What is the added value of more HTA collaboration in Europe?

EUnetHTA JA3 - more than a year later

Wim Goettsch

Director EUnetHTA JA3 Directorate

RedETS (Tenerife), December 4, 2017

eunethta

European Commission

Outline

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

European Commission

EU cooperation on HTA

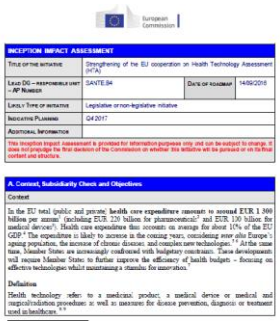
HTA Network

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

Synergy and complementarity

EUnetHTA Joint Action

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



New HTA Initiative

- **Cooperation beyond 2020**
- Inception Impact Assessment
- Description of the status quo
- Options for the future

EU initiative on HTA

Policy options (suggestion EC end 2017)

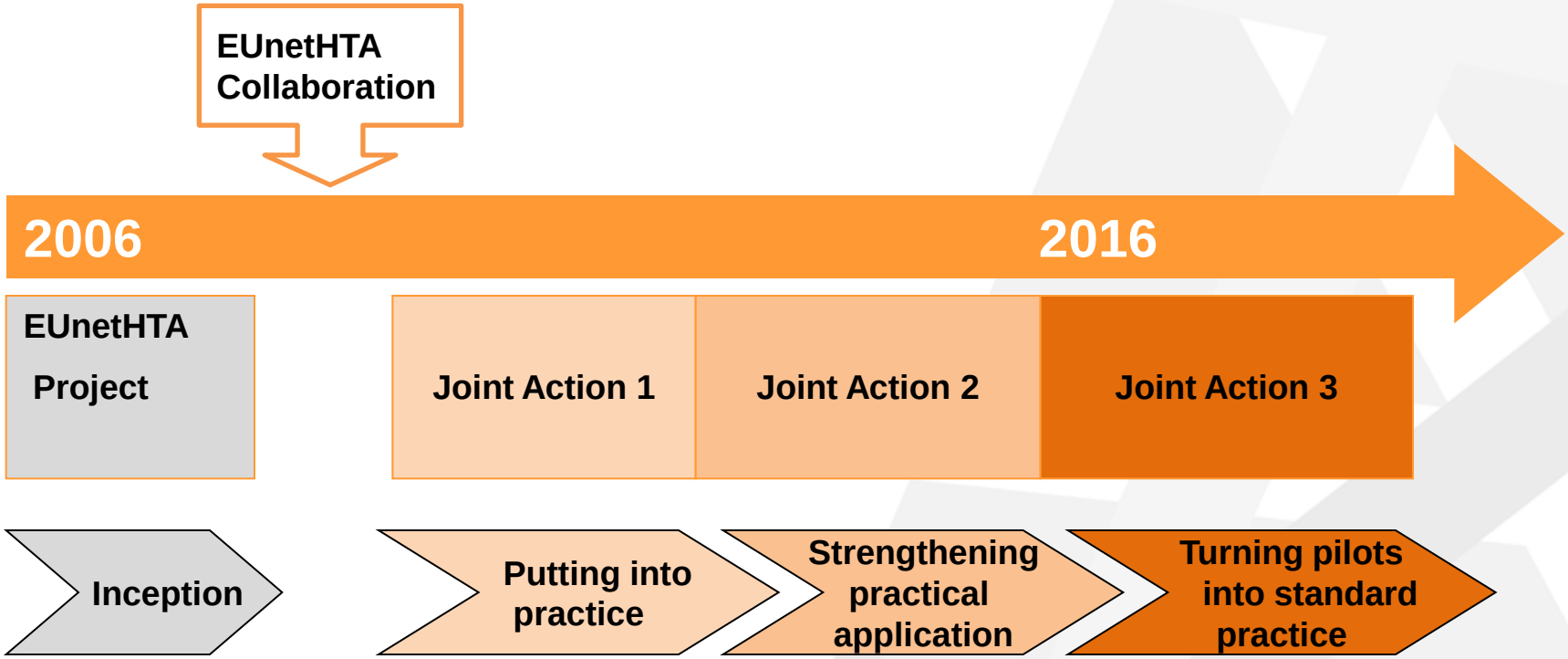
Option 1	Option 2	Option 3	Option 4	Option 5
Status quo – **voluntary cooperation**	**Long-term voluntary cooperation** (beyond 2020)	Cooperation through the **collection, sharing and use of common tools and data**	Cooperation on **production of joint REA (relative effectiveness assessments) reports**	Cooperation on production of **joint Full HTA reports (REA+ economic)**
Non-legislative / *voluntary*		**Legislative / *voluntary* + *mandatory***		

+ Issues to be addressed

- Scope
- Funding mechanism
- Coordination/ secretariat

***Inception Impact assessment available at:**
http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf

EUnetHTA
Historical timeline

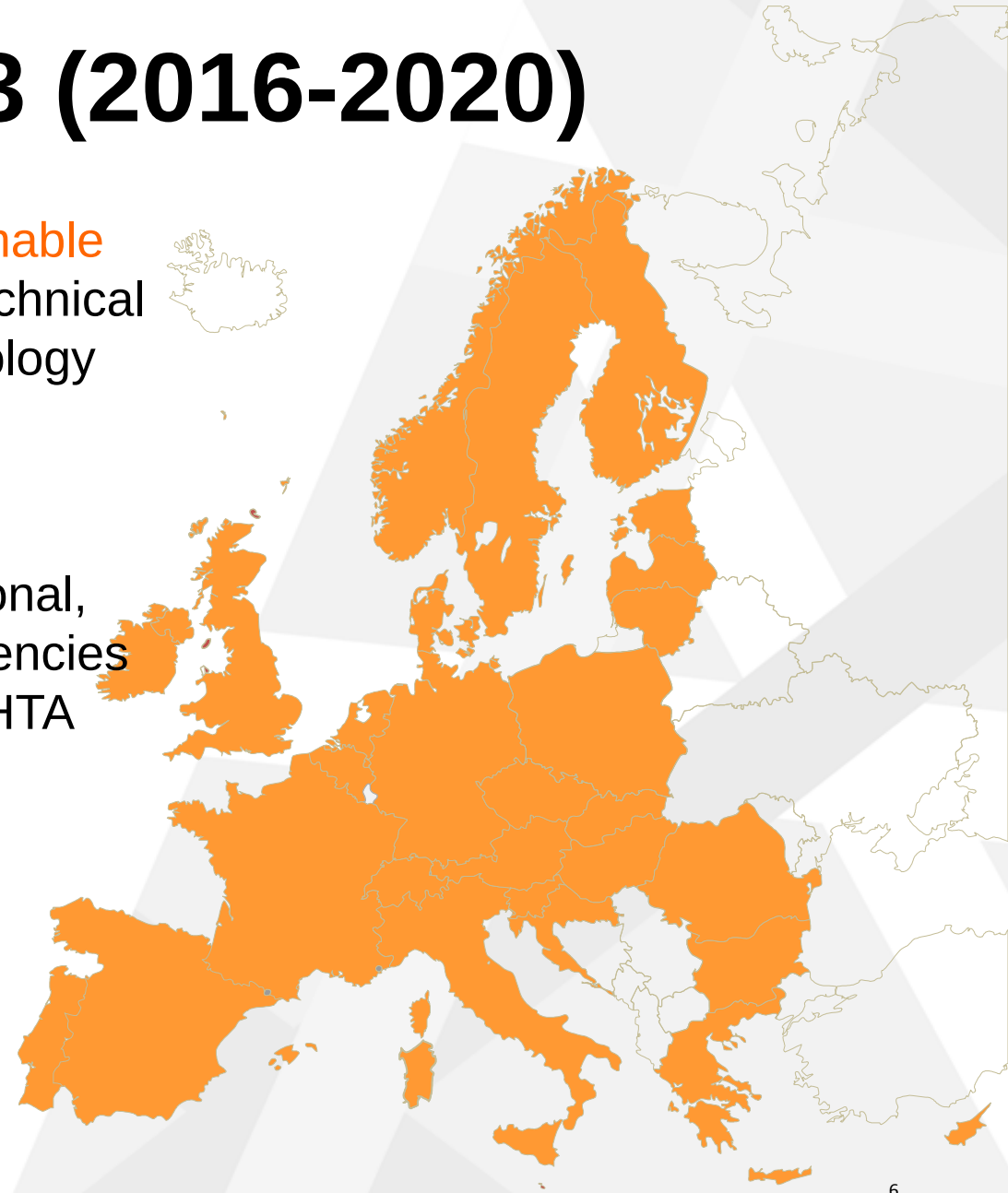


EUnetHTA JA3 (2016-2020)

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

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

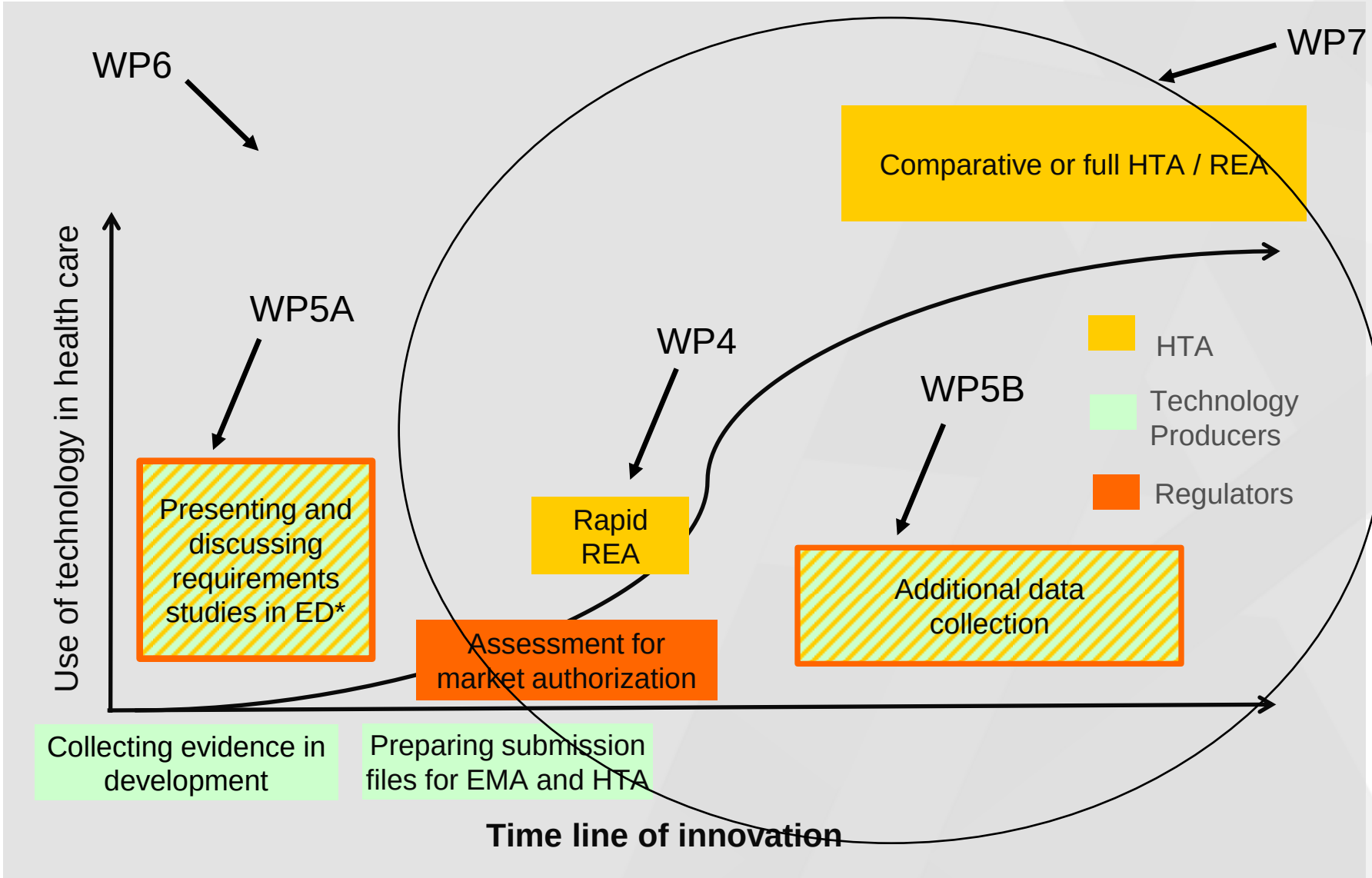
Project Coordinator:
Dutch National Health Care Institute (ZIN)



Summary of Activities in EUnetHTA JA3

- **WP4 Joint Production**
  - To produce **37** rapid REA on pharmaceutical and **43** on other technologies;
  - To provide a system for topic selection and prioritization, e.g. horizon scanning.
- **WP5 Evidence Generation**
  - To conduct Early Dialogues (joint HTA or parallel/joint with regulators);
  - To link additional data collection to several activities (adaptive pathways, MEA, etc.).
- **WP6 Quality Management**
  - To provide quality management for EUnetHTA joint products;
  - To further develop methodologies and tools for joint work if necessary.
- **WP7 National implementation and impact**
  - To facilitate the reuse and implementation of joint products at the national/local level;
  - To measure the impact of joint work in collaboration with other work packages.
- **WP1 Coordination**
- **WP2 Dissemination**
- **WP3 Evaluation**

HTA in the life cycle of technologies



*Early dialogue

Objectives WP4 General

- **Production** of Joint and Collaborative Assessments
- **Refine the production processes** of jointly produced assessments based on lessons learned and experiences from JA2 and current Joint Assessments
- **Facilitate the implementation** of Joint Assessments in national/local practice

Joint Assessments

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

Collaborative Assessments

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

Tools & templates

Model for rapid REA

- HPCU
- DTC
- Clinical effectiveness
- Safety

+ consideration of other Core Model applications

Provides working framework through a set of research questions*

Guidelines provide methodological guidance

Guidelines on Methodological Issues:

Comparators and comparisons
- Criteria for choice of most appropriate comparator(s)
- Methods of comparison: direct and indirect comparisons

Outcomes
- Clinical endpoints
- Surrogate endpoints
- Composite endpoints
- Health-related quality of life
- Safety

Level of evidence
- Internal validity
- Applicability


SUMMARY OF RELATIVE EFFECTIVENESS OF [XXX]

The assessment element ID codes in brackets (e.g. A0001) refer to the result cards in Appendix 1, which give details of the relevant results.

Scope

Population	
Intervention	
Comparator(s)	
Outcome(s)	

Introduction

Health problem

[Describe the incidence/prevalence] (A0023). [Describe risk factors] (A0003).

[Describe symptoms] (A0005). [Describe natural course of disease] (A0004).

[Describe how disease is diagnosed] (A0024). [Describe current treatment] (A0025).

Description of technology

[Describe regulatory status] (A0020). [Describe mode of action] (B0001). [Describe available comparators] (A0025 and/or B0002).

[Describe recommended dose and specific warnings to discontinue treatment] (B0001).

[Describe monitoring requirements for patients treated with intervention] (C0062).

[Describe additional pharmacovigilance activities] (C0007)

Results

Available evidence

[Describe body of evidence] (safety and clinical effectiveness domain)

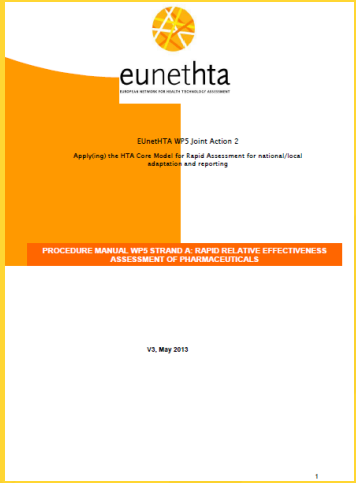
Upcoming evidence

[Describe ongoing trials] (safety and clinical effectiveness domain)

Clinical effectiveness

Assessment template and Project Plan template provide guidance for reporting

Procedure manual describes processes – to be replaced by **SOPs**



Submission File template is submitted by manufacturer (optional for Collaborative Assessments) – to be updated in JA3

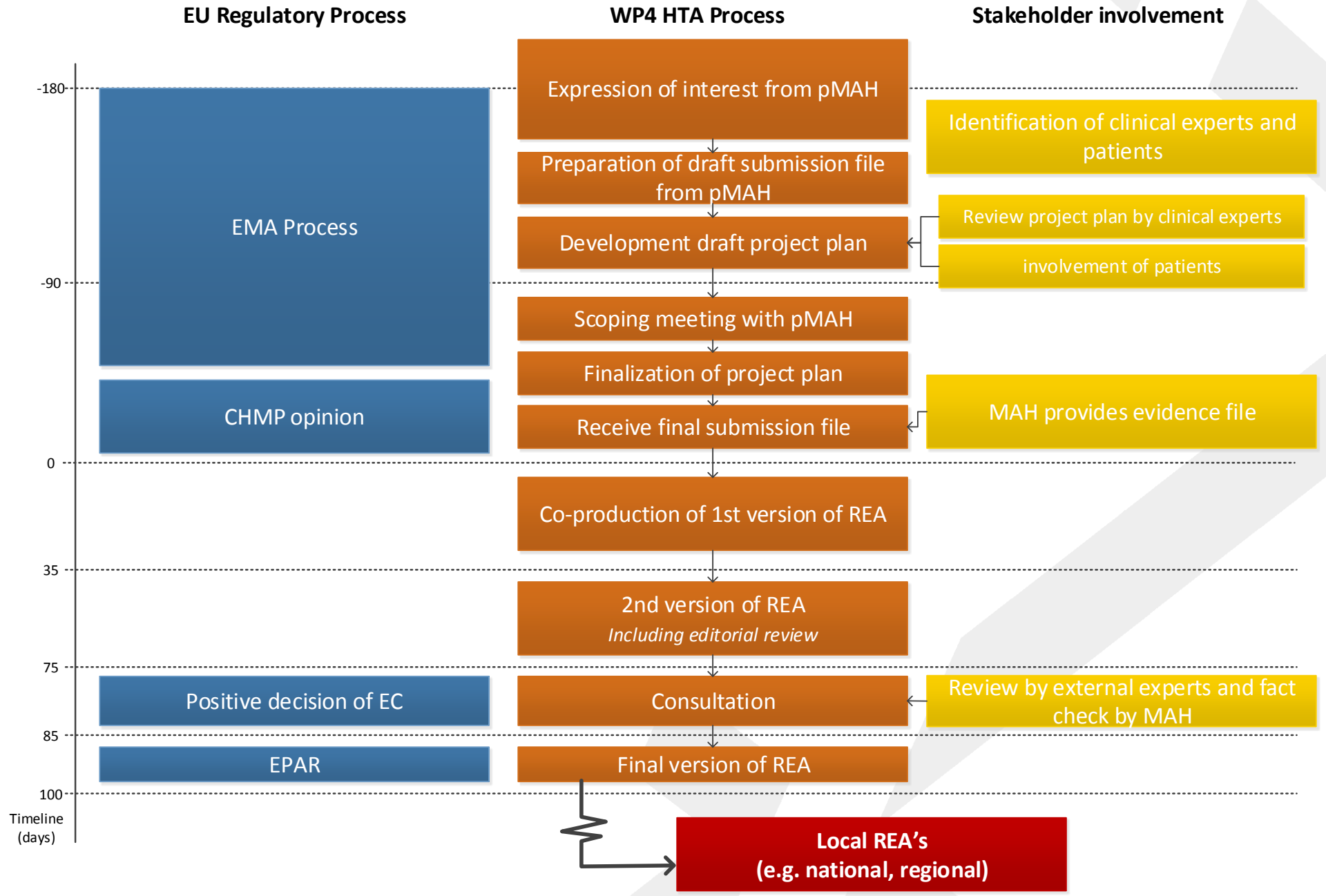
*** + checklist for ethical, organisational, social and legal issues**

WP4 Joint Assessment pharmaceuticals

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

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

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


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

6 Activity Centre Departments

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

- Project management of **Collaborative Assessments**

3 published Collaborative Assessments

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

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

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

4 ongoing Collaborative Assessments

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

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

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

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

No published or ongoing Joint Assessments.

WP5A: Involvement of HTA bodies (HTAB) in Early Dialogues (ED) / Scientific Advice (SA)

- **SA by one single HTAB**
  - Started in 2009
  - NICE, G-BA, AIFA, HAS…
  - HTAB only or in parallel with national regulatory agency
- **SA by multiple HTABs:**
  - Started in 2012: EUnetHTA:
    13 Early Dialogues
  - Dedicated project:
    SEED Shaping European Early Dialogues:
    14 HTABs coordinated by HAS.
    11 EDs, 4 in parallel with EMA
  - Enhanced participation and coordination at the HTA level

eunethta
European network for Health Technology Assessment

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

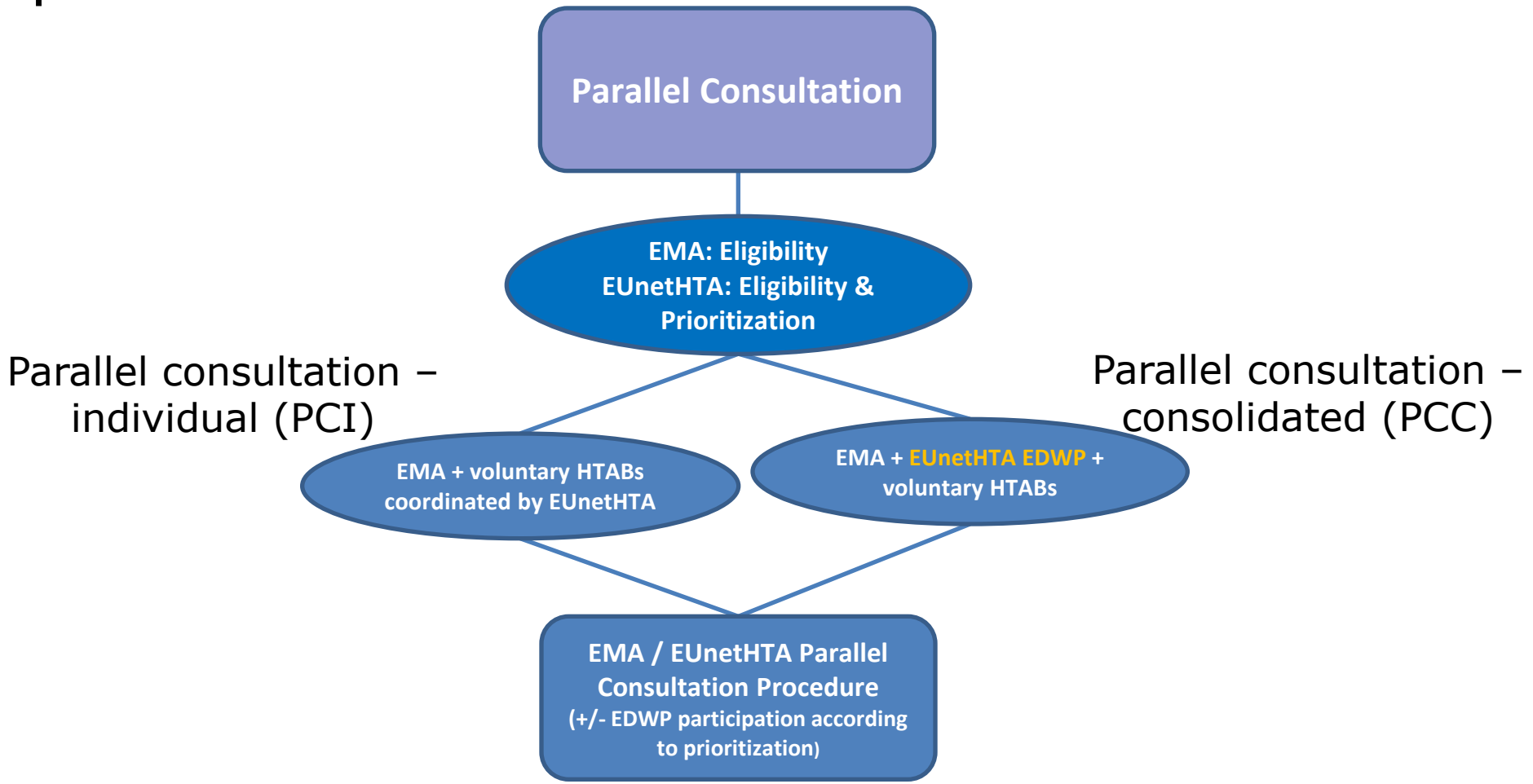
One process for parallel regulator-HTA Early Dialogues/Scientific advice:
EUnetHTA actors and process

Session 1: EUnetHTA JA3 progress

EUnetHTA Forum

presented by Hannah Bruehl
Scientific Officer, Federal Joint Committee

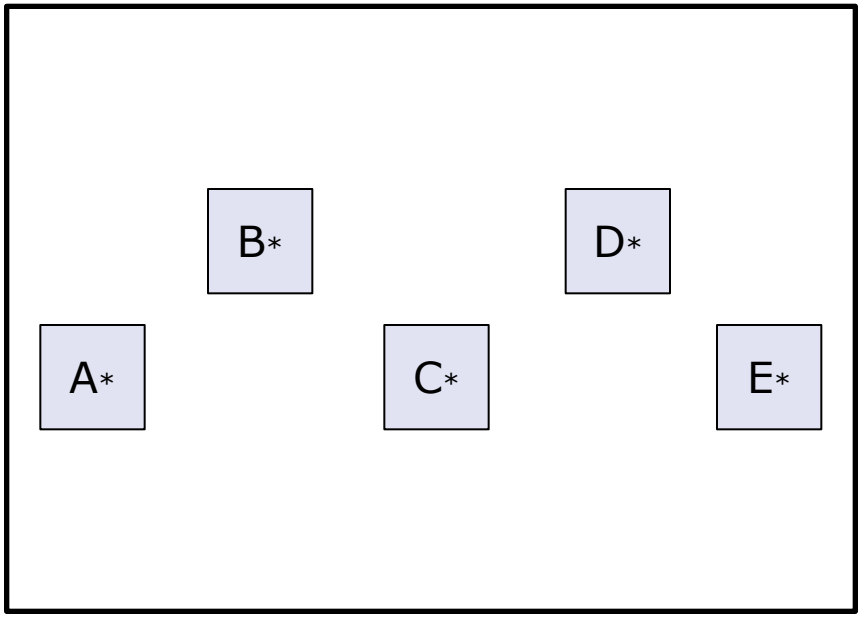
WP5A New Process in JA3 - 2 pathways for parallel consultations



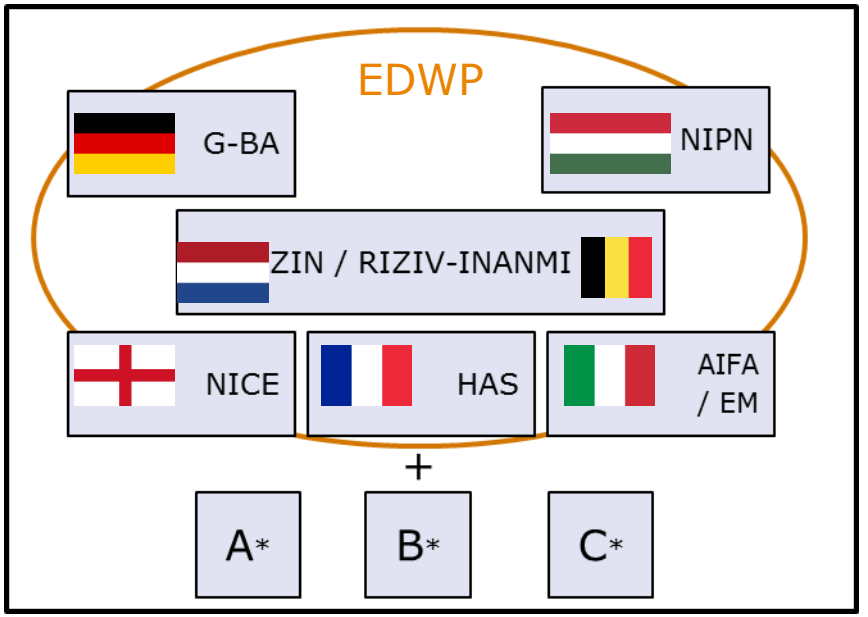
Process - EUnetHTA EDC

The Early Dialogue Committee (EDC) is constituted for a specific product and the members will fluctuate to a degree for each Consultation.

Individual PC



Consolidated PC



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

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

Process - EUnetHTA EDWP selection criteria

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

- →EDs should represent a wide array of topics, therapeutic areas etc.

WP5B: EUnetHTA actions with regard to post-launch evidence generation

Objectives of WP5B

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

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

- Invitation to participate by EMA's new sort of Scientific Advice to qualify disease registries

Procedure = EMA Qualification of novel methodologies for drug development:
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004201.pdf

➢ Outcome: qualification opinion or qualification advice

WP6 – Organisation of work

6A.1

QM Concept Paper
(fundamental aspects and EUnetHTA specific means of QM for joint work)

6A.3

Processes and Process Flows
(e.g. for Rapid REA)

SOPs (incl. Checklists and Templates)
(e.g. data extraction)

6A.4

Training Activities
(on how to apply QM measures)

JA3 WP6

Activities

Activity Centre A
Quality Management
led by IQWiG

Activity Centre B
Sci. Guidance and Tools
led by KCE

Activities

6A.2 QM System

6B.4 Hand-book

WP6

EUnetHTA Companion Guide
(web-based)

Assessment Teams **(WP4)**

6B.1

Inventory & Planning

6B.2

Methodological Guidelines
(e.g. on information retrieval)

6B.3

HTA Core Model®

6B.5 - 6B.9

Practical Tools
(existing tools such as POP database and new tools)

Training Activities
(on how to use tools and methodology)

Overview of WP7 activities

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

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

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

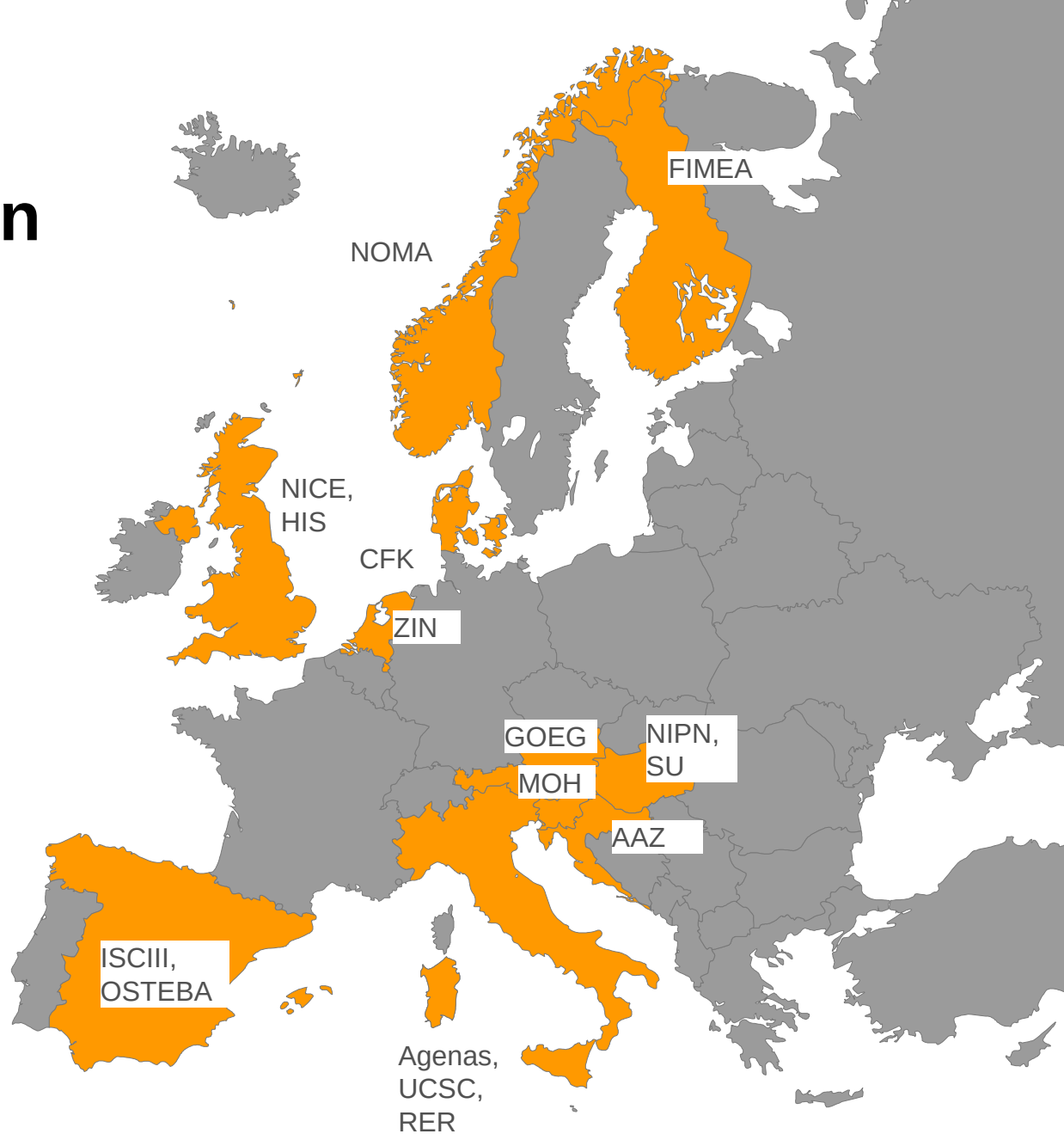
- Implementation network. Support for agencies to use EUnetHTAproducts and feed back issues with the pilot model of HTA cooperation and use of EUnetHTA products, through informal feedback and formally though questionnaires, interviews and case studies.

Aim of the implementation network

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

Implementation leads

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



Conclusions

- EUnetHTA JA3 has delivered many products since its start in June 2016;
- Joint EUnetHTA products can be used on a national and regional level. Implementation will be a key activity;
- How can RedETS help with the implementation of some of these products nationally and regionally?
- Also training activities on EUnetHTA products, tools and processes may be very crucial; RedETS may assist to initiate training activities on EUnetHTA products as part of their activities?