EUnetHTA and relative effectiveness assessments

Introduction and background on the development of the pilots of the Rapid REA model

Simone Warren
Lead Partner EUnetHTA JA2 WP5 on Rapid Assessments
ZIN, The Netherlands

Hustopeče, March 26, 2015

Agenda presentation and discussion

- **Background**
- **EUnetHTA JA1 (2010-2012)**
- **Activities EUnetHTA JA2 (2012-2015)**
- **Discussion**

Pharmaceutical Forum 2008 Recommendations

- Decisions on reimbursement at national level
- Relative effectiveness assessment (REA) vs. cost-effectiveness assessment (CEA)
- Exchange of REA criteria/information
- Implementation of agreed good practice principles for REA
- More effectively done by existing networks

But also: "…Member States, with the involvement of the EMA, should continue their efforts to consider how European Public Assessment Reports can further contribute to relative effectiveness assessments.."

EUnetHTA JA1 WP5 REA Pharmaceuticals

- EUnetHTA was asked to take this work forward by the Steering Committee of the HL PF in autumn of 2008.
- EUnetHTA WP on REA started in 2010
- EUnetHTA decided to work with the definitions that had been agreed upon in PF2008

According to the Pharmaceutical Forum:

Relative effectiveness can be defined as the extent to which an intervention does more good than harm compared to one or more intervention alternatives for achieving the desired results when provided under the usual circumstances of health care practice.

EUnetHTA Joint Action 1: 2010-2012

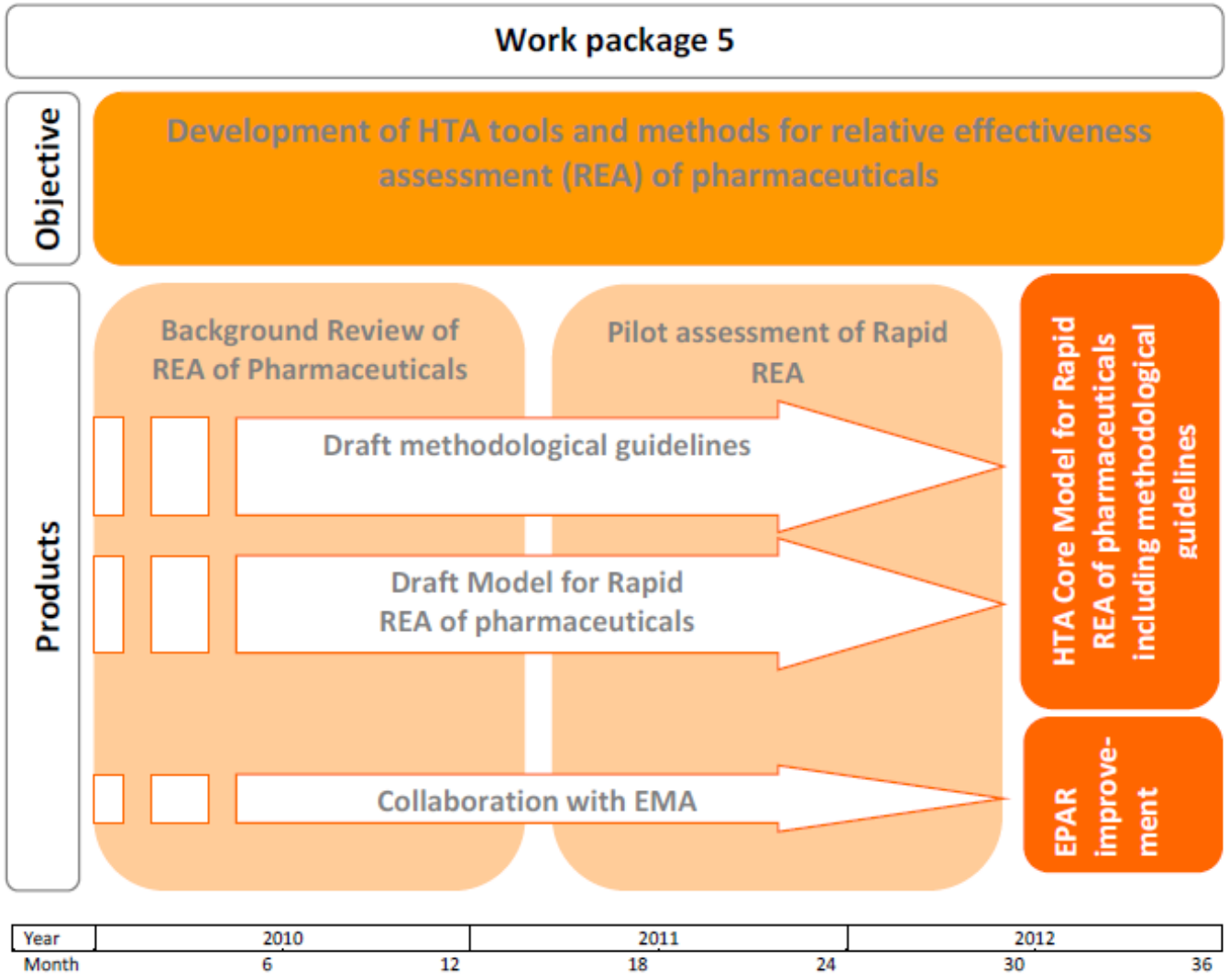
Focus on HTA in Europe to:

- Facilitate efficient use of resources available for HTA
- Create a sustainable system of HTA knowledge sharing
- Promote good practice in HTA methods and processes
- Develop a business plan for a continuous European network for HTA

Work packages

- Coordination, Communication, Evaluation, Core HTA including adaptation, Relative Effectiveness Assessment (REA) of Pharmaceuticals (WP5), New Technologies. Facilitating Evidence Generation and Collaboration on (Pre-coverage) Assessments Information management system, Strategy development (Business model for sustainability including capacity building to do HTA)

EUnetHTA WP5 REA Pharmaceuticals



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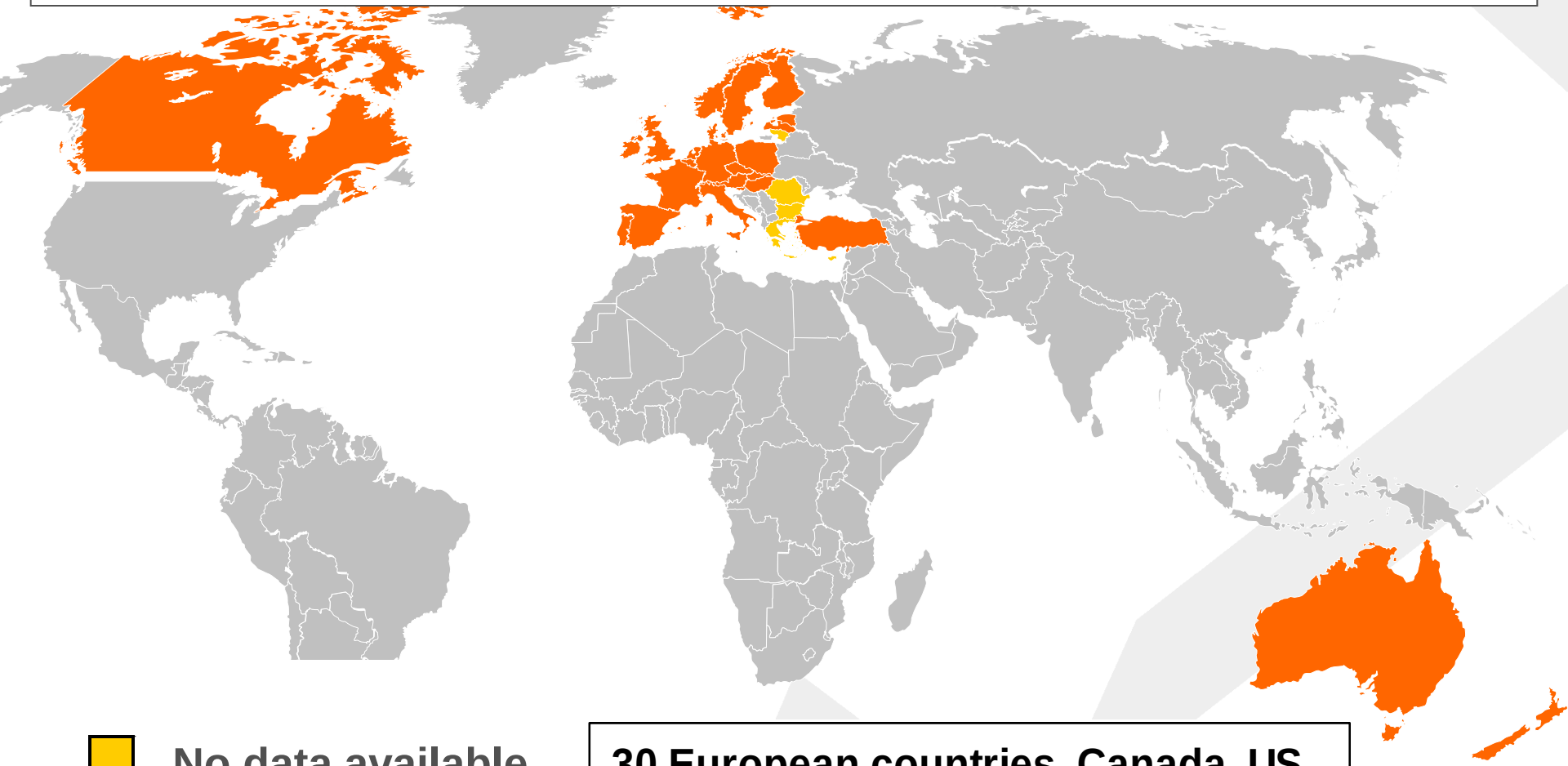
Relative Effectiveness Assessment of Pharmaceuticals: Similarities and Differences in 29 Jurisdictions

Sarah Kleijnen, MSc[1,2,], Elisabeth George, PhD[3], Scott Goulden, MSc[3], Anne d'Andon, MD[4], Pauline Vitré, PD, MSc[4], Boguslawa Osińska, MSc[5], Rafal Rdzany, PhD[5], Steffen Thirstrup, MD, PhD[6], Belen Corbacho, MSc[7], Bence Z. Nagy, MSc[8], Hubert G. Leufkens, PhD[2], Anthonius de Boer, MD, PhD[2], Wim G. Goettsch, PhD[1,2]*

[1]*College voor zorgverzekeringen, Diemen, The Netherlands;* [2]*Division of Pharmacoepidemiology and Clinical Pharmacology, Faculty of Science, Utrecht Institute for Pharmaceutical Sciences, Utrecht, The Netherlands;* [3]*The National Institute for Health and Clinical Excellence, London, UK;* [4]*Haute Autorité de santé, Paris, France;* [5]*Agency for Health Technology Assessment, Warsaw, Poland;* [6]*Institute for Rational Pharmacotherapy, Copenhagen, Denmark;* [7]*Andalusian HTA Agency, Seville, Spain;* [8]*Hungarian National Institute for Quality and Organizational Development, Budapest, Hungary*

A B S T R A C T

Countries included



No data available

Completed

30 European countries, Canada, US, Australia, New Zealand

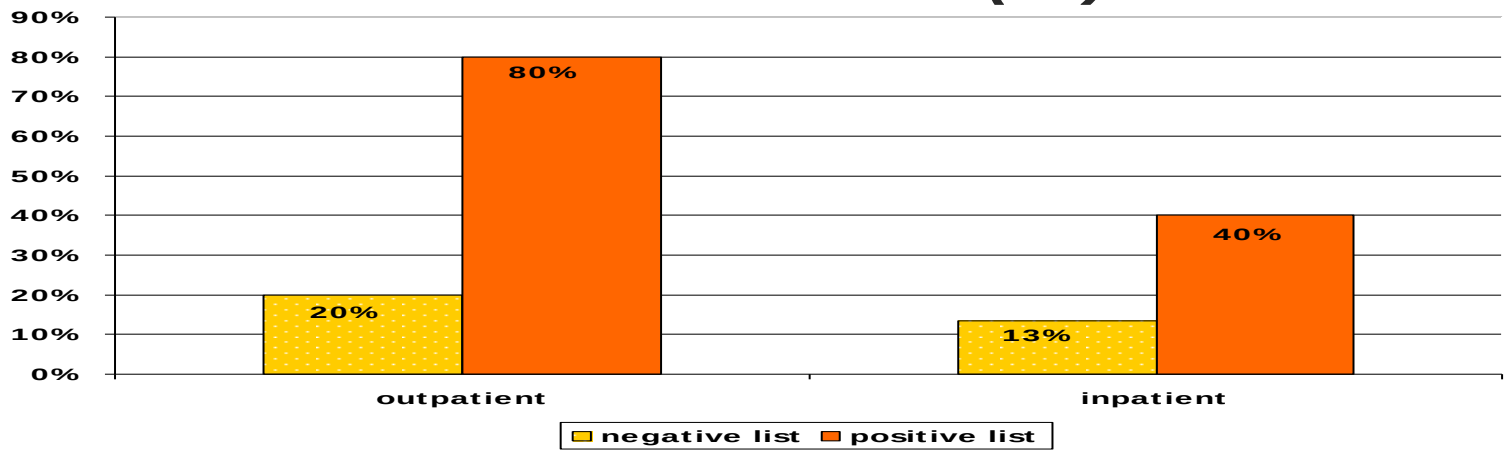
Data collected	No sources	Excluded
29 jurisdictions: *Australia Austria Belgium Canada Czech Republic Denmark England& Wales (UK) Estonia Finland France Germany Hungary Ireland Italy Latvia Luxembourg Malta Netherlands New Zealand Norway Poland Portugal Scotland (UK) Slovakia Slovenia Spain Sweden Switzerland Turkey*	**5 jurisdictions**: *Bulgaria* *Cyprus* *Greece* *Lithuania* *Romania*	**1 jurisdiction**: *USA*

Background review on national REA
Basic information

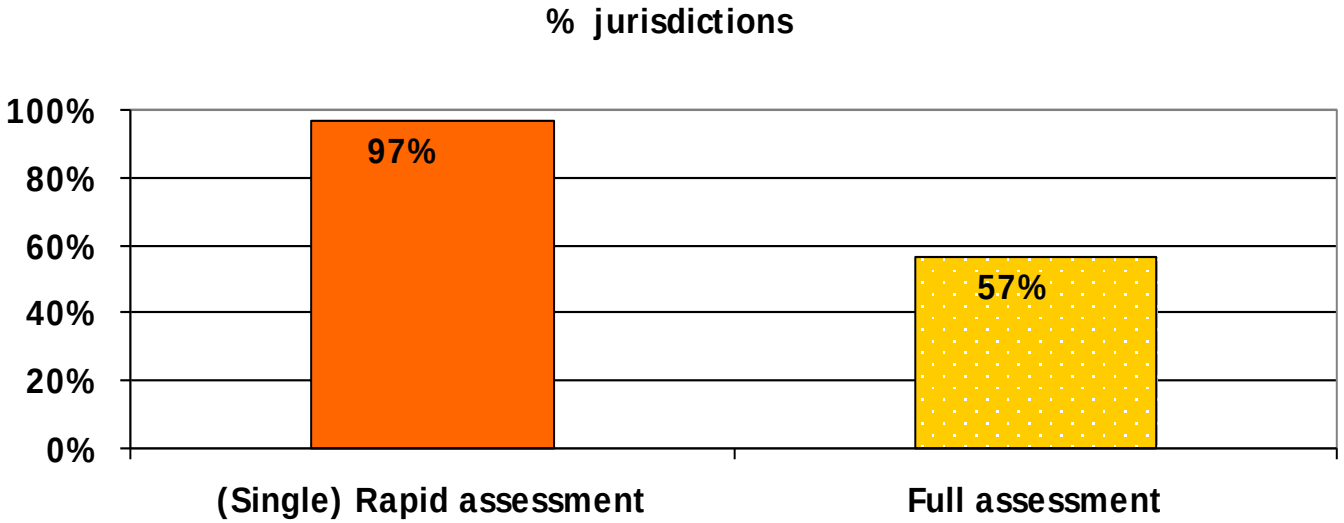
- **Countries have national health service (50%) or insurance based system (50%)**
  - Mostly social health insurance

- **Reimbursement of pharmaceuticals is organised in positive or negative lists**
  - Positive list: only reimbursed when on list
  - Negative list: reimbursed except when on list
  - Difference in assessment between inpatient and outpatient pharmaceuticals

Jurisdictions with national positive/negative reimbursement list (%)

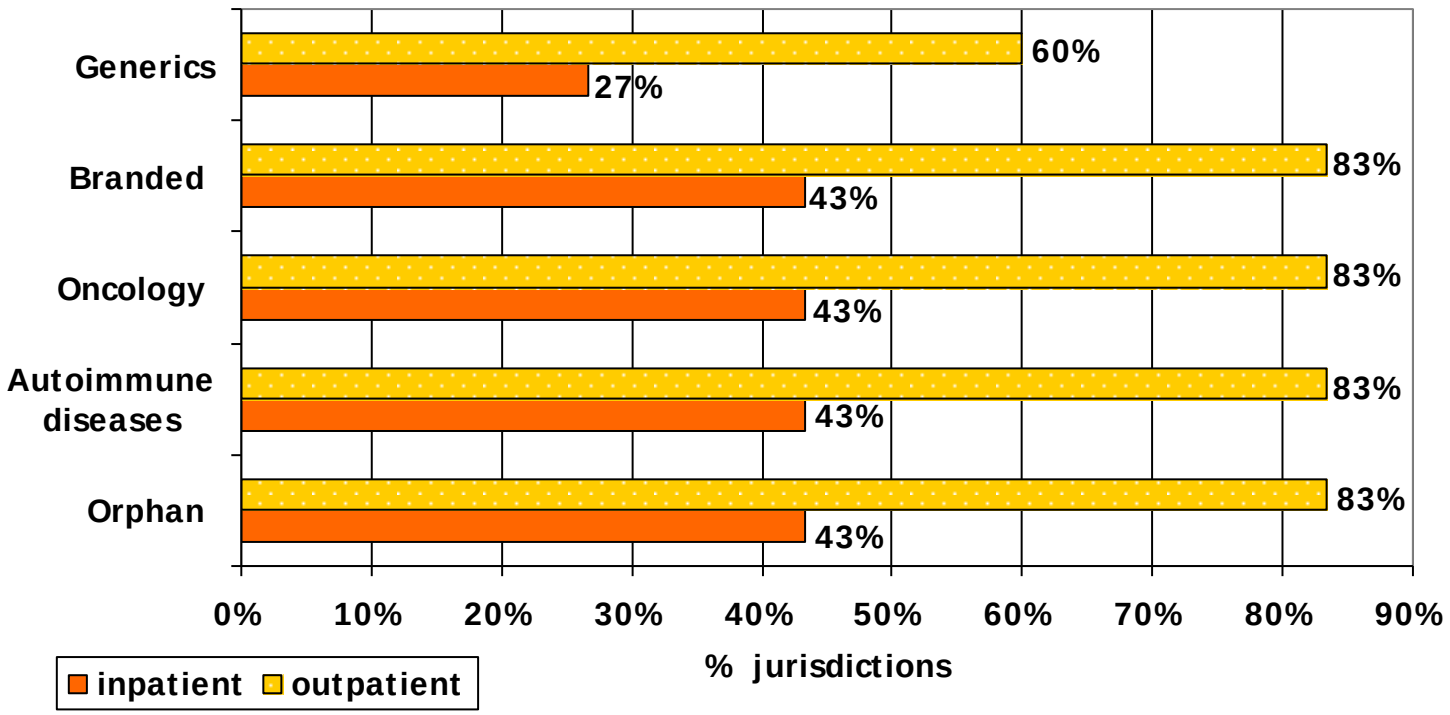


Assessment as *part* of reimbursement decision



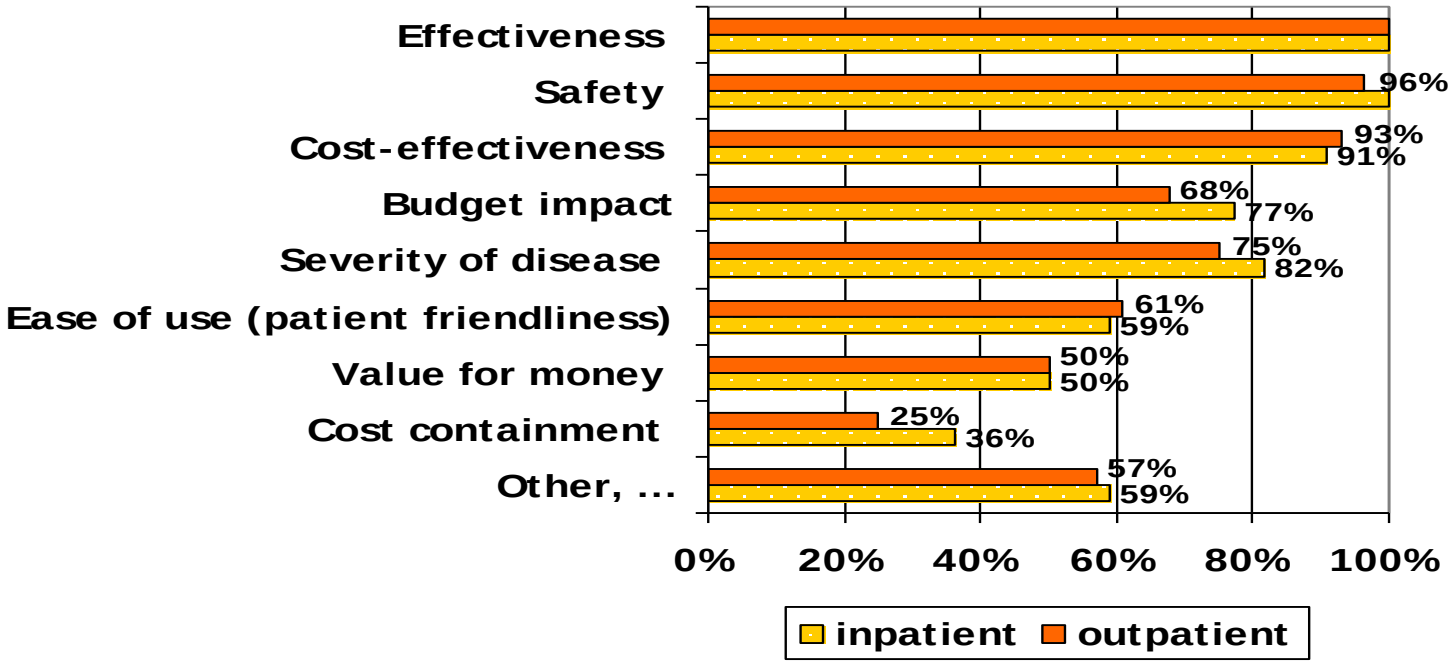
Which pharmaceuticals are ALWAYS evaluated?

Jurisdictions in which specific types of reimbursed pharmaceuticals are always subject to a reimbursement evaluation (%)



Criteria for reimbursement

Jurisdictions in which specific reimbursement criteria are applicable (%)



Results for Rapid Relative Effectiveness Assessment: Efficacy vs Effectiveness

- All jurisdictions consider ‘always’ or ‘sometimes’ applicability of trial data
- If no effectiveness data from clinical studies are available
  - qualitative extrapolation: 75% (sometimes or always)
  - quantitative extrapolation: 50% (sometimes or always)
- In the absence of long-term data, short-term data are extrapolated:
  - qualitative extrapolation: 69% (sometimes or always)
  - quantitative extrapolation: 62% (sometimes or always)

Background Review on national REA: Conclusions and Challenges

- **Most countries carry out some form of REA to support national reimbursement decisions of pharmaceuticals**
- **The scope and the methodology used vary across countries to some extent >> however not that much (TERMINOLOGY!)**
- **Rapid assessments are most common and relevant for reimbursement Purposes**
- **The differences between counties, as well as the reasons behind them, need to be considered in the development of a common European methodology for REA**

Table 1: Most relevant challenges for a European model

Most relevant challenges
Methodology to do assessments is often not explicitly reported
Variation between jurisdictions in terminology and definitions
How to handle lack of effectiveness data
How to present unintended and intended effects
Variance in usual care between jurisdictions

**http://www.eunethta.eu/outputs/methodological-guideline-.....*

Methodological guidelines*

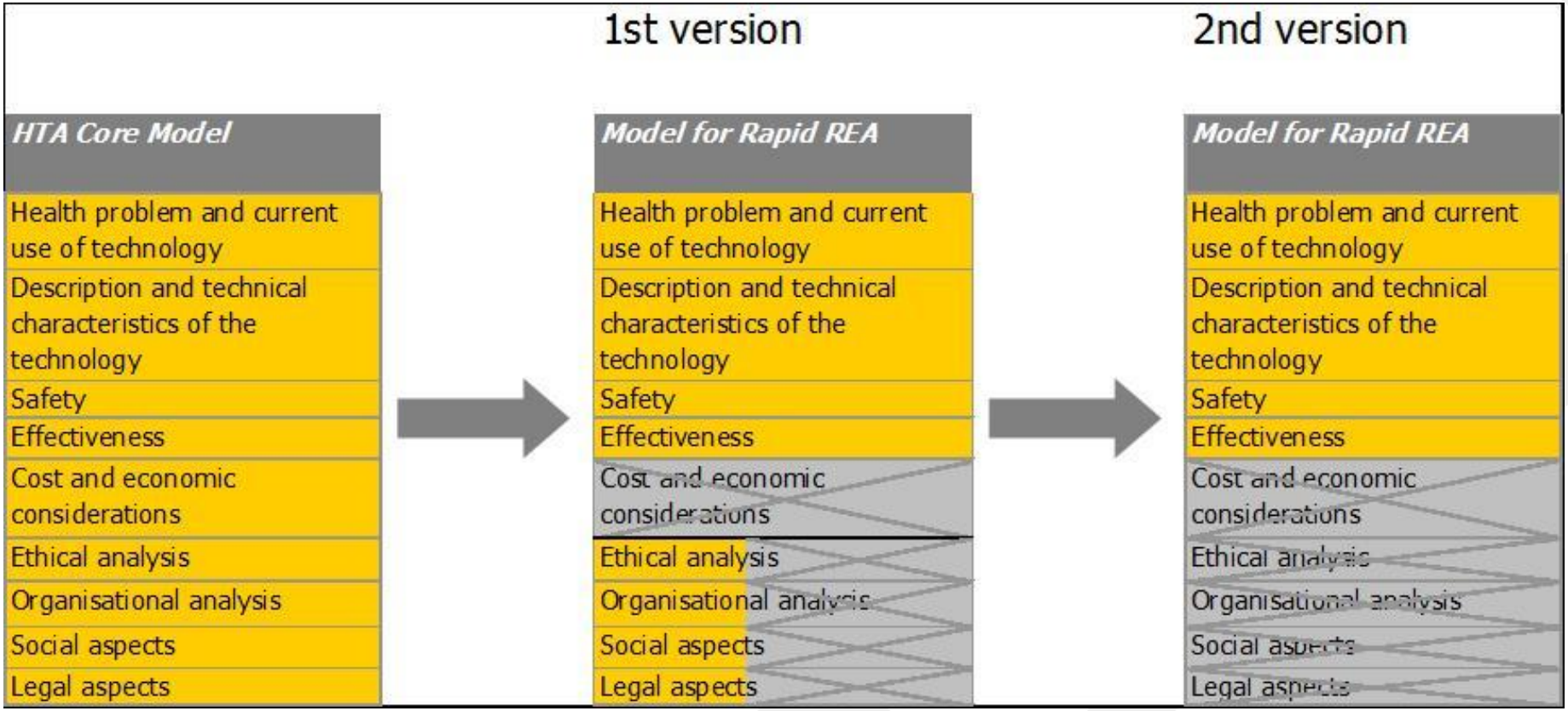
Guidelines

- Choice of comparator
- Composite EP
- Surrogate EP
- Applicability
- Direct and indirect comparisons
- Clinical EP
- HRQoL
- Safety
- Internal validity

- Consultation by Stakeholder advisory Groups and WP5 members
- Public Consultation (industry, public bodies, experts, HTA organizations, EMA)
- Important number of thorough comments received (30 – 40 pages per guideline)
- Meeting with stakeholders (EFPIA and others) February 2013
- Guidelines are finished for JA1 in February 2013 but never finalized!
- Will be further discussed in JA2

**http://www.eunethta.eu/outputs/methodological-guideline-.....*

Model for Rapid REA of Pharmaceuticals*



*http://www.eunethta.eu/outputs/new-application-hta-core-model-hta-core-model-rapid-relative-effectiveness-assessment-pharma

First pilot rapid assessment

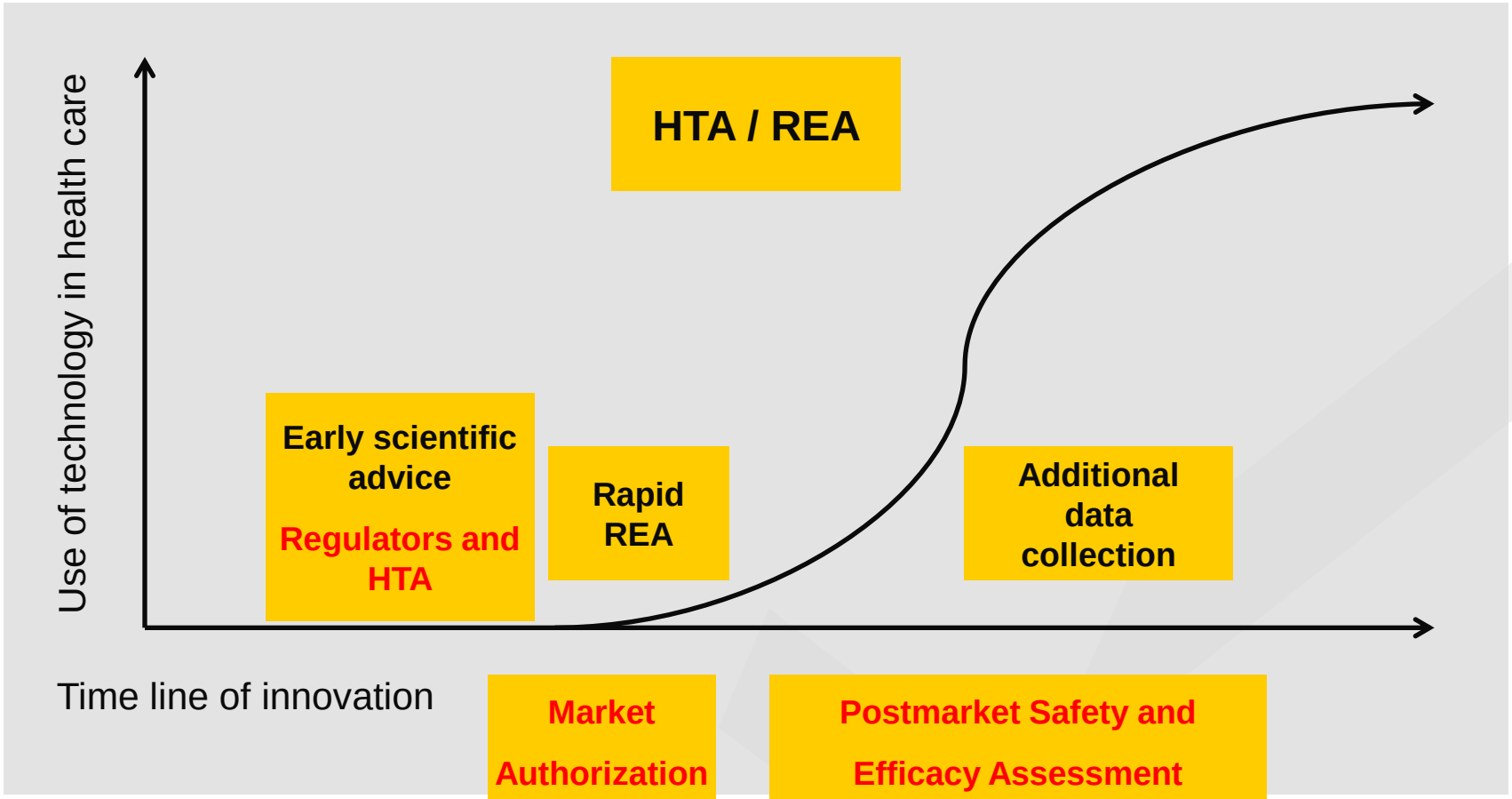
- **Topic selection:**
  - Pazopanib for the first-line treatment of metastatic renal cell cancer.
- **Basic documentation:**
  - Manufacturer submission file, Model for Rapid REA, Methodological guidelines developed in WP5
- **Process:**
  - Traditional model of collaboration in core-HTA was used
  - Domain teams with participants from different organizations
  - Synthesis of data after the collection of data in the different results cards
- **Results:**
  - Participation of 29 organizations requires intense coordination on several levels
  - 3,5 months timelines for scope/assessment phase is not possible in daily practice
  - Relevance of all research questions (assessment elements) for REA?

**http://www.eunethta.eu/outputs/wp5-ja1-pilot-pazopanib-reportappendix*

Collaboration with EMA

- EPARs improvement
- Guidelines (EMA, EUnetHTA)
- Post-licensing studies database, common core protocol
- Parallel scientific advice

Health Technology Life-cycle



Collaboration between EMA and EUnetHTA

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Improving the Contribution of Regulatory Assessment Reports to Health Technology Assessments—A Collaboration between the European Medicines Agency and the European network for Health Technology Assessment

Michael Berntgen, PhD, MDRA[1,], Anne Gourvil, PhD[2], Mira Pavlovic, MD[2], Wim Goettsch, PhD[3], Hans-Georg Eichler, MD, MSc[1], Finn Børlum Kristensen, MD, PhD[4]*

[1]*European Medicines Agency, London, UK;* [2]*La Haute Autorité de Santé, Saint-Denis La Plaine Cedex, France;* [3]*National Health Care Institute, Diemen, The Netherlands;* [4]*EUnetHTA Secretariat, C/o Danish Health and Medicines Authority, Copenhagen, Denmark*

ABSTRACT

In response to a recommendation from the Pharmaceutical Forum, the European Medicines Agency and the European network for Health set of EPARs for recently approved medicinal products was carried out in parallel by both the European network for Health Technology Assess-

WP5 - Applying the HTA Core Model for Rapid Assessment for national adaptation and reporting

EUnetHTA Joint Action 2 (2012-2015)

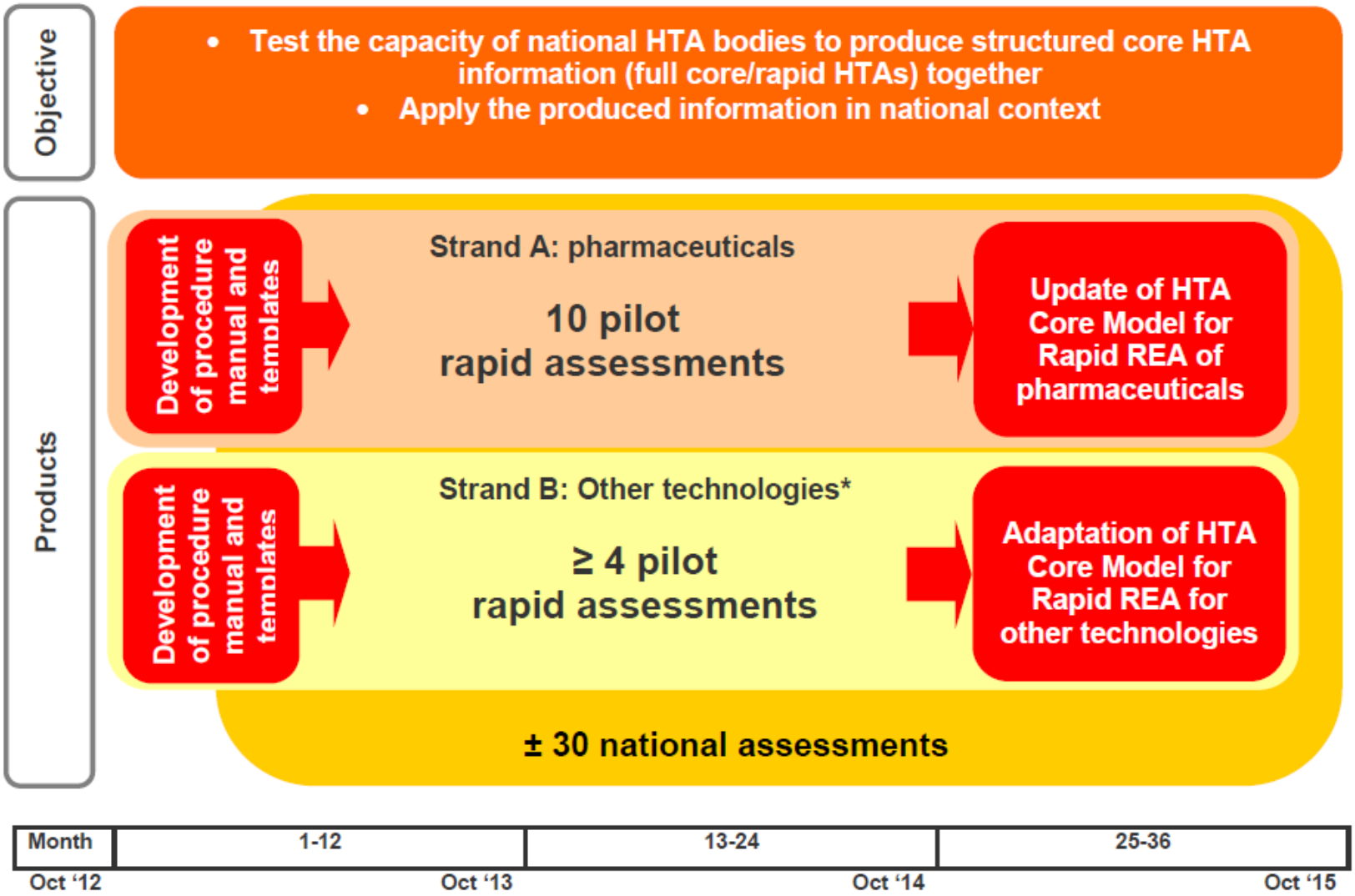
Objective of WP5:

➢***Objective #1 of Grant Agreement (p35): Test the capacity of national HTA bodies to produce structured core HTA information (full core/rapid HTAs) together and apply it in national context (including collection of data on costs and overall efficiency of the production in the network***

➢Output (products) oriented work package in order to prove the capacity of cooperation for increased efficiency of European HTA-production

➢Pilot reports will be produced in order to critically review the applicability of the work done by JA1 WP5 and WP7B

Project → **JA1** → **JA2**



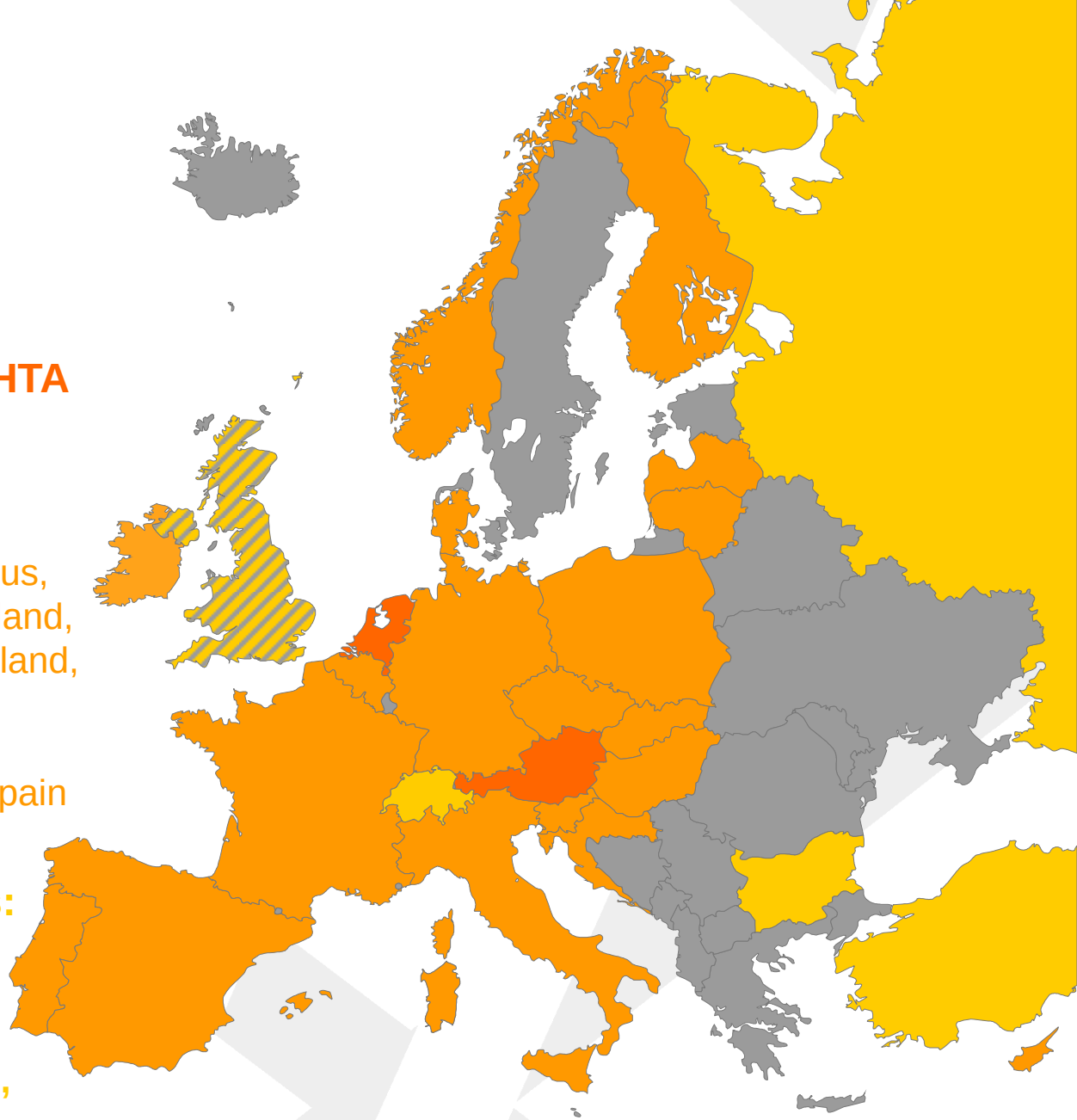
*such as medical devices, diagnostics and medical interventions

WP5 Partners

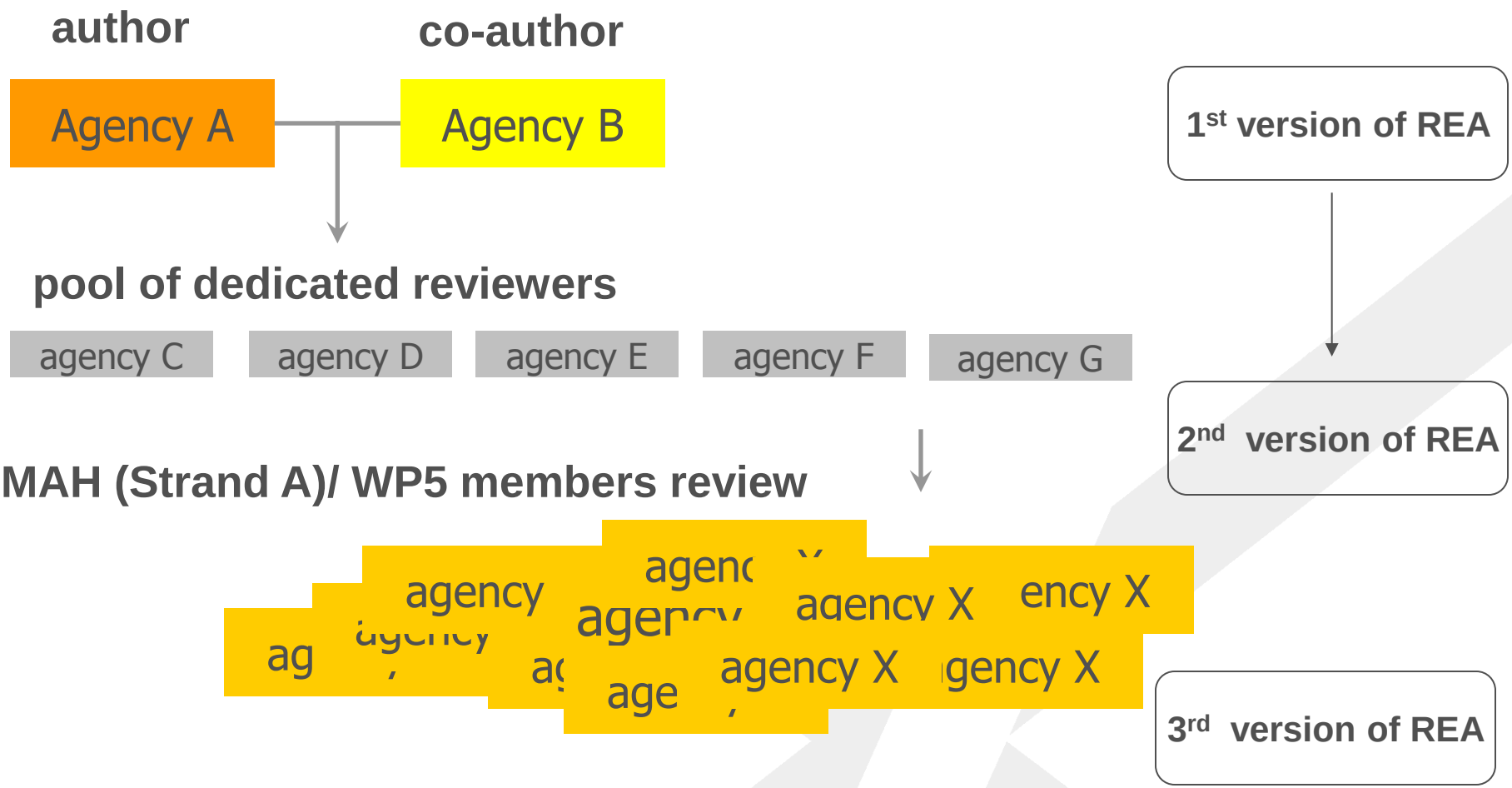
Lead Partner: ZIN
Co-lead partner: LBI for HTA

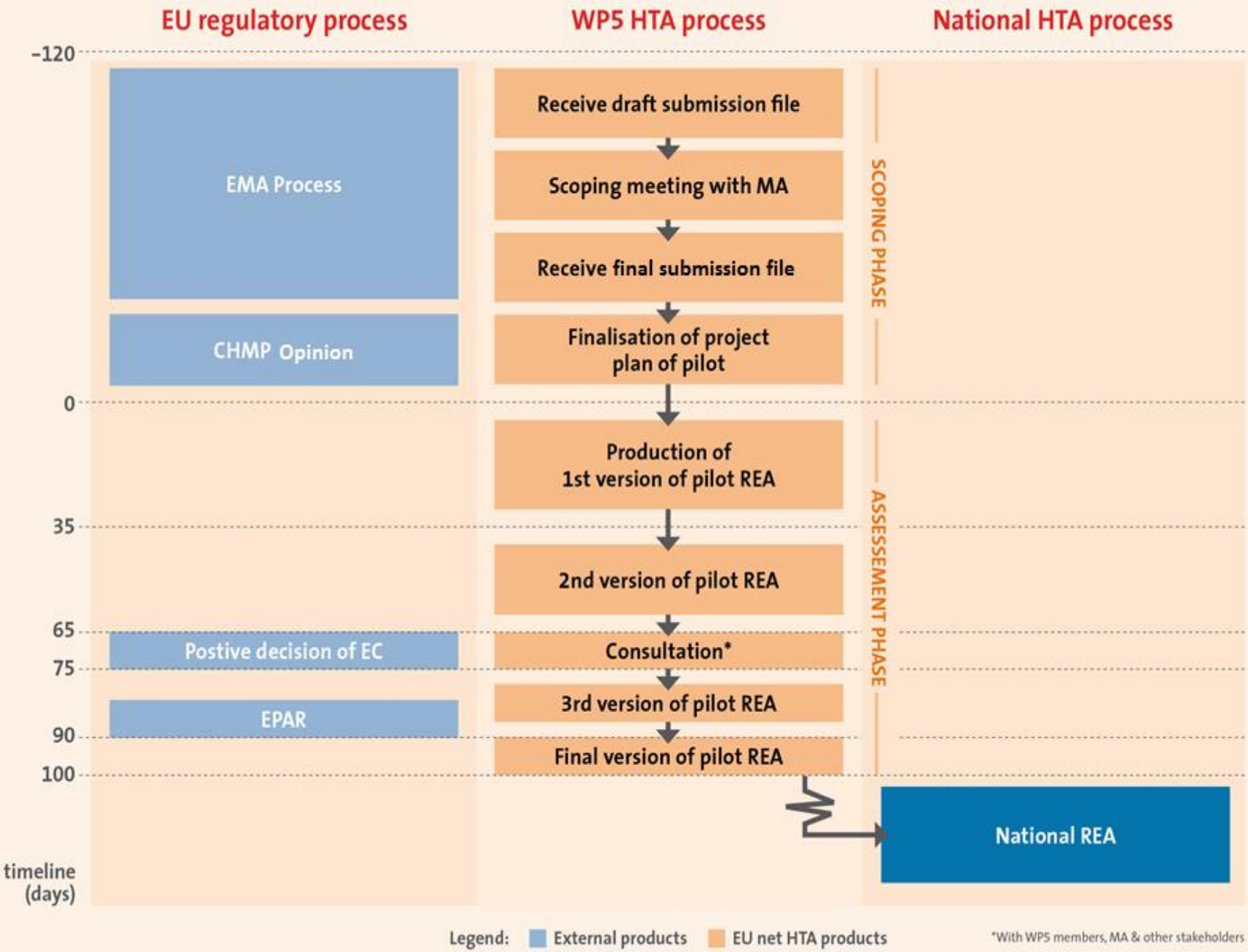
27 Associated Partners:
Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain

19 Collaborating Partners:
Austria, Belgium, Bulgaria, Croatia, Denmark,Germany, Italy, Lithuania Russia, Scotland, Spain, Switzerland, Turkey



Collaboration Model HTA Agencies (both Strands)




EU regulatory process
WP5 HTA process
National HTA process
-120
EMA Process
CHMP Opinion
0
35
65
Postive decision of EC
75
EPAR
90
100
timeline (days)
Receive draft submission file
Scoping meeting with MA
Receive final submission file
Finalisation of project plan of pilot
Production of 1st version of pilot REA
2nd version of pilot REA
Consultation*
3rd version of pilot REA
Final version of pilot REA
SCOPING PHASE
ASSESSEMENT PHASE
National REA
Legend:
External products
EU net HTA products
*With WP5 members, MA & other stakeholders

Submission template (WP7 SG4)

Strand A:

- **Currently working alongside NICE in the development of a manufacturer's submission template.**

- **Template is a collection of submission requirements for reimbursement decisions around Europe**
  - **WP5 works in collaboration with WP7 to test the use of this template in the pilots**
  - **Currently testing 2nd version**
  - **2nd draft submission template, and feedback from that can be included in the development of the final draft submission template over the summer 2015.**

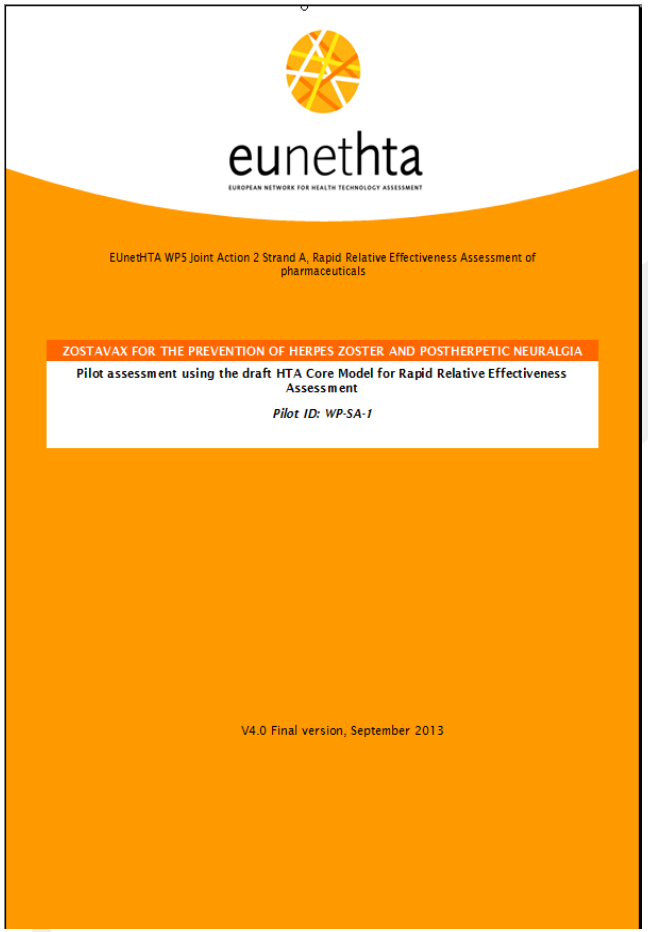
First Pilot: Zostavax

Zostavax for the prevention of herpes zoster and post herpetic neuralgia

- Pilot team:
  - Author: CVZ (NL)
  - Co-author: “A. Gemelli” Teaching Hospital (IT)
  - Dedicated reviewers: HAS (FR), GOG (A), MoH Czech Republic, DPA/MFH (M), RIZIV (B), MSSSI (S), Regio Veneto (IT)

- Duration: 04/2013- published on the EUnetHTA website on 08/2013

- Uptake or use in local/national reports: Austria (twice, 2013), Spain (2013), NL (2014)

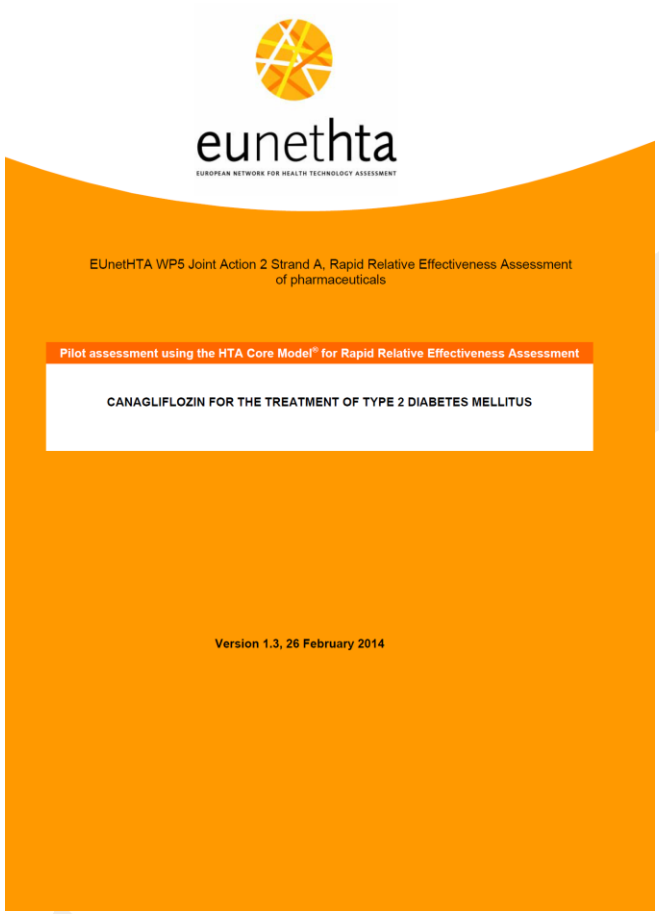


http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/Zostavax_main%20report%20including%20appendices_20130922.pdf

Second Pilot: Canagliflozin

Canagliflozin for the treatment of type II diabetes mellitus

- Pilot team:Authors: AAZ (Croatia), FIMEA (Finland) Regione Veneto (Italy)
- Dedicated reviewers: HAS, HVB; CAHIAQ; Medical University of Sofia; MoH Czech Rep
- Duration: 05/2013 -02/2014
  - Delay mostly due to external factors (i.e. delayed decision of CHMP)
- Local reports:
  - Planned: Czech Republic, Ireland, NL

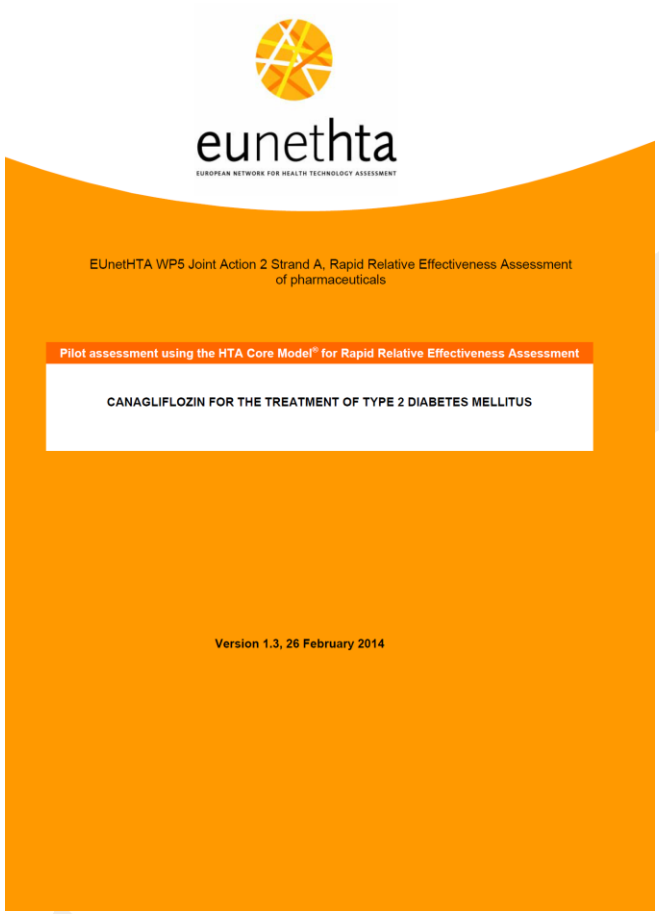


http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/WP5_SA-2_canagliflozin_for_the_treatment_of_diabetes_mellitus.pdf

Third Pilot: sorafenib

sorafenib for advanced thyroid carcinoma (Bayer), authors are AIFA (Italy) and IMFARMED (Portugal)

- Pilot team: Authors: AIFA (Italy), INFARMED (Portugal)
- Dedicated reviewers: Slovak MoH, GYEMSZI; RIZIV; FIMEA; NCPE
- Duration: 11/2014 -03/2015
- Local reports:
  - To be determined

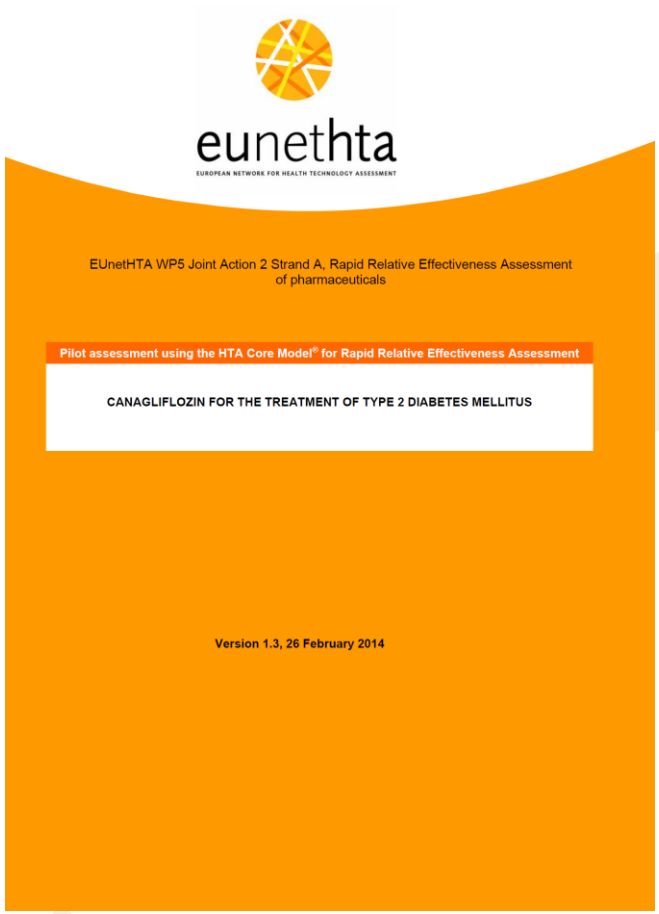


http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/WP5_SA-2_canagliflozin_for_the_treatment_of_diabetes_mellitus.pdf

Fourth Pilot: Ramucirumab

ramucirumab in combination with paclitaxel for previously treated advanced gastric and gastro-oesophageal junction cancer (Eli Lilly), authors are NOKC (Norway) and AAZ (Croatia)

- Pilot team: Authors: NOKC (Norway), AAZ (Croatia)
- Dedicated reviewers: Slovak Ministry of Health, FIMEA, GYEMSZI, A.Gemelli Teaching Hospital, HAS
- Duration: 12/2014 -03/2015
- Local reports:
  - To be determined



http://www.eunethta.eu/sites/5026.fedimbo.belgium.be/files/WP5_SA-2_canagliflozin_for_the_treatment_of_diabetes_mellitus.pdf

joint REAs ongoing

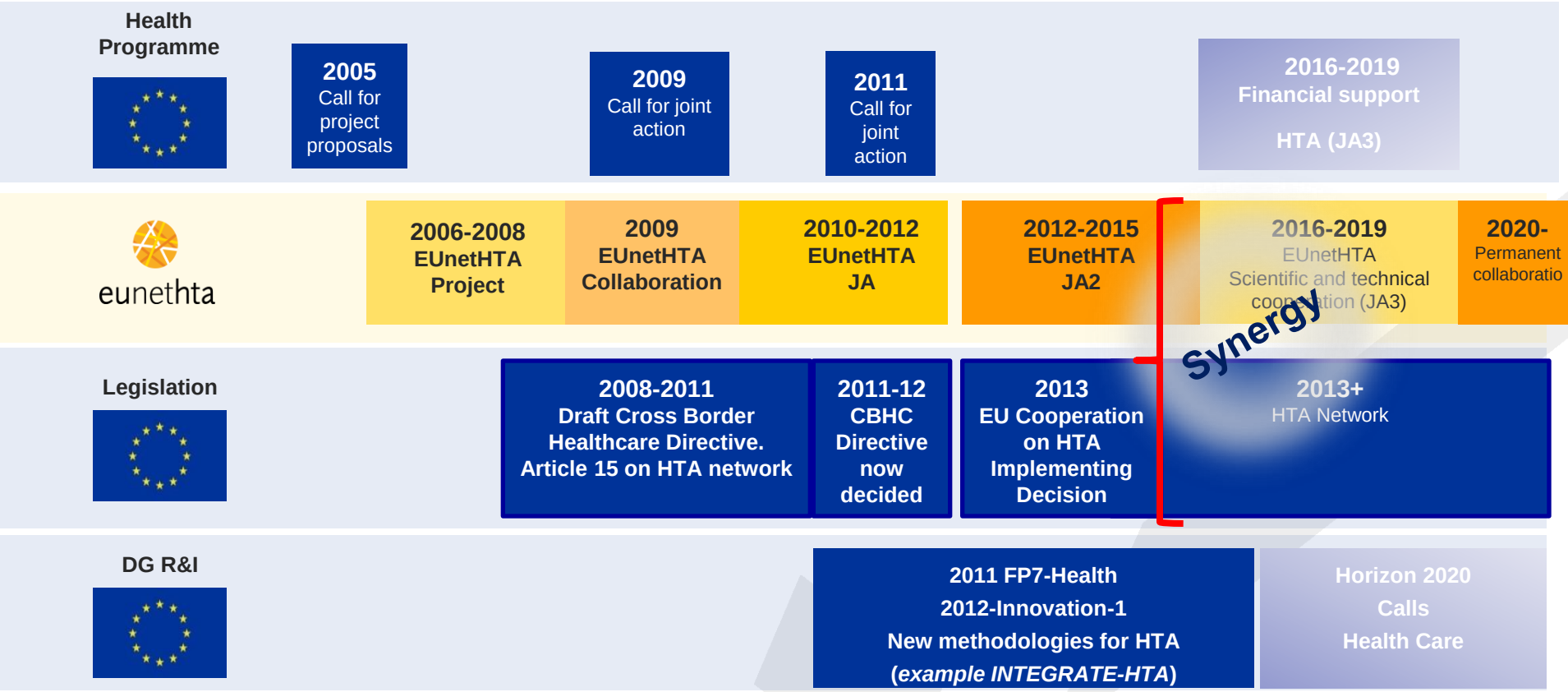
- **Fifth pilot**
  - Vorapaxar for the reduction of thrombotic cardiovascular events in patients with a history of Myocardial Infarction (MI)
  - Assessment began February 2015
  - Expected publication June 2015
- A sixth and seventh pilot are currently under discussion to be completed before the end of JA2 (December 2015)

The Future of EUnetHTA and Joint Assessments

JA3:

- Currently under discussion, but will most likely go ahead
- Planned for 4 years: 2016-202
- Joint rapid assessments will most likely play a major role in JA3.

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



Thank you

Any questions?

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