non-binding
- Confidential
- Capacity building
- Exchanges between HTA bodies
  - Consensus
  - Different views
- No fees for industry

EUnetHTA Early Dialogues

- 2 preparatory pilots (2012) and 8 pilots (2013) on drugs
  - Coordinated and hosted by HAS, France
  - 12 HTA bodies and 9 companies
  - Both small and big companies
  - EMA invited as observer
  - One-day face-to-face meeting
  - 10 drugs in various therapeutic fields
  - **1 remaining ED to conduct for a medical device**

EUnetHTA Early Dialogues Main topics

- Population
- Comparator
- Design of the trial (duration, dosing)
- Endpoints
- Statistic analysis (subgroups, stratification)
- Economic data (population, comparator, model, utility values, resource utilisation)

EUnetHTA Early Dialogues

Outcomes

- Successful experience
  - Improvement of collaboration between partners
  - Improvement of process efficiency
- A survey was addressed to participants to refine the procedure
- Procedure was revised by partners taking into account results of the survey

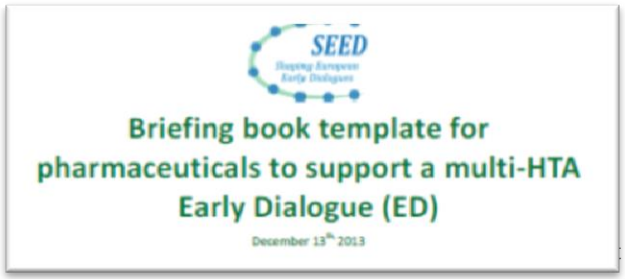
Related activity

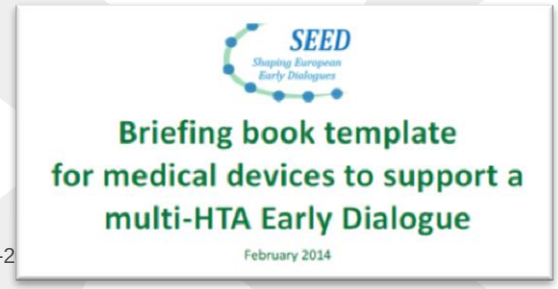
- Production of disease-specific guidelines
- Disease specific approach complementary to the product specific approach
- Not confidential
- First pilot ongoing on **osteoarthritis**.

SEED: Shaping European Early Dialogues

Context

- Project selected by European Commission (call for tenders)
- Consortium HAS (lead) + 13 partners (UK, Italy, Netherlands, Spain, Germany, Belgium, Austria, Ireland, Hungary)
- Regulators, payers, patient representatives as observers
- Procedures and templates for drugs and medical devices have been produced





SEED: Shaping European Early Dialogues

Tasks

- 10 early dialogues for drugs and for medical devices/diagnostics/procedures
  - 7 multi-HTA early dialogues (4 on drugs and 3 on devices)
  - 3 multi-HTA early dialogues with EMA (drugs only)
- One early dialogue per month between May 2014 and February 2015
- Feedback will be asked from all participants
- Proposal for a permanent model at the end of the project
- To be presented for discussion and comments at EUnetHTA plenary assembly

Project funded by the European Union in the frame of the EU Health Programme (2008-2013)

SEED: Shaping European Early Dialogues

Criteria for selection

- New drug or non-drug technology
- The technology should bring benefit to patients compared to existing methods
- Product in initial development phase
- Advice prospective in nature – only planned trials
- Only one indication per product can be discussed

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

SEED: Shaping European Early Dialogues

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

Exchanges among HTA bodies

- E-meeting to identify the need for additional information or clarification in the briefing book
- Written draft positions of each HTA body exchanged
- 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

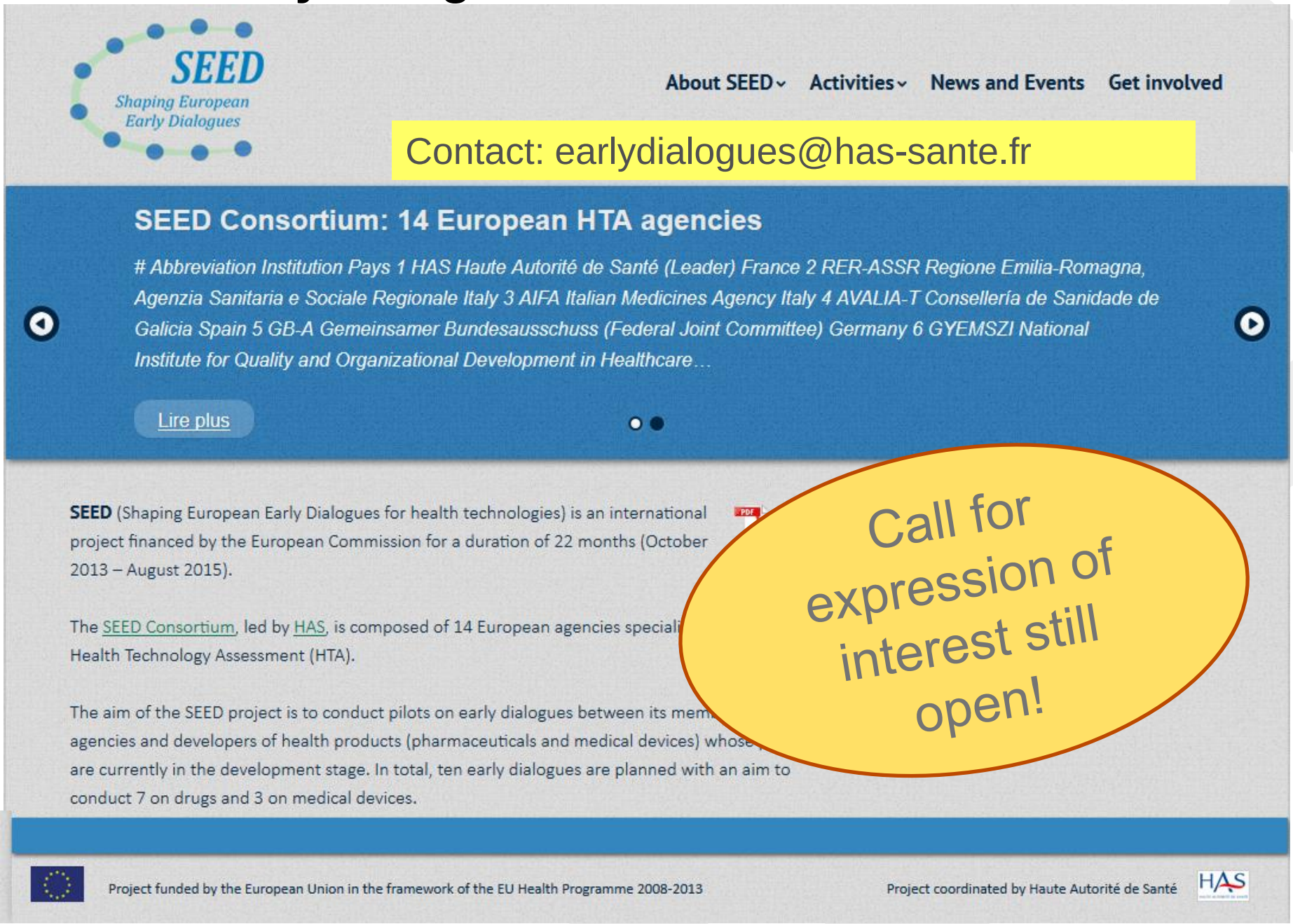
SEED: Shaping European Early Dialogues

Procedure

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

  - Meeting: 2-hr discussion among HTA bodies followed by 3-hr discussion with the company focused on divergent views
- Outcome: Minutes of the meeting produced by the company, reviewed by participating HTA bodies

www.earlydialogues.eu



Relative merits of Existing EUnetHTA Pilots

Across Pharmaceuticals and Medical Technologies

Sector	Rapid Relative Effectiveness Assessments	Early Dialogues
Pharmaceuticals	HTA is routine activity to access market Collaboration could reduce duplication Clear value in exploring	HTA is routine access procedure Therefore HTA Evidence routinely required
Medical Technologies	HTA is not a routine activity to access market Reimbursement often by procedure & Procurement (funding) often local What would 'collaboration' inform?	HTA is not a routine process to Funding & Reimbursement Early dialogues with few exceptions do not inform an access point

COCIR

edma
DIAGNOSTICS FOR HEALTH

Eucomed
Medical Technology

Potential value of EUnetHTA programmes

according to COCIR EDMA EUCOMED

	Pharma	Medical Devices	IVD's	Medical Imaging & Health ICT
Core HTA			?	?
Rapid REA			?	?
Early Dialogue			?	?

Clear decision points for EUnetHTA activities to inform in pharmaceutical access pathways

The existing EUnetHTA activities do not 'map' to consistent decision points for Medical Technologies access pathways

Questions from COCIR EDMA Eucomed

Discussion Questions on Early Dialogues

- Strategically – Is there a role in the 'access pathway'
  - Does relevance vary by type of technology?
    - Medical device category, diagnostics etc.?
  - Does the role of collaborative HTA need to be addressed before scope of early dialogue?

- Tactically - Lack of capacity where there is existing demand
  - Pharmaceuticals

Thank you

Appendix 11:

WP7 SG4: Template development for medical devices: Presentation by Zoe Garrett (NICE)

EUnetHTA WP7 SG4

Manufacturers' submission templates to support production of core HTA information and rapid assessments

Zoe Garrett

National Institute Health and Care Excellence

Introductory words – context setting

- Aim of WP7 SG4: to develop a submission template that includes the evidence requirements from European HTA organisations and reflects the HTA Core Model, to support production of core HTA information and rapid assessments.
- Could be used to support national HTA processes in European countries, and where appropriate, joint assessments.
- Starting point: all current national evidence requirements across Europe
  - Eventual customer: national agencies that make reimbursement decisions
- Ideal situation: final template could be used by any country for their HTA.
  - addresses the questions that individual national agencies ask

Introductory words (cont.)

- This session focuses on the practical, technical issues of
  - Generating a complete set of evidence requirements for REA
  - Dealing with the challenge of packaging them all in one template.

- Link to the WP5 pilots – step in developing the submission template

- EUnetHTA has no authority to stipulate the use of a submission template by any national agency, or that any national agency must adapt their existing practice in any way.
- Work to promote use of the EUnetHTA tools is an important future step, but outside the remit of SG4 and the discussions today

Collection of evidence requirements

Evidence requirements requested from 33 countries

30 countries responded

Confirmation of evidence requirements from 27 countries (28 programmes)

12 had device-specific evidence requirements

7 had evidence requirements not device specific

9 had no standardised evidence requirements

Evidence requirements for devices

Non-device specific evidence requirements	Device-specific evidence requirements	No evidence requirements	No confirmation of requirements
England (TA)	England (MTEP)	Lithuania	Greece
Croatia	Turkey	Luxembourg	Cyprus
Estonia	Switzerland	Malta	Portugal
Ireland	France	Romania	Finland
Latvia	Germany	Scotland	Denmark
Norway	Hungary	Spain	Bulgaria
Poland	Netherlands	Austria	
	Slovenia	Russia	
	Sweden	Italy	
	Belgium		
	Slovakia		
	Czech Rep		
N=7	N=12	N=9	N=6

Methods of analysis

- Framework developed to categorise the information in the evidence requirements
- Each set of national evidence requirements ‘data extracted’ twice (that is, information in the evidence requirements coded under headings in framework)
- Any differences between the pairs of data extractions reconciled to create a final version
- Pieces of information coded under the same heading counted, to enable:
  - Analysis of similarities and differences
  - Identification of range of information requested

Example of analysis

From France:

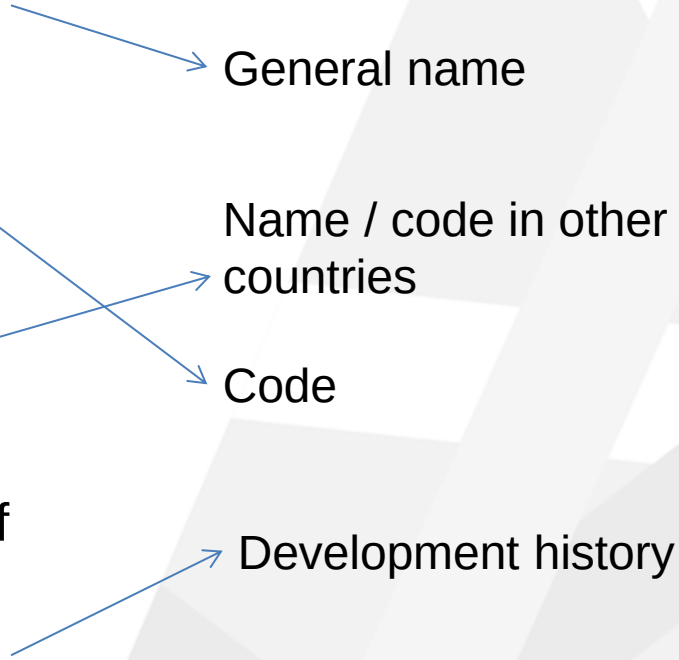
Name of the product or service

Commercial models and references concerned by the application

Current name or commercial references of the product in

France, within EU, other countries

Development history: state of the art in field, development stages, successive improvements and origins of these improvements.



General findings

- Varying level of details across the national evidence requirements: specific questions, general headings, checklists of documents
- Some templates reflect all medical devices, some are for only specific types of device
- Less guidance on completing submissions and fewer English language documents than for pharmaceuticals
- Completed template only one part of the submission package (as for pharmaceutical submissions)
- Safety and clinical effectiveness considered together (same searches, study description and results sections)
- Similar information requested for domains 1,3 and 4 for pharmaceuticals and medical devices
- More differences in information requested in domain 2

Template development

- Starting point the draft submission: template for pharmaceuticals
- Using current analysis identified whether existing information in the template was appropriate or needed to be amended
- Development of de novo sections of the template that were device specific
  - mainly domain 2 technical features of technology
  - also domain 3 manufacturer vigilance data

Introduction to the submission template

- Uses the 4 CORE model domains:
  1. Health problem and use of the technology
  2. Description and technical characteristics of the technology
  3. Safety
  4. Clinical effectiveness
- Clinical effectiveness will be discussed before safety as submission templates follow this order
- For each domain SG4 WP7 have developed a series of modules
- Each module has a group of questions or headings: SG4 WP7 developed questions and headings using the information from the national evidence requirements

1. CORE model domain
   - 1.1 Modules – related to a CORE model topic or domain methodology
   - Questions – related to CORE model assessment element issues and clarifications

Introduction to the submission template (cont)

- A module (and its questions) can:
  - Be generic and suitable to all applications, device-specific or pharmaceutical-specific
  - Request nationally specific information or information that could be relevant across Europe
- A set of modules will form the template for an application e.g. a pharmaceutical or a medical device, in a hypothetical scenario:
  - a new pharmaceutical uses modules 1.1, 1.2 1.3, 2.1, 2.2, 2.3 etc
  - a licence extension uses modules 1.1, 1.2, 1.5, 2.1, 2.2, 2.3 etc
  - a medical device uses modules 1.1, 1.2, 1.3, 2.4, 2.5, 2.6 etc
  - possibility of developing modules for different types of medical device

1. Health problem and use of the technology

	Modules	Relation to CORE model
1.1	Overview of the disease or health condition	Topic: Target condition
1.2	Effects of the disease or health condition on the individual and society	
1.3	Target population	Topic: Target population
1.4	Current clinical management of the disease or health condition	Topic: Current management of condition
1.5	Current use of the technology and comparator(s)	Topic: Utilisation

Modules relating to target condition and target population

1.1 Overview of the disease
- Describing the health problem the technology is used for and classification of disease
- Risk factors, course and prognosis of disease
- Estimates of incidence and prevalence of disease

1.2 Effects of the disease on individual and society
- Symptoms and consequences of disease for individual
- Burden of disease for society
- Aspects of burden targeted by technology

1.3 Target population, to include
- Definition
- Place in care pathway and justification for target population
- Number of people in the target population

Modules relating to use of technology and current management of condition

1.4 Current management of the condition

- Aims of current management, current management strategies and differences in management at different disease stages
- Variations in management and unmet needs
- List of alternatives to the treatment
- How the technology may meet unmet needs and change clinical practice

1.5 Current use of the technology and comparator

- Experience and scale of current use of the technology in clinical practice
- Scale of use of each comparator

2. Description and technical characteristics of the technology

	Modules	Relation to CORE model
2.1	Overview of the technology and comparators	Topic: Features of the technology
2.2	Detailed characteristics of the technology	
2.3	Regulatory status	Topic Regulatory status
2.4	Reimbursement status	
2.5	Details of manufacture, distribution, follow up	Topic: Features of the technology
2.6	Duration of life, guarantees and warrantees	
2.7	Procedures required to use the technology	Topic: Investments and tools required to use the technology
2.8	Personnel and tools required to use the technology	
2.9	Investments, disinvestments and changes in services	

Modules relating to features of the technology

2.1 Overview of the technology and comparators
- Product name, reference codes, manufacturer

2.2 Detailed characteristics of the technology
- Characteristics, package contents
- Different models available and development history
- Mechanism of action

2.5 Details of manufacture, distribution and follow up
- Manufacture, distribution channels and maintaining availability
- Spare parts, replacements, repairs
- Maintenance and servicing

2.6 Duration of life, guarantees and warrantees
- Lifetime of the medical device and/or parts of the device
- Guarantees and warrantees

Modules relating to regulatory and reimbursement status

2.3 Regulatory status of the technology and comparators

- Authorisation status in other countries
- Dates of approval, indications, contraindications
- Launch information

2.4 Reimbursement status of the technology and comparators

- Reimbursement status in other countries
- Recommendations and restrictions

Modules relating to tools, personnel and investments

2.7 Procedures required to use the technology

- Only for medical devices that require a procedure
- Description of procedure, technical platform, anaesthesia, comparison of procedures where more than one exists

2.8 Personnel and tools required to use the technology

- People who administer the technology
- Skills required to administer the technology (including training and quality assurance measures)
- Equipment and supplies required

2.9 Investments, disinvestments and changes in services

- Additional infrastructure, human resources, tests, investigations and equipment needed and possible disinvestments
- Changes to other programmes (for example rehabilitation), and impact on other services

4.Clinical Effectiveness

	Modules	Relation to CORE model
4.1	Identification and selection of studies	Relation to CORE model domain methodology Results of studies relevant to CORE model topics: Mortality; Morbidity; Change-in management; Health related quality of life; Patient satisfaction
4.2	Relevant studies	
4.3	Characteristics of studies	
4.4	Individual study results	
4.5	Risk of bias study level: RCTs	
4.6	Risk of bias study level: non-RCTs	
4.7	Risk of bias outcome level	
4.8	Methods of evidence synthesis	
4.9	Conclusions on clinical effectiveness	Topic: Mortality; Morbidity; Change-in management; Health related quality of life; Patient satisfaction
4.10	Subgroup analysis	Relation to CORE model domain methodology
4.11	Strengths and limitations	

Modules relating to identification and appraisal of studies

4.1 Identification and selection of studies

- Search strategy, databases, limits, inclusion and exclusion criteria

4.5 Risk of bias study level: RCTs

- Includes questions from EUnetHTA guideline on risk of bias: randomisation, blinding, allocation concealment etc

4.6 Risk of bias study level: non-RCTS

- Determination of treatment group, minimisation of bias, comparability of groups at baseline etc
- To be updated following work of WP7 SG3

4.7 Risk of bias outcome level

- Includes questions from EUnetHTA guideline on risk of bias: blinding, ITT, selective outcome reporting

Modules relating to study characteristics

4.2 Relevant studies

- List of relevant studies and administrative details, study ID, dates, conflicts of interests, status, linked publications

4.3 Characteristics of the studies

- Aims, study population, intervention, comparator, study design, follow up, outcome measures
- Study methodology, method of randomisation, allocation concealment, statistical analysis etc

4.4 Results of individual studies

- Power, withdrawal, baseline comparability
- Clinical outcomes data

Modules relating to synthesis of evidence

4.8 Methods of synthesis

- Approach to synthesis and justification of approach
- Studies and outcomes included
- Methods used

4.9 Conclusions on clinical effectiveness

- Effects of treatment versus comparator on mortality, morbidity, disease progression, management, QoL and patient satisfaction

4.10 Subgroups

- Subgroups considered and justification of these
- Methods of analysis and findings

4.11 Strengths and Limitations

- Internal validity of evidence base and consistency of effects
- Relevance of the evidence base to assessment
- References EUnetHTA guideline on external validity

3.Safety

	Modules	Relation to CORE model
3.1	Details of the studies (safety-specific information)	Related to domain methodology Results of studies includes study data relevant to CORE model topic patient safety
3.2	Results of the studies (safety-specific information)	
3.3	Study quality (safety specific information)	
3.4	Methods of evidence synthesis (safety)	
3.5	Manufacturer vigilance data (devices)	Topics: Patient safety, Occupational safety and Environmental safety
3.6	Conclusions on patient safety	
3.7	Strengths and limitations	Related to domain methodology

Study identification written up in clinical effectiveness section

Modules relating to domain methodology

3.1 Details of the studies

- Safety specific information only
- Details of studies providing safety data
- Methods of collecting safety endpoints

3.2 Results of studies

- Safety endpoint data

3.3 Assessment of study quality

- Risk of bias in safety endpoints (EUnetHTA guideline)

3.4 Methods of evidence synthesis

- Same section as clinical effectiveness

Modules relating to assessment elements

3.5 Manufacturer vigilance data

- List of serious incidents and other incidents
- Measures taken as a result of incidents
- Limitations or measures to be taken to reduce risk of adverse events

3.6 Conclusions on patient safety

- Harms to patient from use and administration of technology
- Differences in risks between technology and comparators
- Dose relationship, onset, changes over time, susceptible patient groups
- Risks caused by behaviour of people who apply or maintain technology

3.7 Strengths and limitations

- Same section as clinical effectiveness

Discussion and Questions

- Are our analyses complete?
- Is there anything we are missing?
- Are there any issues with any of the evidence requirements?