CIRS- Centre for Innovation in Regulatory Science

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Mapping of HTA in Europe
" Regulatory and Reimbursement Atlas"

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Introduction to CIRS

Background of comparative process mapping project

Methodology

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About CIRS

Mission

To maintain a thought leadership role in identifying and applying scientific principles for the purpose of advancing regulatory and HTA policies and processes.

CIRS provides a neutral, independent, international forum for industry, regulators, HTA and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy through the innovative application of regulatory science*

Regulatory science is the science of developing new tools, standards and approaches to inform decision making pertinent to the quality, safety, efficacy and effectiveness of medicinal products.

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Member Companies

USA	Europe	Japan
AbbVie	Actelion	Astellas
Amgen	AstraZeneca	Eisai
Biogen	Bayer	Takeda
Celgene	GlaxoSmithKline	Zeria
Eli Lilly and Co.	Merck Serono	
Johnson & Johnson	Novartis	
Pfizer	Novo Nordisk	
Shire	Roche	
	Sanofi	
	Servier	
	UCB	

HTA and Coverage Bodies

Country	Organisation
Australia	PBAC
Belgium	INAMI; KCE
Brazil	CONITEC
Canada	CADTH; DSEN, Canadian Institutes of Health Research, INESSS, Alberta Health Services
Croatia	AAZ
Denmark	Danish Health and Medicines Authority
England, Wales	NICE
Europe	EUnetHTA
France	HAS
Finland	THL
Italy	AIFA
Lithuania	VASPVT
Norway	NOKC
Poland	AHTAPol
Portugal	INFARMED
Scotland	Scottish Medicines Consortium
Spain	CAHIAQ, Osteba
Sweden	TLV
Switzerland	BAG
The Netherlands	ZIN
United States	UnitedHealth Group; TEC; Blue Cross/Blue Shield Association; Kaiser Permanente Institute for Health Policy; AHRQ; OPTUM

Participating Regulatory Authorities

Country	Authority
Argentina	ANMAT
Australia	TGA
Brazil	ANVISA
Canada	Health Canada
Chile	ANAMED
China	SFDA; CDE
Chinese Taipei	TFDA; CDE
Colombia	INVIMA
EU	EMA
India	CDSCO
Indonesia	NAFDC
Israel	MoH
Japan	MHLW, PMDA
Jordan	JFDA
Kuwait	KDFC
Malaysia	NCPB
Mexico	COFEPRIS
Oman	MoH
Peru	DIGEMID
Philippines	DOH, FDA
Qatar	SCH
Saudi Arabia	SFDA
Singapore	HSA
South Africa	MRA
South Korea	MFDS
Sweden	MPA
Switzerland	Swissmedic
Turkey	MARA
United Arab Emirates	MoH
United Kingdom	MHRA
United States	FDA

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HTA Programme at CIRS

Key objectives of the programme

to improve understanding of HTA and coverage processes and decision making and to promote best practice by the application of tools developed by the Centre

to advance HTA and regulatory agency interaction in terms of scientific advice and alignment of technical requirements

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The HTA Steering Committee

Chairman

Dr Brian O'Rourke, Canadian Agency for Drugs and Technologies in Health (CADTH), Canada

Agency Members

Dr Meindert Boysen, National Institute for Health and Clinical Excellence (NICE), UK

Professor Hans-Georg Eichler, European Medicines Agency (EMA), UK

Professor Finn Børlum Kristensen, European Network of Health Technology Assessment (EUnetHTA); National Board of Health, Denmark

Dr François Meyer, Haute Autorité de Santé, (HAS), France

Andrew Mitchell, Department of Health and Ageing, Australia

Industry Members

Dr Indranil Bagchi, Pfizer Inc., USA

Lars Brüning, Bayer Healthcare Pharma, Germany

Adrian Griffin, Johnson & Johnson, UK

Dr Jens Grueger, Roche Pharmaceuticals, Switzerland

Dr Michael Happich, Eli Lilly and Company, Germany

Academic and Research Members

Prof Bruno Flamion, University of Namur, Belgium

Prof Adrian Towse, Office of Health Economics (OHE), UK

Dr Sean Tunis, Center for Medical Technology Policy (CMTP), USA

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Complexity of the review process (e.g. EU)

Regulatory: European Medicines Agency

- One agency, decision applies across EU

HTA: 30+ HTA agencies in Europe:

- Both national and regional level HTAs
- Different methodologies, processes and requirements
- Different outcomes

Payers: 30+ payer agencies in Europe:

- Both national and regional level payers
- Different abilities to pay
- Different resource allocation decisions

Patients: 501 million people across EU[1]

- Unequal access to the same medicines

European Union:
27 Member States in 2010

European Economic Area Members:
Iceland, Liechtenstein, Norway, Switzerland

Source: EuroStat (http://epp.eurostat.ec.europa.eu)
Population of 501,103,425 as at 1 January 2010

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"If you have seen one HTA system, you have seen one HTA system."

Health Technology Assessment: Lessons Learned From Around the World An Overview
[Value in Health Special Issue, June 2009]

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Establishment and progress of the project

There is a need to systematically characterise the organisations and their activities within each country in order to be able to understand, compare, measure and identify the most effective and efficient practises.

2011 a pilot project was conducted for the purpose of testing and refining the methodology of this programme. The pilot study successfully demonstrated the feasibility and utility of this exercise.

In 2012, the process maps have been developed to examine the reimbursement systems of 33 jurisdictions in Europe.

From 2013 onwards, comparative maps are developed for more than 70 jurisdictions.

Objectives

- To identify the key stakeholders that had direct or indirect involvement with respect to the decision-making outcome.
- To understand the criteria and method of evaluation for HTA in each country.
- To identify the process archetypes of HTA systems in 33 European jurisdictions

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Process mapping methodology

In order to maximise the comparability of these process maps, **the scope of this study was limited to**: The regulatory and reimbursement processes for the review of New Active Substances (NAS)

The maps were designed to contain a hierarchy of information:

❑ The first level is the **identification of the agencies involved in the process** and whether they are within government or independent.

❑ The second level identifies **the movement of information from the sponsor of the new medicine to the agencies** and thus specifies the key milestones of regulatory approval, HTA evaluation, recommendation, decision making and adoption.

❑ The third level acknowledges that even within milestones, processes are potentially different, and hence **identifies key activities** (such as scientific advice, price consideration) that are utilised in the systems.

Process mapping methodology

Step 1 → Step 2 → Step 3
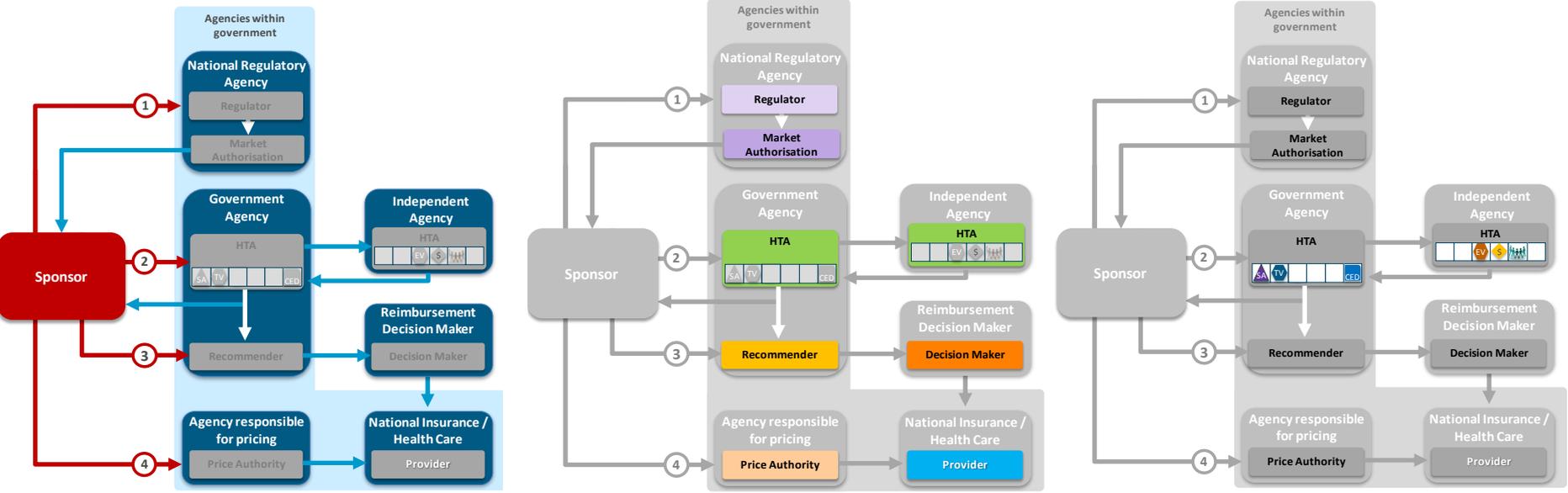
This model indicates the construction of the first step of the process maps. The Sponsor is shown in red and the connections with the agencies are numbered to indicate the typical order in which these contacts occur. The Agencies are shown in blue with internal connections in white and external connections in blue. The light blue shading indicated those agencies that are within the national level government.

Seven functions that represented significant and measureable key components of the system were defined and then mapped onto the agencies that conducted those functions. This allowed the identification of where in the system such functions occurred and how they related to one another.

For the HTA function, a "task bar" of key activities was developed in order to characterise a selection of defining elements of the HTA process. Each activity was
given an identifying icon that was shown in the HTA task bar if it was a normal part of that agency's actions

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Core Functions:

Regulator

Regulator: where scientific evaluation based on safety, quality and efficacy is conducted to determine if market authorisation should be recommended.

Market Authorisation

Market Authorisation: where the decision to grant market authorisation to the new medicine is made.

HTA

HTA: where assessment of the new medicine is conducted in relation to the therapeutic value and/or economic value of the new medicine to the healthcare system in question.

Price Authority

Price Authority: where the list price for the new medicine is either determined or otherwise controlled such as in the form of a voluntary price agreement or by imposing a price ceiling.

Recommender

Recommender: where the HTA appraisal results in a recommendation for reimbursement but the decision itself is made elsewhere.

Decision Maker

Decision Maker: where the decision to reimburse the new medicine is made in relation to the national coverage scheme.

Provider

Provider: where the new medicine is adopted based upon outcome of the decision maker.

HTA Key Activities:

SA

Scientific Advice: Provision of scientific advice to the sponsor in relation to the drug development program or the submission of evidence to that agency.

TV

Therapeutic Value: Evaluation of the clinical evidence in order to determine if there is added-therapeutic value in the new medicine.

EV

Economic Value: Determination of the cost-effectiveness, cost-utility, cost-benefit and/or budget impact of the new therapy.

$

Reimbursement rate: Determination of the rate of reimbursement for the new medicine, usually into pre-defined categories.

Public consultation: Involvement of patients, patient advocates and/or public representatives, this includes both formal and informal forms of consultation.

CED

Coverage with Evidence Development: Provision of release of the new medicine where data is limited with the condition of further evidence development.

France
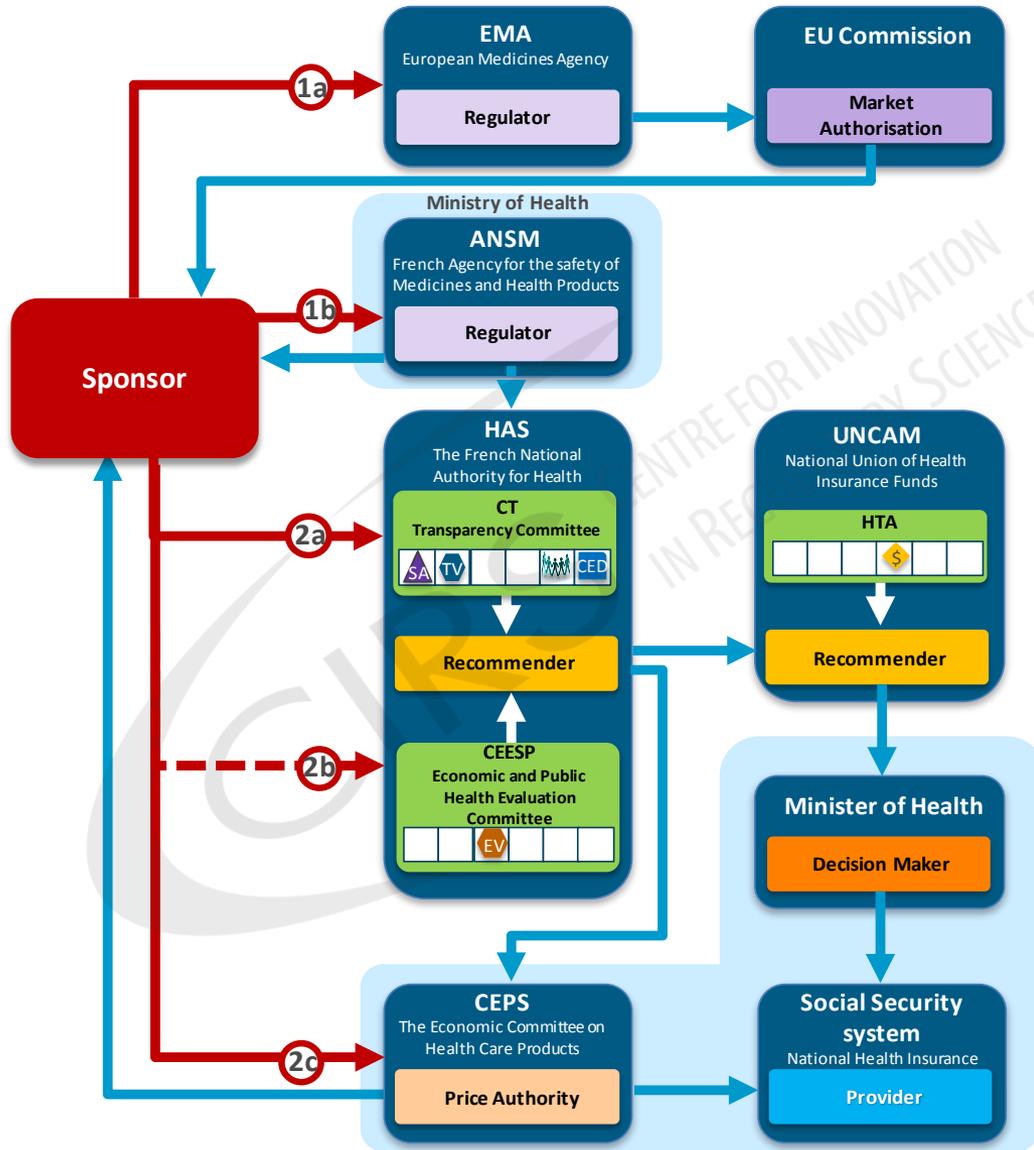
Manufacturer dossier is submitted simultaneously to the *Commission de la Transparence* (CT, Transparency Committee), the *Commssion d'Evaluation Economique et de Santé Publique* (CEESP, Economic and Public Health Evaluation Committee), the *Comité Economique des Produits de Santé* (CEPS, Economic Committee for Healthcare Products), and the *Union Nationale des Caisses d'Assurance Maladie* (UNCAM, National Union of Health Insurance Funds).

CT (Transparency Committee) determines the drug's *service médical rendu* (**SMR; medical benefit**) and *amélioration du service médical rendu* (**ASMR, improvement in medical benefit**). CEESP (Economic and Public Health Evaluation Committee) issues opinion on c**ost-effectiveness**.These two assessments are submitted to the CEPS.
UNCAM (National Union of Health Insurance Funds) determines whether a drug will be reimbursed and at what rate (15%,30%, 65% or 100%).

The CEPS (Economic Committee for Healthcare Products) and the manufacturer negotiate the price based on the drug's ASMR ratings, the prices of drugs with similar indications, actual/forecas sales, and actual/forecast consumption.

The Ministry of Health takes final decision. Details of reimbursed drugs are published in the *Journal Officiel.*

Production / validation flow

Data collection/ synthesize

CIRS searches from public domain
Data collection from internal resources

Creation of process map

CIRS creates draft map based on the standard methodology
Draft map undergoes internal SOP and QC

Draft map sent to HTA agency for review and comments

No comments from agency →

Comments sought from local expert

Finalization

Comments integrated into maps
Final map created and posted on Atlas

Maintenance

Map reviewed and updated every year, ad hoc update if significant changes occur in the system

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Comparison of process maps
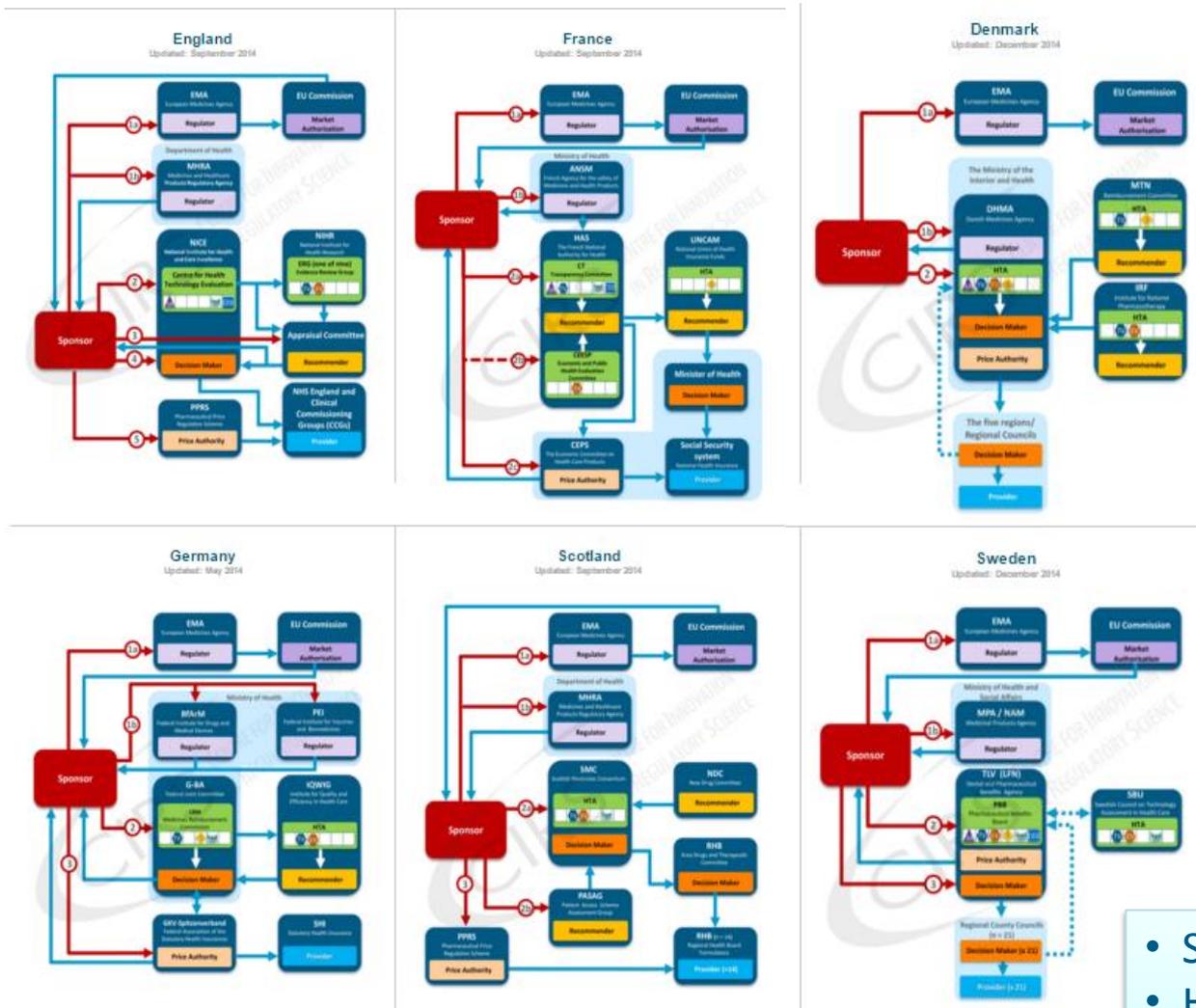
- Systematic design
- Hierarchical comparison
- Visual and simple

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Outcome of the comparative mapping exercise

❑ Identification of key stakeholders in the reimbursement system, and the extent of independence of the agencies from government

❑ Understanding the interactions of key stakeholders and the position of HTA in the decision making pathway

❑ Comparison of methodology used by HTA and to understand the extent of independence between clinical and economic assessment, the final HTA recommendation and the coverage decision

❑ Identification of the location of the decision-maker in the process

❑ Illustration of multi-step, multi-stakeholder approaches in the reimbursement systems.

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Online Platform – Regulatory and Reimbursement Atlas

Atlas · **Methodology** · **Compare Multiple Maps** · **Instructions** · **Information**

CIRS Regulatory and Reimbursement Atlas

CIRS Regulatory and Reimbursement Atlas™

- More than 70 jurisdictions
- National vs. regional
- Emerging countries

Select a country to view map

- Ireland
- Italy
- Japan
- Latvia
- Liechtenstein
- Lithuania
- Luxembourg
- Malta
- Netherlands
- New Zealand
- Norway
- Peru
- Philippines
- Poland

The CIRS Regulatory and Reimbursement Atlas™ has the following features:

- The colour coded world map indicates which jurisdictions currently have process maps available in the CIRS Regulatory and Reimbursement Atlas™
- The list of countries contains clickable links to direct the user to the relevant process map.
- The main menu is positioned at the top of the page and consists of five clickable icons: Atlas, Methodology, Compare multiple maps, Instructions and Information. The comparison function allows the user to view two or four countries for comparison.

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Output of the Atlas – Case studies

The Regulatory and Reimbursement Atlas has been used to underpin research studies within CIRS.

Three case studies :

1. Educational tool for participating stakeholders
2. Development of archetype of EU systems
3. HTA Assessment routes and timelines comparison

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Case study 1
Stakeholder survey – How can knowledge of HTA systems be effective translated to meet stakeholder needs?

HTA Agency View points

• *"One-stop shop, easy to use, comparability"*

• *"The flow chart kind of illustration is most helpful in terms of user friendliness etc. I guess you might come to a point where the flow chart will get too complicated but so far it works for these purposes"*

• *Great job. I think this work fills an important gap in the resources and tools available for industry, HTA bodies, payers and academics. This is a fast growing field and getting increasingly complex with time and this tool (Atlas) provides a one stop experience for people who are keen to understand the*

• *Regulatory-HTA-Payer landscape, different interaction points and similarities and differences across different systems. Finally, the methodology and standardised format is quite sophisticated yet simple and user-friendly."*

Pharmaceutical company View points

• *"Uniform methodology"*
• *"Clarity and ease of use"*
• *"The graphical representation of the Atlas would be a good choice for discussions with internal colleagues and external audiences to provide a common point of discussion"*

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Case study 2
Development of archetypes to facilitate comparative analysis of reimbursement and decision-making processes in Europe

2 sets of taxonomy was developed when comparing the similarities and differences between regulatory to reimbursement system

The '**System taxonomy**' set contains 4 groups including HTA and an additional fifth group for systems that use external HTA:
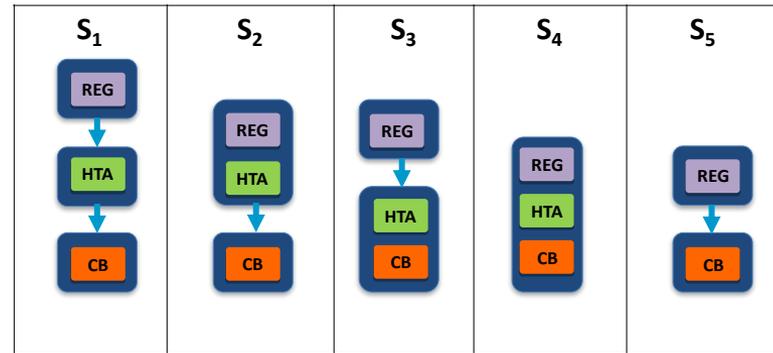
The '**HTA taxonomy**' set focuses on the relationship between the HTA appraisal, therapeutic assessment and the economic evaluation if present.

S_1	S_2	S_3	S_4	S_5
REG				
	REG	REG		
HTA	HTA		REG	REG
		HTA	HTA	
CB	CB	CB	CB	CB

H_1	H_2	H_3	H_4
TV EV	TV EV	TV	External HTA
AP	AP	AP	AP

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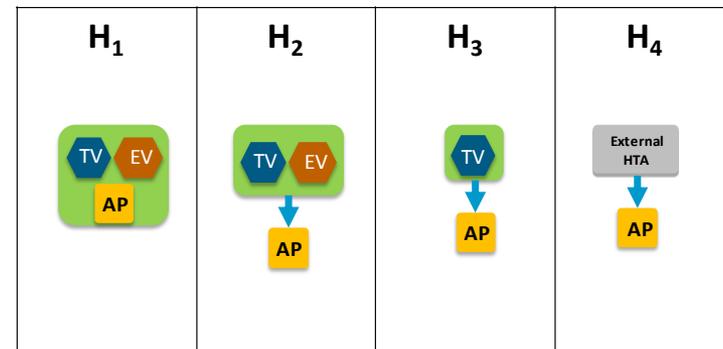
CASE STUDY 2

Case study 2
Development of archetypes to facilitate comparative analysis of reimbursement and decision-making processes

Objectives

1) Compare positive, restricted and negative HTA recommendations for NAS's granted EMA approval from 2008 to 2012

2) Assess the relationship between System taxonomy with HTA recommendations

3) Assess the relationship between HTA process taxonomy with HTA recommendations

Conclusion

❑Congruence between dissimilar Process Archetypes ranged from **47% to 96%** and suggest the reimbursement recommendations by these is likely to be influenced by factors other than the process.

❑This study identified the greatest level of congruence for HTA recommendations from the A taxonomy agencies.

❑Other factors likely play a role in the divergences of reimbursement recommendations among dissimilar processes

Case study 3
Assessment routes and timelines

France

Timelines for each step
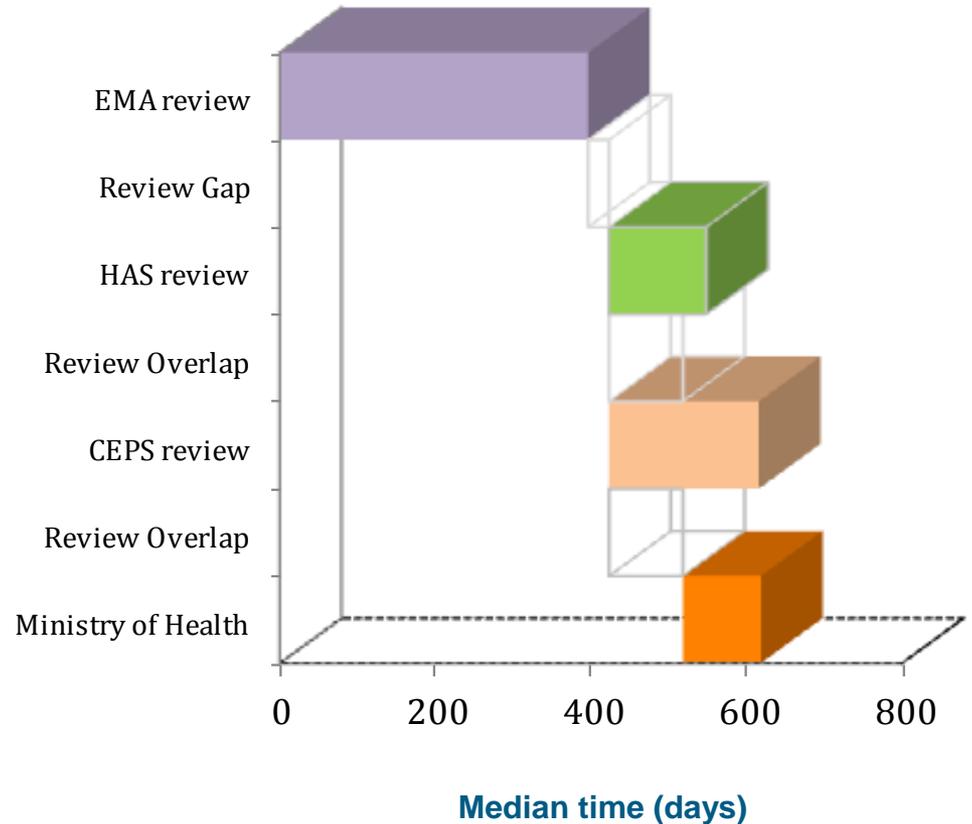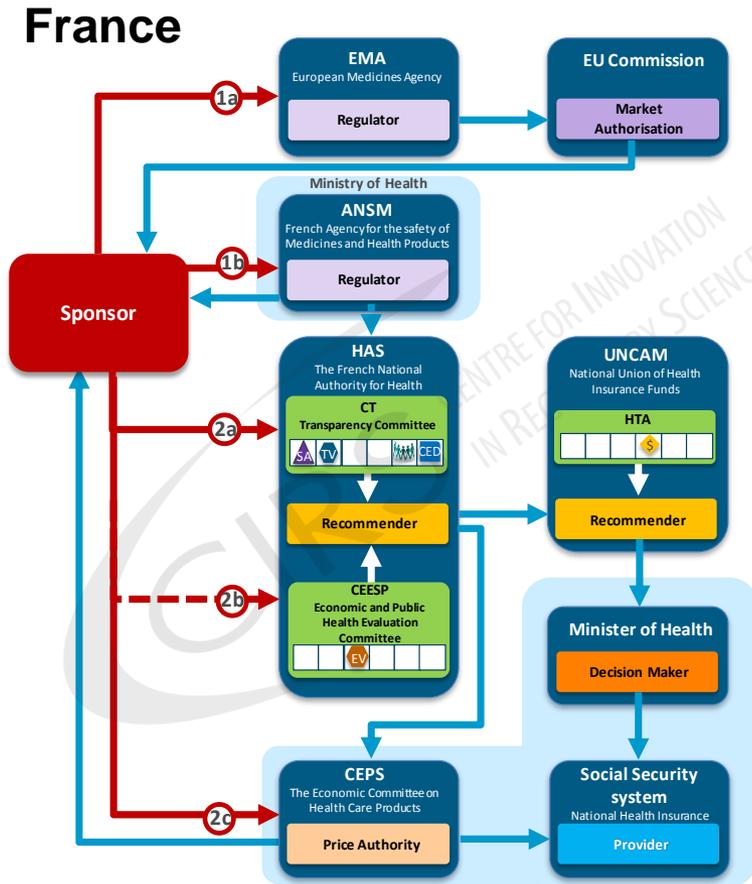
Median time (days)

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Comparative mapping project

Current status

☐ Process Maps have now been produced for over <u>70 jurisdictions</u> over the world

☐ The process maps have been built into <u>an online platform – Regulatory and Reimbursement Atlas</u> that provides easily interpretable, hyperlinked, graphical representations and interactive digital format allows comparison of multiple maps -

☐ A number of research projects have been derived from the Atlas maps

Future plan

☐ The process maps <u>are continuously maintained and updated</u> to reflect the most up-to-date information of the systems

☐ <u>Monitor the HTA environment</u> and changes of systems

☐ Utilize process map to <u>underpin future researches</u>

☐ <u>Enhance granularity</u> of the map with a focus of certain HTA activities (Patient engagement, early scientific advice etc)

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