Overview of what is changing on HTA in Europe

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Aims of Health Technology Assessment

HTA is a useful tool to

- Support decision makers in their efforts to achieve sustainable healthcare systems

HTA provides

- Evidence-based information useful in making decisions on how to allocate resources

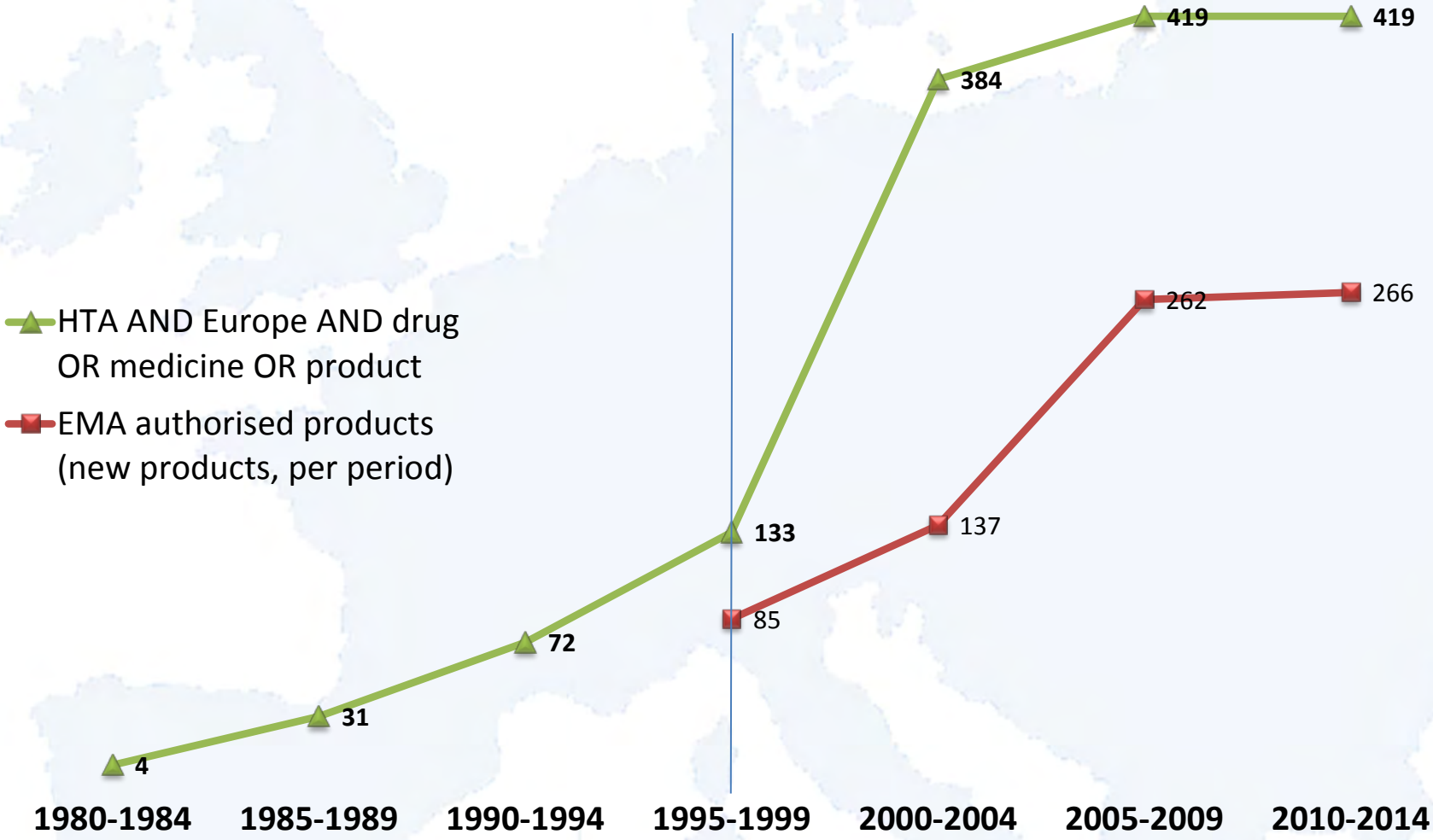
HTA is instrumental to

- Promote real innovation that deliver better outcomes

HTA can also be seen as a tool to recover control on new medicines (“sovereignty”)

- Since 1995, 750 new medicines approved via the centralised procedure at EMA
- ALL EU MS are collaborating in the evaluation of medicines
- The marketing authorisation decision lies in all
- Yet, MS are tempted to recover some control on the flow of new medicines as this impacts the balance of their healthcare system

Articles on HTA in Europe (PubMed)



Different outcomes from RD drugs assessments across HTA agencies

Brand name	Glivec®	Tasigna®	Avastin®	Revlimid®	Lucentis®
	Imatinib	nilotinib	bevacizumab	lenalidomide	ranibizumab
	RD oncology	OMP oncology	Off-label in RD	OMP oncology	RD in ophthalmology
GBR	🟢	✖	✖	🔴	🟠
FRA	🟢	🟢	🟢	NA	🟠
ITA	🟠	🟠	🟠	🟠	🟠
ESP	🟠	🟠	🟢	🟠	🟢
CZE	🟢	🟢	🟠	🟠	🟠
POL	🟠	🟠	🟠	🟠	🔴

Approved for reimbursement
- 🟢 As per indication
- 🟠 With restrictions
- 🔴 With severe restrictions

✖ Not reimbursed

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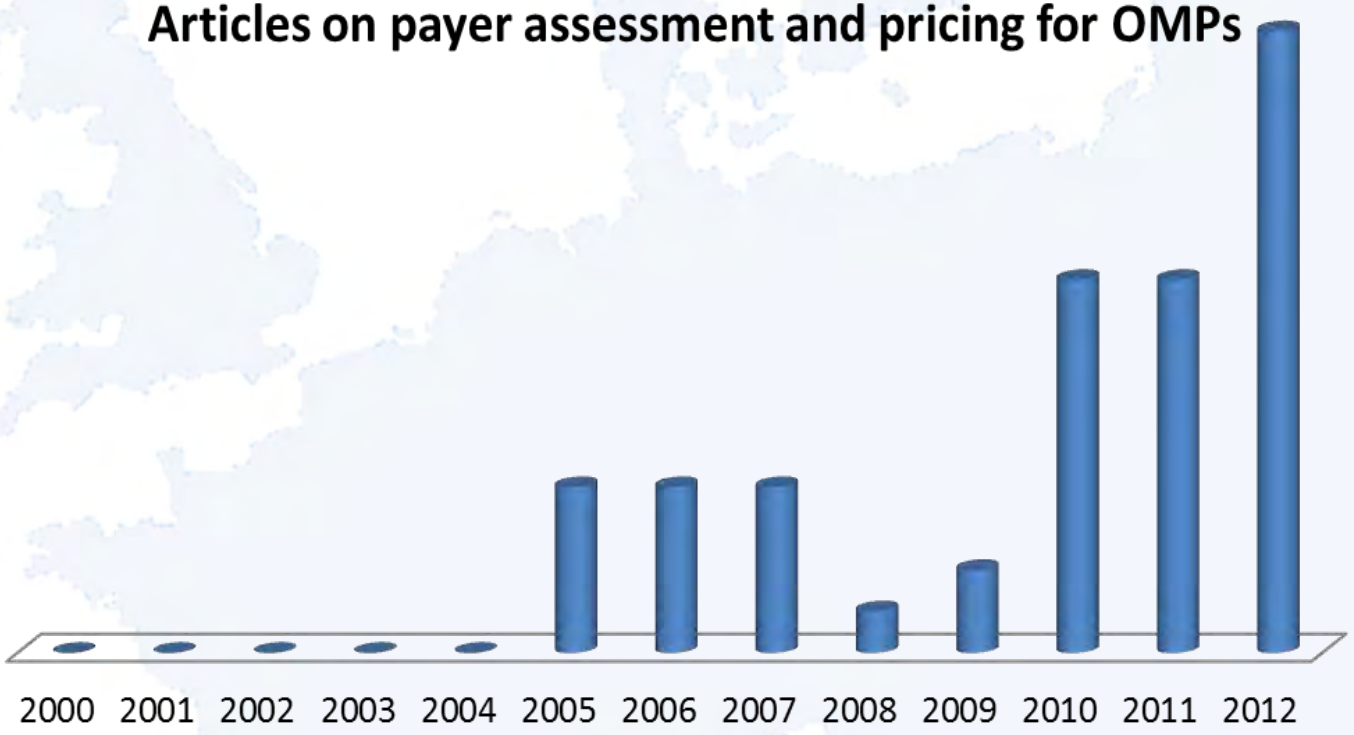
HTA activity on OMPs since 2008



13 published before 2008 (average 1.4/year) versus 35 after 2008 (average 8.8/year), or 6.25 fold more articles in the recent period, as an indication of more acute difficulties with OMPs since the onset of the economic crisis.

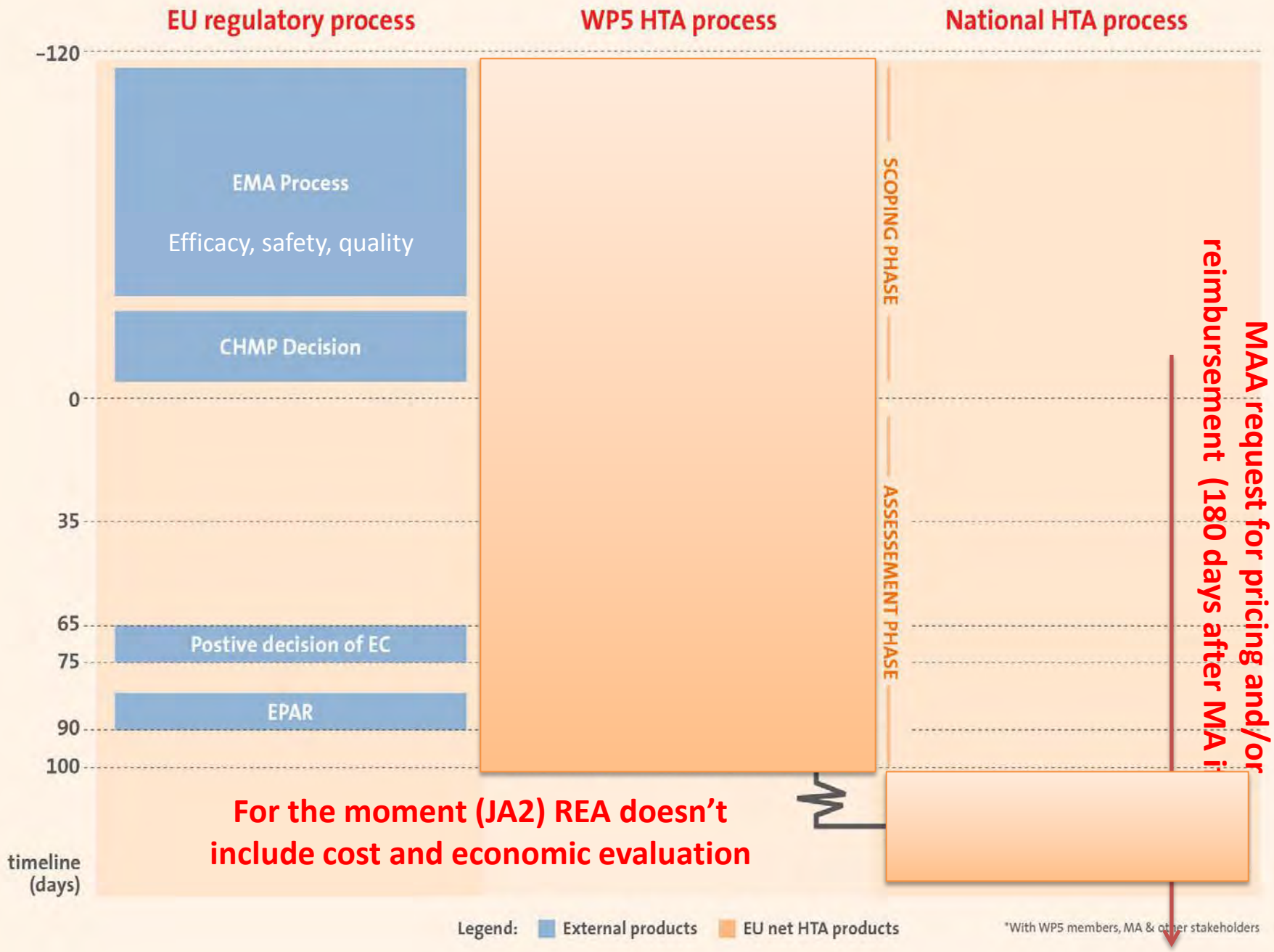
Hutchings et al : Payer Assessment and reimbursement policy for rare diseases: a review of the literature. ISPOR 16th Annual European Congress, Dublin

Intro: HTA domains

Rapid

Full

1. **Health problem and current use of technology**
2. **Description and technical characteristics**
3. **Safety**
4. **Clinical effectiveness**
5. **Costs and economic evaluation**
6. **Ethical analysis**
7. **Organisational aspects**
8. **Social aspects**
9. **Legal aspects**


EU regulatory process
WP5 HTA process
National HTA process
-120
EMA Process
Efficacy, safety, quality
CHMP Decision
0
35
65
Postive decision of EC
75
EPAR
90
100
timeline (days)
SCOPING PHASE
ASSESSEMENT PHASE
MAA request for pricing and/or reimbursement (180 days after MA i
For the moment (JA2) REA doesn't include cost and economic evaluation
Legend:
External products
EU net HTA products
*With WP5 members, MA & other stakeholders

Fair priority setting

A fair HTA process should ensure	Publicity	Availability of decisions to the wider public for scrutiny
	Relevance	Stakeholders agreeing upon the “relevance” of the inputs for the decision
	Appeals	Objections and contributions to the revision of decisions
	Enforcement	“publicity”, “relevance”, “appeals” appropriately followed

A 7-step policy framework for rare diseases

Principles of accountability for reasonableness (Daniels & Sabin)	Confirm disease is truly rare (COMP)	< 5 /10,000 in the EU severe/life-threatening
	Understand the disease	Listen to patients, interview some, collect info from many
	Understand potential value of candidate drug	Evaluation of all accessible clinical data. Bradford Hill criteria may be used
	Estimate its clinical effectiveness	In the absence of adequate RCT evidence: Markov modelling
	Estimate costs and generate funding reco.	Cost minimisation, incremental cost per life year gained, budget impact…
	Review assessment with experts and stakeholders	Areas of significant disagreement or error, face validity of the model
	Reassess if new data come in	

From Clarke et al. Drugs for Rare Diseases Working Group, Ontario Public Drug Program

When we are proposed to join a clinical trial

- The investigators always explain that in a clinical trial, all subjects receive the best possible care
  - Subjects in the comparator arm receive best possible care and a placebo
  - Subjects in the experimental arm receive best possible care and the experimental product
- So, if the treatment we receive in a clinical trial is the best possible care, both in the experimental and the comparator arm, why do HTA agencies claim they need to evaluate the experimental product compared to a different treatment then the comparator used in the trial?

Why are we facing a problem?

Regulators: benefits (efficacy)/risks

HTA: safety and relative effectiveness

Experimental drug compared to placebo or comparator

New technology compared to how disease is treated

Comparator defined by investigators, i.e. treating physicians

In theory, in the best interest of patients.

Comparator defined by standards of care or what is available

Why should they differ?

Usually: same comparator across all participating countries

Usually: SoC differs by country

Because equal rights to treatment in all EU states is not a reality (yet)

Illustration: experimental treatment X

Regulatory trial: the easiest comparator is B, as to recruit patients in all 3 countries X should be compared to B

Country 1 available treatments	Country 2 available treatments	Country 3 available treatments
• A: first line antibiotic • B: only if resistance to A	• B: first line antibiotic • C: only if resistance to B	• B: first line antibiotic
HTA body country 1 Needs to assess X versus A & B	HTA body country 2 Needs to assess X versus B & C	HTA body country 3 Needs to assess X versus B

Maybe A is obsolete, and B and C are the best treatments.
If offer for care was more homogenous across EU MS, both B & C would be available everywhere

We inherited from a very heterogeneous situation where SOC differs by country. This explains why HTA bodies make different assessments

Orphan drugs, cost-effectiveness and QALYs

- Some say rare diseases are not “special”
- Organ Transplant
- Limits of cost-effectiveness

35 years of QALY

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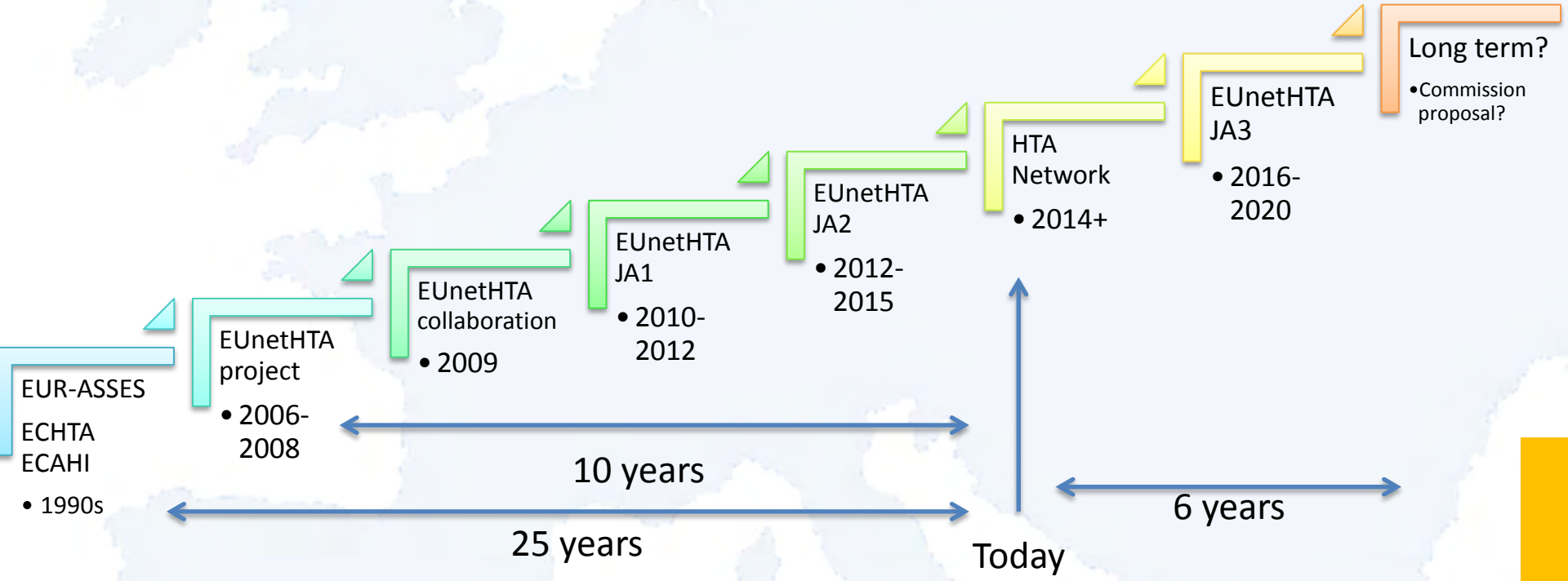
HTA network: timelines (25 years+)



EUnetHTA Joint Action 2 (2012-2015) Planned deliverables

- Recommendations on the implementation of sustainable European network for HTA
- Full Core HTAs
- Pilot rapid assessments
- Methodological guidelines and Templates to support production of core HTA information and rapid assessments
- Guidelines and pilots to improve quality and adequacy of initial and additional evidence generation
- Report on yearly training courses on EUnetHTA tools and methodology
- Report on evaluation of project completion including assessment of impact on secondary users of HTA information

The future: Scope of EU cooperation on HTA

The full life cycle

- From horizon scanning, to early dialogue, parallel scientific advice, rapid assessment, full assessment, and disinvestment (obsolete technologies)

The whole range of health technologies

- Pharmaceuticals, medical devices, combination of diagnostics and pharmaceuticals, surgical procedures, preventive and health promotion programmes, ICT tools, integrated care processes

All different domains of HTA

- Clinical (HTA Core model for REA, time limits Transp. Dir.), and also economic, social, ethical, organisational, legal

Feedback to a wide range of decision makers

A clear framework for priority setting

- Reflecting the added value of cooperation, synergies with national activities, level of commitment of relevant players

Common tools: the POP database
(Planned & Ongoing Projects)

POP Statistics: Quarterly Updates

In Spring 2014, POP Database contained: **1,230** planned, ongoing and recently published projects from **44** EUnetHTA JA partners and **24** countries

(Oct/Dec 2013) POP Request

Out of 63 EUnetHTA JA partners:

- **28 responded** and **entered/updated projects** in the database
- **11 responded** but **DID NOT feed** the database
- **24 did not respond at all** (38%)
- **Total number of projects: 1,219**
- Alert (SAME) topics: 101 (8%)
- **Similar projects** (within alert topics): **249**
- **Access-rights: 41** partners

(Jan/March 2013) POP Request

Out of 68 EUnetHTA JA partners:

- **35 responded** and **entered/updated projects** in the database
- **8 responded** but **DID NOT feed** the database (no current changes in the projects)
- **25 did not respond at all** (37 %)
- **Total number of projects: 1,216**
- Alert (SAME) topics: 103 (8 %)
- **Similar projects** (within alert topics): **247**
- **Access-rights: 46** partners

Other tools

- EVIDENT database
  - Sharing and storage of information on reimbursement / coverage and assessment status of promising technologies and
  - Additional studies requested further to a HTA
- Common guidelines on
  - Clinical, composite and surrogate endpoints
  - Safety, health-related quality of life
  - Criteria for the choice of the most appropriate comparator(s)
  - Direct and indirect comparison
  - To come: economic and cost evaluation, observational data
- Disease specific guidelines (to come)

Long term host of the EU HTA collaboration: possible alternatives

Within the the EC DG Sanco	Part of the EMA	Rotating HTA agency	Part of the E-CDC	Within CHAFEA

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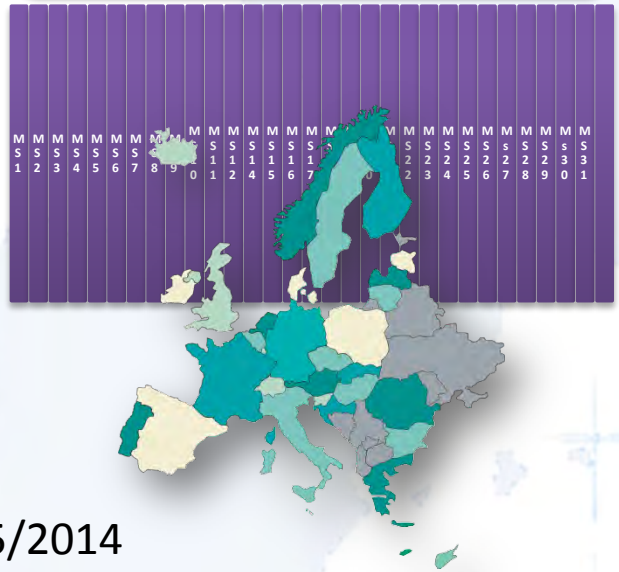
Today

New health technology

Different methods, conclusions and additional studies requested, not all domains



Horizon 2020

New health technology

POP database, common guidelines

Joint assessment

Joint report used by 15+ other agencies

National level to be added

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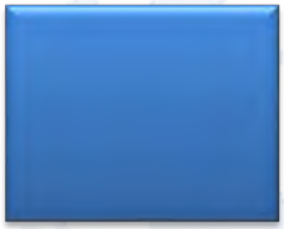
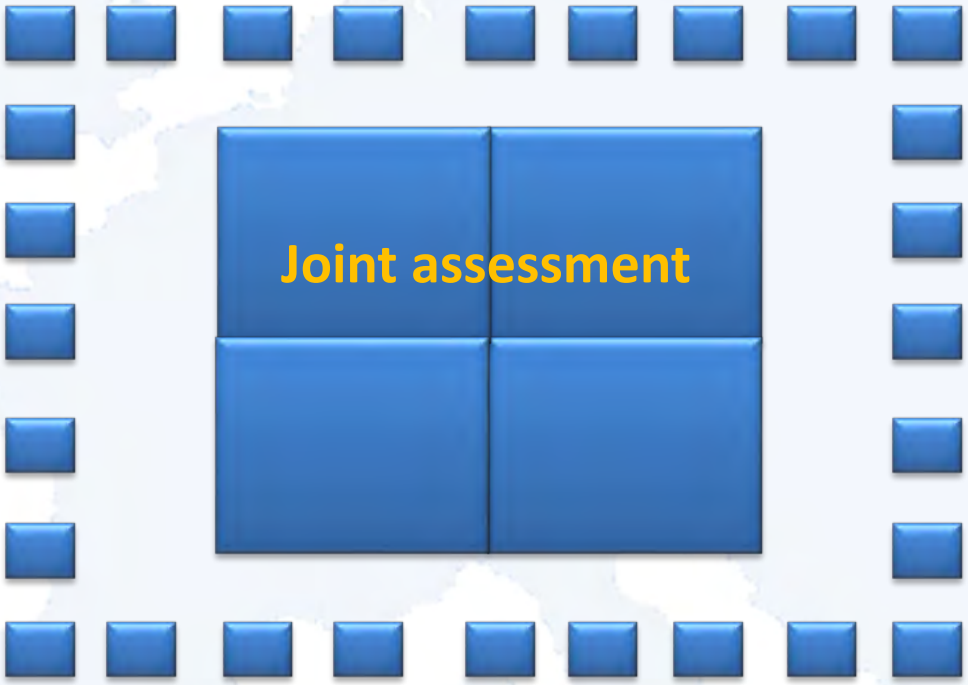


If this surface would represent the amount of work to be done by one agency in one country to assess a new technology

This would represent the work done by 28 agencies independently

And this would represent the amount of work done by joint collaboration



National level part (not all at once)

Example of national barriers

- AMNOG in Germany
  - IQWIG cannot share which projects they have
  - None of the 8 OMPs assessed since AMNOG made it
    - For 5 OMPs, G-BA rated “unquantifiable additional benefit”, in further 5 cases “minor a. b.” and in 1 sub-pop. considerable ben.
  - Price negotiation 15 months
  - Includes the Czech Rep., Slovakia and Greece in the country basket for international reference pricing
  - The German price is again referenced by 19 other MS
  - G-BA choice of comparator often differs from that chosen for the development programme after EMA consultation
  - Good point: full transparency on price and rebates
- Austria
  - Until recently, HTA experts were not authorised to use English

Patients are engaged at all steps

Orphan Drug Designation
COMP
Criterion on significant benefit

Protocol Assistance

Opinion on benefit/risks
CHMP
T0

Opinion on significant benefit
COMP
Assessment of significant benefit

Marketing authorisation
European Commission
T0 + 90 Days

Additional data HTA
Updated core HTA
Relative effectiveness assessment

Scientific Advice
EMA/EUnetHTA
Early dialogue

Report and
evidence generation plan

Assessment of new
Evidence

Time

Early dialogue	Exchange and defining what's missing	Evidence generation	Assessment
• EMA • EUnetHTA • Sponsor • Patients (CAB-PRO) • Experts	• EMA • EUnetHTA • Sponsor • Patients & doctors	• EMA • EUnetHTA • MAH • ENCEPP • Centres of Expertise • European Reference Networks	• EUnetHTA • EMA • MAH • Patients • Centres of Expertise

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How do we organise ourselves to find experts?

- Patients, among other, are invited to contribute to EUnetHTA HTA reports (scientific advice)
- Unlike most medicines at EMA, technologies are not disease specific
- For example:
  - Balloon Eustachian tuboplasty / dilation of Eustachian tubes to treat Eustachian tube dysfunction
  - Biodegradable stents for benign refractory esophageal stenosis
  - Duodenal-jejunal bypass sleeve to treat obesity
  - Renal sympathetic denervation to treat resistant arterial hypertension

"OK, all those in favour of delegating decision-making, shrug your shoulders"

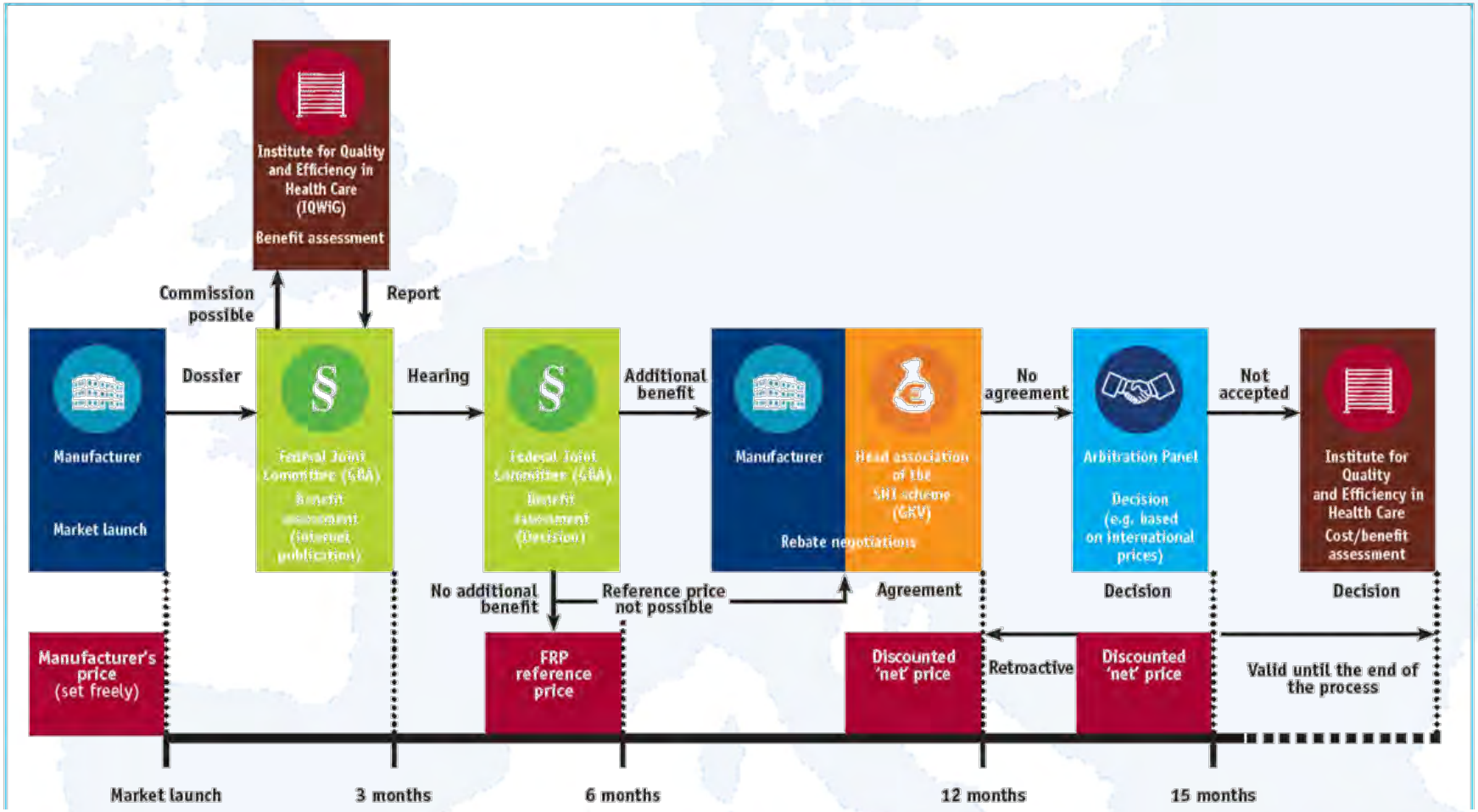
THANK YOU

43 EMA authorised OMPS: varying reimbursement decisions (OHE Oct. 2009)

	France	Germany	Italy	Spain	Sweden	The Netherlands	England and Wales
Authorised	43	43	43	43	43	43	43
Launched	38	35	34	30	35	40	39
Of which reimbursed	38	35	32	30	24	39	39
% reimbursed /launched	100%	100%	94%	100%	69%	97%	100%

Martina Garau and Jorge Mestre-Ferrandiz
Office of Health Economics Briefing, No 52 October 2009

Germany well over 90 days



Since AMNOG came into force in Germany

Total number of finalised assessments	66
Major additional benefit	0
Considerable additional benefit	11
Slight additional benefit	23
Additional benefit not quantifiable	11
No additional benefit	70
Less benefit	1

As of Feb 2014. The difference between the number of finalised assessments and the number of the Committee's decisions results from the fact that some decisions refer to more than one subpopulation.

Among these assessments were 8 OMPs. As far as OMPs are concerned, the Joint Federal Committee **only assesses the extent of the additional benefit without determining the additional benefit against a comparator therapy** in the first place.

Funds needed: hypothesis

- Production
  - Large HTA bodies can conduct 20-30 assessments/year
  - Others: 10
  - Current HTA production capacity: 180 / year
  - Full speed HTA network production: 600 / year
- Rapid assessment: 30 000 €
- Full HTA report: 100 000 €, to increase to 300 000 € for joint production (less for national full HTA reports using common methodologies)