European Commission

Study on impact analysis of Policy Options for strengthened EU cooperation on Health Technology Assessment (HTA)

Annexes

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Annexes

Annex 1: Expert consultation

Introduction

This document is a consultation document for the expert group of the 'Study on impact analysis of policy options for strengthened EU cooperation on HTA'. It includes background information as well as a range of questions regarding the identified policy options for cooperation on HTA on EU level and possible impacts.

As a member of the expert group established for the duration of this project we kindly invite you to respond to these questions to support us in ensuring the quality, feasibility and relevance of the policy options on HTA cooperation.

The document is structured in 4 parts:

1. Background information to this study
2. Description on baseline scenario and related questions
3. Information on policy options and related questions
4. Questions regarding impacts for assessing the policy options

Background information

The European Commission (EC) is exploring options for a new, sustainable mechanism for HTA in Europe after 2020. Consequently, the Directorate General for Health and Food Safety (DG SANTE) of the European Commission started an **impact assessment process** and launched a public consultation on 21 October 2016([1]).

In the framework of this process, the EC commissioned the consortium of Sogeti, the Austrian Public Health Institute (GÖ FP) and the London School of Economics and Political Science (LSE Health) to conduct an impact analysis of policy options for strengthened EU cooperation on HTA in order to **support the Impact Assessment process of the EC with data and evidence**.

Possible policy options for cooperation on HTA on EU level have been identified within the Inception Impact Assessment published by the EC([2]). These are further developed by the Commission in the course of the study and expert input is required to ensure their validity and reliability.

In the course of the study a systematic literature review as well as a desk research of HTA and its use in EU Member States will be performed. A detailed case study covering 40 health technologies including pharmaceuticals, medical devices and other technologies (such as screening programs) will be conducted to assess the status quo. Data for this case study will be retrieved by literature review and an additional survey process to complement information retrieved.

Moreover, data will be collected to assess the impacts that the different possible implementation mechanisms for the five policy options in question (so called business models) will have on all relevant stakeholder groups. Data collection will be performed by a thorough literature research as well as a survey addressing all stakeholder groups.

We like to emphasize that the data collection will be from a public health perspective focusing on facts and figures to underpin the different policy options, not on opinions of any stakeholder group.

([1]) http://ec.europa.eu/health/technology_assessment/consultations/cooperation_hta_en.htm

([2]) An inception impact assessment has been published: **http://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf**

Description of Baseline Scenario

The baseline scenario is defined as the status quo of European HTA cooperation in 2016 taking the possible developments until 2020 (end of EUnetHTA Joint Action 3) into account. This status quo is characterized by

- a heterogeneous situation regarding the relevance of HTA in the national decision making processes;
- strictly voluntary cooperation between the European Commission and the EU Member States through (1) Joint Actions (Scientific and technical- developing methodologies and tool and performing joint assessments) and (2) HTA Network (providing strategic guidance).
- No guarantees that any joint output is taken up in national HTA activities.

Planned Work until 2020 – expected outcomes

The general objective of the EUnetHTA Joint Action 3 (2016 – 2020) is to support voluntary cooperation at scientific and technical level between Health Technology Assessment Bodies to validate the model for joint work to be continued after EU funding under the Health Programme. The cooperation between national and regional HTA Bodies is to meet the provisions set out by Article 15 of Directive 2011/24/EU[1] on patient's right in cross-border healthcare and to create synergy with the strategic HTA Network set up under this Directive.

The Joint Action 3 is aiming to establish an inventory on the available methodological documents and tools and, consequently, identifying gaps and adjusting or maintaining existing guidelines and tools. Moreover, all tools should be integrated in an **Online Handbook for HTA-Doers, early dialogue** communication should be provided and a tool for post-launch **evidence generation** and a **prioritisation process** for the topics of Joint Assessments should be developed.

In EUnetHTA Joint Action 3 a higher number of joint production work, than in the last Joint Actions; namely 51 **Joint Assessments**([3]) (33 on pharmaceuticals and 18 on other technologies) and 29 **so called "Collaborative Assessments"**([4]) (4 on pharmaceuticals and 25 on other technologies) are planned.

Until 2020 the Joint Action is financed by the 3rd Health Programme and Member States' contributions in kind. A new Joint Action is not foreseen, as it is a mechanism that should pilot new cooperation mechanisms, but not fund them on a long term. Therefore, it is anticipated that after expiration, and without further EU action, Member States would depend solely on their national/regional HTA procedures and budgets. Although Member States will be free to cooperate regarding HTA it is not sure on what scale joint work might continue.

Questions addressing the Baseline Scenario:

([3]) A Joint Assessment is defined as a prioritized topic, submission-based (using the submission templates as were developed in EUnetHTA JA2), an authoring team of 2-3 agencies and at least 5 dedicated reviewers, English as working language, use of HTA Core Model and Guidelines, EUnetHTA procedures on stakeholder involvement (scoping meeting with manufacturer etc.), internal and external quality assurance. A Joint Assessment can be a REA or a Full HTA.

([4]) A collaborative assessment is defined by a lower level of centralized work organization, but equal criteria in quality assurance: the collaborative assessments shall include at least 3-5 partners, however in justified cases two partners would be acceptable. Such constitutes a less centralised topic selection/priority selection process. English as working language, use of HTA Core Model and Guidelines, not necessarily submission based, internal QA by review by at least 2 other EUnetHTA partners (support by WP 4) + QA by external peer review, stakeholder involvement at 1 point in time (further criteria to be agreed upon).

1) Are you missing important aspects in the description of the Baseline Scenario? If yes, please state them shortly:

2) If there is no further financing by the EU after 2020, do you expect that the EU cooperation work will continue?

3) If yes, on what scale? Do you expect the following outputs to be produced through a MS-driven cooperation?

Outputs	**Yes**	**Partly (please elaborate)**	**No**
Maintenance of common tools and procedures			
Performing joint Early Dialogues			
Performing joint Relative Effectiveness Assessments([5])			
Performing joint Full Health Technology Assessments([6])			

([5]) REA can take place at time of market access, or later (re-assessment)

([6]) Full HTA can take place at time of market access, or later (re-assessment)

Key characteristics of policy options for cooperation on HTA after 2020
The different policy options for cooperation on HTA after 2020 are defined along several key characteristics focusing on 1. HTA output, 2. participation and uptake organizational aspects, 3. organizational aspects, 4. funding aspects as well as 5. timelines. These are described in the following.

1) The scope of the cooperation is defined by several **outputs**([7]) produced in joint collaboration, comprising:

- Maintenance of common tools and procedures, incl. common submission templates, an IT system with planned and ongoing assessments, common methodologies (e.g EUnetHTA Core Model), a joint prioritization process, and cooperation regarding data requirements and Horizon Scanning
- Performing joint Early Dialogues
- Performing joint Relative Effectiveness Assessments (REA can take place at time of market access, or later (re-assessment)
- Performing joint Full Health Technology Assessments (Full HTA can take place at time of market access, or later (re-assessment))

2) The engagement in participation and uptake([8]) of jointly produced outputs can be either **voluntary** or **mandatory**:

- voluntary participation/ voluntary uptake (V/V): both participating in the production of outputs and uptake of the respective output is entirely voluntary
- voluntary participation/mandatory uptake (V/M): the participation in the production of joint work is voluntary, meaning that Member States can decide to opt-in([9]) to the joint cooperation. However, once a Member State has opted-in the uptake of the joint work into the national setting is mandatory
- mandatory participation/mandatory uptake (M/M): both participation in the production of outputs and the uptake of these into the national setting are mandatory

For each of the policy options different combinations of **voluntary or mandatory** participation and uptake per output are possible.

([7]) The scope of the activities may differ for pharmaceuticals, medical devices and other technologies.

([8]) Please note that Up-take concerns the using or considering of the results and findings of the HTA cooperation, reaching from jointly developed submission templates to outcomes in full HTA. The subsequent pricing and reimbursement decision remains purely on national level. Also providers / developers need to adhere to this process.

([9]) Opt-in by MS is by output, not by individual products e.g. once a MS has opted in for joint REA, they take part in all joint REAs – but not necessarily as an author.

3) For organizing the production of these joint HTA outputs a number of different **implementation mechanism** are conceivable:

- Project based cooperation: there is voluntary cooperation, but no permanent coordination mechanism (i.e. Secretariat).
- MS secretariat (rotating): a permanent Secretariat is established, which will be rotating between the Member States.
- Existing EU agency: a permanent Secretariat is integrated in in an already existing EU agency. This Secretariat will coordinate the work of national experts in HTA bodies, to carry out the assessments.
- New EU agency: a permanent Secretariat is integrated in a NEW EU agency. This Secretariat will coordinate the work of national experts in HTA bodies, to carry out the assessments.

4) For financing the joint cooperation several **funding mechanisms** are conceivable:

- EU funding, either through Public Health program or another financial instrument
- Funding by Member States joining the collaboration
- Funding through industry fees

5) **Timelines**:

Timelines for implementation of the proposed policy options post 2020 reach from immediately, without delay, for option 1 (i.e. 2021) to appropriate transitional periods for implementing options 4 or 5 in a new legal framework).

Table 1 provides an overview of each policy option and the envisaged implementation funding mechanism. A short summary for each policy option can be found afterwards.

Please note that the final policy option does not have to be exactly one that was presented but it can combine elements. (E.g. It is possible to have option X, but combine it with the implementation model of option Y.) So at this point it needs to be ensured that 5 policy options cover all elements (e.g. all feasible implementation models should be covered), in a combination that is logical.

Table 1: Overview of Policy Options

		Baseline	Non-legislative	Legislative			
		PO 1	PO 2	PO 3	PO 4		PO 5
		No EU action after 2020	Voluntary cooperation through Public Health Programme	Legislation covering common tools and early dialogues	Legislation covering Joint work on REA Plus common tools and early dialogues		Legislation covering Joint work on Full HTA (incl. REA) Plus common tools and early dialogues
					4.1 REA V/M	4.2 REA M/M	
Outputs	Common tools, incl. templates, methodology	V/V	V/M	M/M	M/M	M/M	M/M
	Early dialogue([10])	V/V	V/M	V/M	V/M	M/M	M/M
	Joint REA([11])	V/V	V/M	V/V	V/M	M/M	M/M
	Joint Full HTA([9])	V/V	V/V	V/V	V/V	V/V	V/M
Implementation		No EU input	Project based cooperation	MS secretariat (rotating)	Existing EU agency	Existing EU agency	New EU agency
Financing		None from EU	EU+MS	EU+MS+fees from industry for early dialogues, joint REA and full HTA			
Scope			All medicines, medical and other technologies	Tools: all medicines, MDs , other technologies (phasing in), ED: industry submission	Tools and ED see PO 3. REA: certain categories of medicines (centrally authorised, high value/budget impact, agreement between MS), certain categories of MDs (similar criteria) and other technologies (agreement and prioritisation between MS) – phasing in([12])		Tools and ED see PO 3, REA see PO4. For others: ad hoc agreement and prioritisation between MS

(10) Early Dialogue: Here mandatory uptake means that the MS cannot repeat an ED that was done at EU level. Technology providers need to agree to Early Dialogue before it commences.

(11) Either at time of market or re-assessment

(12) A gradual introduction of products during a transitory period that allows to manage the workload while the structures/implementation model are being developed.

Short description of policy options:

Policy Option 1. Baseline scenario - No EU action after 2020:

- Non-regulatory framework
- Participation/uptake entirely voluntary
- No EC action & no EU funding. MS are free to cooperate in any kind

Policy Option 2. Voluntary cooperation supported by the Public Health Programme:

- Non-regulatory framework
- Participation entirely voluntary
- Mandatory uptake of (some of the) common (IT-) tools, templates, methodologies + Early Dialogue + joint REA EU contribution can only be obtained if contractually agreed by the participants.
- Voluntary uptake of joint Full HTA
- Coordination organised on a project basis
- EU & MS funding but perhaps no long-term stability, as budgets have to be negotiated between EU and MS [13].
- Scope: All medicines, medical and other technologies

Policy Option 3. Legislation covering Common Tools and Early Dialogues:

- Regulatory framework will be established
- Mandatory participation and uptake in common (IT-) tools, templates, methodologies (question: what about registries for collection of data)
- Opt-in (foreseen in legislation) in early dialogues and reassessments, mandatory uptake for those who opted in
- Voluntary participation in and uptake of joint REA + joint Full HTA
- Coordination organised by a rotating secretariat run by MSs
- Funding by EU, MS and by other sources (e.g. company fees for early dialogues or registries for reassessment)
- Scope: for tools: all medicines, MDs, other technologies (phasing in), for early dialogue: industry submission

Policy Option 4.1. Opt-in for Joint REA plus option 3:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies – see option 3
- Opt-in (foreseen in legislation) in joint REA and early dialogues and mandatory uptake by those who opted in
- Voluntary participation and uptake of joint Full HTA
- Coordination organised in an existing EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for joint REAs)
- Scope: for tools and ED see policy option 3. For REA: certain categories of medicines (centrally authorised, high value/budget impact, agreement between MS), certain categories of MDs (similar criteria) and other technologies (agreement and prioritisation between MS) – phasing in period foreseen

Policy Option 4.2. Mandatory Joint REA plus option 3:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies + early dialogues + joint REA

(13) Through the Multiannual Financial framework (MFF)

- Voluntary participation in and uptake of joint Full HTA
- Coordination organised in an existing EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for joint REAs)
- Scope: for tools and ED see policy option 3. For REA: certain categories of medicines (centrally authorised, high value/budget impact, agreement between MS), certain categories of MDs (similar criteria) and other technologies (agreement and prioritisation between MS) – phasing in period foreseen

Policy Option 5: Option 4.2 and Opt-in for Full HTA:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies + Early Dialogue + joint REA – option 4.2
- Opt-in (foreseen in legislation) participation in joint Full HTA and mandatory uptake for those who opted in
- Coordination organised in a new EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for Full HTA)
- Scope: for tools and ED see policy option 3. For REA see policy option 4. For others: ad hoc agreement and prioritisation between MS.

Questions regarding the policy options:

We kindly invite you to comment on the respective Policy Options described in the previous section (Table 2 and short description above).

Feedback is guided by the questions within Table 2. For closed questions, please indicate your opinion by using 'X'. Within free text fields please keep you answer as short as possible.

Table 2: Questions regarding the policy options (note: please keep your answers as short as possible) – In this section you are invited to respond irrespective of the policy options presented in table 2 apart from questions directly referring to table 2.

Question	PO 2		PO 3		PO 4.1 and 4.2				PO 5	
	IMPLEMENTATION									
Is the Implementation Mechanism described in Table 2 suitable for this policy option?	yes	no	yes	no	yes		No		yes	no
If not, which implementation mechanism would you consider more suitable for the respective policy option and why?										
Which Implementation mechanism do you consider the most preferable for HTA bodies? (single choice: please insert 'X')	Project based cooperation		Project based cooperation		Project based cooperation				Project based cooperation	
	MS secretariat (rotating)		MS secretariat (rotating)		MS secretariat (rotating)				MS secretariat (rotating)	
	Existing EU agency		Existing EU agency		Existing EU agency				Existing EU agency	
	New EU agency		New EU agency		New EU agency				New EU agency	
Which Implementation mechanism do you consider the most preferable for Industry? (single choice: please insert 'X')	Project based cooperation		Project based cooperation		Project based cooperation				Project based cooperation	
	MS secretariat (rotating)		MS secretariat (rotating)		MS secretariat (rotating)				MS secretariat (rotating)	
	Existing EU agency		Existing EU agency		Existing EU agency				Existing EU agency	
	New EU agency		New EU agency		New EU agency				New EU agency	
Is there another implementation mechanism not stated yet that you										

Question	PO 2		PO 3		PO 4.1 and 4.2				PO 5	
consider relevant?										
	SCOPE									
For which product group do you think the respective Policy option is feasible? (multiple choice: please insert 'X')	Centrally authorised plus high value/budget impact pharmaceuticals, based on agreement between MS		Centrally authorised plus high value/budget impact pharmaceuticals, based on agreement between MS		Centrally authorised plus high value/budget impact pharmaceuticals, based on agreement between MS				Centrally authorised plus high value/budget impact pharmaceuticals, based on agreement between MS	
	Other pharmaceuticals		Other pharmaceuticals		Other pharmaceuticals				Other pharmaceuticals	
	Medical Devices		Medical Devices		Medical Devices				Medical Devices	
	Other technologies		Other technologies		Other technologies				Other technologies	
	FINANCING OF POLICY OPTIONS									
Do you think the financing mechanism is feasible for the respective policy option?	yes	no	yes	no	yes		no		yes	no
If not, which financing mechanism do you consider more suitable for the respective policy option and why?										
	INCENTIVES, BARRIERS									

Question	PO 2		PO 3		PO 4.1 and 4.2				PO 5	
What incentives would be needed for HTA bodies to engage within the respective policy option?										
What incentives would be needed for industry to engage within the respective policy option?										
What barriers can be expected for HTA bodies to engage within the respective policy option?										
What barriers can be expected for industry to engage within this policy option?										
	VOLUNTARY AND MANDATORY PARTICIPATION AND UPTAKE									
For each policy option, is the combination of voluntary and mandatory participation and uptake reasonable?	yes	no	yes	no	yes		no		yes	no
If not, what would you change within the policy option with regards to voluntary/mandatory participation and uptake?										
	OTHER ASPECTS									

Question	PO 2	PO 3	PO 4.1 and 4.2		PO 5
Is there a relevant aspect missing within the matrix of policy options (Table 2)? If yes, please explain.					
Additional Comments					

1. Impacts of the respective policy options

Within this study we aim to collect and provide key input for assessing the impact of different identified policy options for EU cooperation on HTA beyond 2020 from the perspective of different stakeholders. A range of general impacts to be considered are stated within the Impact Assessment guidelines provided by the EC. A first set of indicators to assess these impacts was established. To ensure that all relevant impacts and indicators for all stakeholder groups are covered, we kindly ask you to go through Table 3 and:

1. Rate the indicator with regard to its relevance for assessing the policy options' impacts
2. Comment on the indicator
3. Add sources of information or references to literature if known
4. Add indicators you consider being relevant but are missing in Table 3

Table 3: Impacts to assess policy options

Impact	Indicator	Rating of relevance ++=high relevance + =low relevance 0 =no relevance	Comment	Sources of information / references to literature
Economic Impacts				
Operating costs and conduct	Costs of performing a health technology assessment for **technology developers** (incl. pharmaceutical and medical device industry and SMEs)			
	Costs of performing a health technology assessment for **HTA bodies**			
	Transaction costs for technology developer (costs for preparing multiple dossiers for HTA assessment bodies in different MS)			
	Changes in timelines affecting technology developers' revenue			
Administrative burden	Duplication of assessments per technology on EU level			
	Changes in administrative costs for **industry** induced by the respective policy option			
	Changes in administrative costs for **MS** induced by the respective policy option			
SME's growth	Cost of performing a technology assessment for SME technology developers			
	Revenue of SME technology developers Revenue of SME technology developers			
Impact on EU Health Technology sector competitiveness	Predictability of HTA framework attracting investments			
	Technology developers capacity to innovate (positively/negatively affecting investment decisions/R&D)			
Functioning of the internal market and	Fragmentation of HTA system			

Impact	Indicator	Rating of relevance ++=high relevance + =low relevance 0 =no relevance	Comment	Sources of information / references to literature
competition	Effects on the attractiveness of the European market at international level			
Innovation and research	Incentives for Industry to innovate			
	Diversity of research in the field of HTA			
Consumer and households/patients	Involvement of patients in the HTA process			
	Time for access to market			
	Level of consumer/patient information on the technology			
	Price patients pay for good/service			
Macroeconomic environment	Consequences on economic growth and employment			
Social Impacts				
Employment and labour markets	Influence on jobs related to health technology sector			
Governance, participation and good administration	Responsibilities of public institutions and administration in HTA on MS level			
	Public's access to information on the decision-making process			
	Involvement of stakeholders in HTA governance issues			
Access to and effects on social protection and health systems and Sustainability of health systems	Financing of expensive treatments with little or no added value			
	Negotiation power for MS in setting prices			
	Access to health technologies (especially pharmaceuticals and medical devices)			
Public health and safety	Availability of health technologies on the market			
Additional indicators that should be				

Impact	Indicator	Rating of relevance ++=high relevance + =low relevance 0 =no relevance	Comment	Sources of information / references to literature
investigated:				
Additional indicators that should be investigated:				
Additional indicators that should be investigated:				

Annex 2: Search strategy

Search strategy Medline, Cochrane via OVID

Search date: 11.11. 2016

Databases:
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present,
EBM Reviews - Cochrane Database of Systematic Reviews
EBM Reviews - ACP Journal Club
EBM Reviews - Database of Abstracts of Reviews of Effects
EBM Reviews - Cochrane Central Register of Controlled Trials
EBM Reviews - Cochrane Methodology Register
EBM Reviews - Health Technology Assessment
EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2015

1	(health adj2 technology adj2 assessment).ti,ab.	3608
2	(European adj2 public adj2 assessment adj2 report).af.	37
3	"relative effectiveness assessment*".af.	10
4	joint assessment.af.	244
5	(outcome adj2 assessment).ti,ab.	5602
6	(outcome adj2 assessment).ti.	855
7	(clinical adj2 assessment).ti,ab.	28074
8	(process adj2 assessment).ti,ab.	2892
9	(health adj2 services adj2 research).ti,ab.	3267
10	(evidence adj2 based adj2 medicine).ti,ab.	11324
11	exp Technology Assessment, Biomedical/	11026
12	Decision Making, Organizational/	11623
13	(international adj2 comparison*).ab,ti.	2515
14	(international adj2 cooperation*).ab,ti.	1618
15	health policy.ab,ti.	14596
16	(european adj2 cooperation*).af.	116
17	(european adj2 collaboration*).af.	236
18	Health Policy/	61143
19	International Cooperation/	44957
20	1 or 2 or 3 or 4 or 7 or 8 or 9 or 10 or 11	58616
21	12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	127090
22	20 and 21	2205
23	limit 22 to yr="2012 - 2016"	**495**

Search strategy Embase

Search date: 11.11. 2016

Databases: Embase

1	(health adj2 technology adj2 assessment).ti,ab.	3728
2	(European adj2 public adj2 assessment adj2 report).af.	30
3	"relative effectiveness assessment*".af.	24
4	joint assessment.af.	367
5	(outcome adj2 assessment).ti,ab.	5870
6	(outcome adj2 assessment).ti.	1023
7	(clinical adj2 assessment).ti,ab.	37347
8	(process adj2 assessment).ti,ab.	3799
9	(health adj2 services adj2 research).ti,ab.	3600
10	(evidence adj2 based adj2 medicine).ti,ab.	14440
11	exp Technology Assessment, Biomedical/	11795
12	Decision Making, Organizational/	140609
13	(international adj2 comparison*).ab,ti.	3209
14	(international adj2 cooperation*).ab,ti.	1965
15	health policy.ab,ti.	17242
16	(european adj2 cooperation*).af.	533
17	(european adj2 collaboration*).af.	314
18	Health Policy/	139998
19	International Cooperation/	51926
20	1 or 2 or 3 or 4 or 5 or 7 or 8 or 9 or 10 or 11	73628
21	12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	329992
22	20 and 21	3625
23	limit 22 to yr="2012 - 2016"	**588**

Search strategy Cinahl

Search date: 11.11. 2016

Databases: Cinahl

S6	(S2 OR S3) AND (S1)	Limiters - Published Date: 2012_01_01-2016_12_31 **Results (180)**
S5	(S2 OR S3) AND (S1)	Results (898)
S4	S2 OR S3	Results (62,545)
S3	AB (international AND comparision*) OR AB (international AND cooperation*) OR AB (health AND polic*) OR AB (european AND cooperation*) OR AB (european AND collaboration*)	Results (28,582)
S2	(MH "Decision Making, Organizational") OR (MH "Health Policy") OR (MH "International Relations")	Results (39,135)
S1	AB (Health AND Technology AND Assessment*) OR AB (European public assessment report) OR AB (relative effectiveness assessment*) OR AB (outcome assessment) OR AB (clinical assessment) OR AB (health services research) OR AB (evidence-based medicine) OR AB (joint assessment)	Results (42,545)

Search strategy Econlit

Search date: 11.11. 2016

Databases: Econlit

S4	(AB (Health AND Technology AND Assessment*) OR AB (European public assessment report) OR AB (relative effectiveness assessment*) OR AB (outcome assessment) OR AB (clinical assessment) OR AB (health services research) OR AB (evidence-based medicine) OR AB (joint assessment)) AND (AB (international AND comparision*) OR AB (international AND cooperation*) OR AB (health AND polic*) OR AB (european AND cooperation*) OR AB (european AND collaboration*))	Limiters - Published Date: 2012_01_01-2016_12_31 **Results (31)**
S3	(AB (Health AND Technology AND Assessment*) OR AB (European public assessment report) OR AB (relative effectiveness assessment*) OR AB (outcome assessment) OR AB (clinical assessment) OR AB (health services research) OR AB (evidence-based medicine) OR AB (joint assessment)) AND (AB (international AND comparision*) OR AB (international AND cooperation*) OR AB (health AND polic*) OR AB (european AND cooperation*) OR AB (european AND collaboration*))	Results (124)

S2	AB (international AND comparision*) OR AB (international AND cooperation*) OR AB (health AND polic*) OR AB (european AND cooperation*) OR AB (european AND collaboration*)	Results (12,913)
S1	AB (Health AND Technology AND Assessment*) OR AB (European public assessment report) OR AB (relative effectiveness assessment*) OR AB (outcome assessment) OR AB (clinical assessment) OR AB (health services research) OR AB (evidence-based medicine) OR AB (joint assessment)	Results (36,876)

Search strategy Scopus

Search date: 11.11. 2016

Databases: Scopus

(TITLE-ABS (health PRE/2 technology PRE/2 assessment) OR (INDEXTERMS (health technology assessment)) OR TITLE-ABS (european PRE/2 public PRE/2 assessment report) OR TITLE-ABS (relative PRE/2 effectiveness PRE/2 assessment*) OR (INDEXTERMS (relative effectiveness assessment)) OR TITLE-ABS (outcome PRE/2 assessment) OR TITLE-ABS (clinical PRE/2 assessment) OR TITLE-ABS (evidence PRE/2 based PRE/2 medicine) OR (INDEXTERMS (evidence based medicine)) OR TITLE-ABS (joint PRE/2 assessment)) AND (TITLE-ABS (international PRE/2 comparision*) OR (INDEXTERMS (international comparison)) OR TITLE-ABS (international PRE/2 cooperation*) OR (INDEXTERMS (international cooperation)) OR TITLE-ABS (health PRE/2 polic*) OR (INDEXTERMS (health policy)) OR TITLE-ABS (european PRE/2 cooperation*) OR TITLE-ABS (european PRE/2 collaboration*)) OR (INDEXTERMS (european collaboration)) AND NOT INDEX (medline) AND NOT INDEX (embase) AND (LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012))	**83** document results

Annex 3: Questionnaire addressed to Public administration and others

Introduction to the survey

Purpose of the survey
The European Commission (EC) is exploring options for a new and sustainable mechanism for Health Technology Assessment (HTA) in Europe after 2020. Consequently, the Directorate General for Health and Food Safety (DG SANTE) of the European Commission started an impact assessment process. In the framework of this process, the EC commissioned the consortium of Sogeti, the Austrian Public Health Institute (GÖ FP) and the London School of Economics and Political Science (LSE Health) to provide **data and evidence** to identify the impact of policy options for strengthened EU cooperation on HTA in order to support the Impact Assessment process of the EC**.**
This survey is part of the data collection process, which focuses on the insights of key stakeholders (HTA bodies, healthcare providers, public healthcare payers and competent authorities as well as patients/consumers). There is an additional version of the survey for completion by industry stakeholders.

Aim
We would like you to assess, from your perspective, the potential impacts of different policy options for strengthened EU cooperation on HTA after 2020.

Outline of the questionnaire
The survey is split into four parts:
Part 1: General questions on your institution.
Part 2: Questions regarding the costs incurred as a result of the HTA process
Part 3: Information about the preliminary policy options. Assessment of possible impacts of 5 policy options (scenarios) for strengthened EU cooperation on HTA after 2020
Part 4: Indicating your option with regard to the relevance of defined impacts and scope

How we will process the information you provide
The results will be gathered and clustered and will finally feed into a Multi-Criteria Decision Analysis (MCDA) model. The MCDA is a method, based on mathematical algorithms, for evaluating individual, often conflicting, criteria. The criteria are then combined into one matrix for general assessment to help decision-makers consider multiple conflicting factors, or "impacts", in a rational and consistent manner. The objective of the MCDA is to identify policy options which take into account the preferences of the involved stakeholders as well as account for the conflicting nature of related impacts.

Confidentiality clause
We would like to assure you that the European Commission's statuary obligation of confidentiality is in place. The final report will only present aggregated or anonymized data.
If you include confidential information/business secrets, please clearly identify/mark the section; non-marked sections are assumed to be not confidential. A non-confidential version is also welcome. According to the framework contract with the consortium, the European Commission may request the data gathered by the contractor.

Deadline for the survey
This online survey will be active until January 22 2017.

In case you have questions or need any support please contact:
Gesundheit Österreich Forschungs- und Planungs GmbH (GÖ FP)
Stubenring 6, 1010 Vienna (Austria)

E-Mail: EU.HTA@goeg.at
Phone: 0043 (0)151561 – 285

Part 1: General Questions

Please fill in the name of the organisation/association and your function within:
Organisation/association:
Role:
Your contact details (E-Mail):

Operational level
Please indicate the operational level of your organisation/association (one answer possible):

- *International (e.g. representative at EU level)*
- *National (e.g. national agency)*
- *Regional (e.g. representative of a specific region).*

Country:
Please indicate the country where your organization is based.
(List of countries will be available)

Personal /institutional capacity:
We kindly ask you to fill out the questionnaire from your organisational/institutional point of view. If this is not possible, please state that your answers represent your personal perspective*.*

- Personal perspective
- Organisational perspective

Organisation
Please state your main field of work:

- Government
- Public Administration
- HTA Body/Organisation
- Payer
- Pricing/reimbursement body
- Healthcare provider
- Patient/patient advocate
- Other (please specify)

Is your organization performing or commissioning an health technology assessment process?

- Yes
- No

Part 2: Questions regarding the status quo

Costs of performing a health technology assessment (HTA) (this will only be asked to organisations/association that perform HTAs)

General instructions:

- Please refer to the timeframe that is stated within the question.
- Please use € if available, otherwise use your local currency
- All figures should be in the Continental European format (e.g. 3,4.)
- All dates should be given in the format YYMMDD

Please specify the activities undertaken by your Agency (please tick all that apply):

- HTA
- Production of clinical guidance
- Development of quality standards
- Evidence generation
- Early engagement
- Horizon scanning
- Other

General Costs

Q4: Is there a fixed budget on an annual basis allocated to your agency for HTA activities?

A. €

B. % of total budget

Q5: What proportion of your budget is expended on operating costs?

% of total budget

Q6: What are the annual audit costs?

% of

For the purpose of the study internal audit is defined as follows: an internal audit is used to assess operational efficiencies and resource management. It is often compulsory for public bodies to verify cost records and adherence to acceptable cost accounting procedures.

Q7: Approximately what overall expenses are associated with an HTA process, per technology?

A. REA (if applicable)

B. Full HTA

   a. Single technology assessment

   b. Multiple technology assessment

Q8: Are there any other essential costs related to HTA process? *Please specify*

Workforce allocation related to the HTA process

Q10_1: How many staff do you employ in your agency exclusively for the purpose of HTA?

Q10_2: If possible, please state how many person months are invested in one HTA process on average (person month meaning one person working full time for one month).

Q11: What are the costs associated with REA process?

A. Staff costs

B. Outside consultancy/sub-contracting

C. Other general expenses (i.e. travel costs)

Q12: What are the costs associated with full HTA process?

A. Staff costs

B. Outside consultancy/sub-contracting

C. Other general expenses (i.e. travel costs)

Stakeholder costs

Q13: What are the approximate costs of stakeholder involvement in the HTA process?

A. Fees for participation (e.g. per diem)
B. Travel costs
C. Interview/ workshop expenses
D. Other expenses (please specify)

Implementation and Dissemination of HTA recommendations

Q14: Approximately how much do you spend on the dissemination of the final report?

A. Reports (paper format)
B. Guidelines (paper format)
C. Digital services (e.g. website maintenance)

Q15: Are there any expenses associated with the monitoring/implementation process of HTA recommendations?

A. Yes

If yes, please specify:

B. No

Part 3: Information about the preliminary policy options on HTA cooperation after 2020

In this part, we provide you with key information to assess the impact of the different preliminary policy options.

Please read carefully through the short description of each policy option in order to understand the scope of the questions asked in part 3.

Please note:

For assessing the impacts of the various options and the various implementation mechanisms /business models, fine-tuned options were created within the course of the study. These combine the options with the implementation mechanisms (for details see below).

The fine-tuned options in this section are provisional. They are merely examples of the possible combinations of the IIA options with the IIA implementation mechanisms that were developed in order to facilitate the analysis. In any event, they do not represent the preferred combinations of the European Commission nor the contractor and other combinations are possible. Furthermore, the policy options may need to be revised following the input of Member States and stakeholders through public consultation and discussions. The final policy option does not have to be exactly in line with one that was analysed, but it can combine elements. (E.g. it is possible to have option X, but combine it with the implementation mechanism of option Y.)

Key characteristics

The different **policy options** for cooperation on HTA after 2020 are defined along several key characteristics focusing on 1. HTA output, 2. Participation and uptake from Member States' perspectives, 3. Organizational aspects, 4. Funding aspects as well as 5. Timelines. These are explained in the following:

1) The scope of the cooperation is defined by several **outputs**([14]) created by a joint collaboration, comprising of:

- Common tools and procedures, including common submission templates, an IT system with planned and ongoing assessments, common methodologies (e.g EUnetHTA Core Model), a joint prioritization process, and cooperation on data requirements, including Horizon Scanning
- Performing joint Early Dialogues
- Performing joint Relative Effectiveness Assessments (REA can take place at time of market launch, or later (re-assessment))
- Performing joint Full Health Technology Assessments (Full HTA can take place at time of market launch, or later (re-assessment))

2) The engagement in participation and uptake([15]) of jointly produced outputs can be either **voluntary** or **mandatory**:

([14]) The scope of the activities may differ between pharmaceuticals, medical devices and other technologies.

- Voluntary participation/ voluntary uptake (V/V): Member States can decide if they wish to participate in the production of outputs and take up the respective output; cooperation is entirely voluntary.
- Voluntary participation/mandatory uptake (V/M): The participation in the creation of joint work is voluntary, meaning that Member States can decide to opt-in([16]) to the joint cooperation. However, once a Member State has opted-in the uptake of the joint work into the national setting is mandatory.
- Mandatory participation/mandatory uptake (M/M): Both participation in the production of outputs and the uptake of these into the national setting are mandatory.

For each of the policy options, different combinations of **voluntary or mandatory** participation and uptake per Output are possible.

3) For organizing the creation of these joint HTA outputs a number of different **organizational mechanisms** are conceivable:

- Project based cooperation: The secretariat is set up by the Member States that participate (similar to EUnetHTA).
- EU/MS secretariat: A permanent Secretariat is established.
- Existing EU agency: A permanent Secretariat is integrated in an already existing EU agency. This Secretariat will coordinate the work of national experts in HTA bodies in carrying out the assessments.
- New EU agency: A permanent Secretariat is integrated in a NEW EU agency. This Secretariat will coordinate the work of national experts in HTA bodies in carrying out the assessments.

4) For financing the joint cooperation several **funding mechanisms** are conceivable:

- EU funding, either through a Public Health program or another financial instrument
- Funding by Member States joining the collaboration
- Funding through industry fees

5) **Timelines**:

Timelines for implementation of the proposed policy options after 2020 range from immediately, without delay, for option 1 (i.e. 2021) to transitional periods for implementing options 4 or 5 in a new legal framework).

Table 4 provides an overview of each policy option and the envisaged implementation/funding mechanism. A short summary for each policy option can be found afterwards.

([15]) Please note that Up-take concerns using or considering the results and findings of the HTA cooperation, reaching from jointly developed submission templates to outcomes in full HTA. The subsequent pricing and reimbursement decision would remain purely on national level. Also providers / developers need to adhere to this process.

([16]) Opt-in by MS is by output, not by individual products e.g. once a MS has opted in for joint REA, they take part in all joint REAs - but not necessarily as an author.

Table 4: Overview of Policy Options

		Baseline	Non-legislative	Legislative			
		PO 1	PO 2	PO 3	PO 4[17]		PO 5
		No EU action after 2020	Voluntary cooperation through Public Health Programme	Legislation covering common tools and early dialogues	Legislation covering Joint work on REA Plus common tools and early dialogues		Legislation covering Joint work on Full HTA (incl. REA) Plus common tools and early dialogues
					4.1 REA V/M	4.2 REA M/M	
Outputs	Common tools, incl. templates, methodology	V/V	V/M	M/M	M/M	M/M	M/M
	Early dialogue([18])	V/V	V/M	V/M	V/M	M/M	M/M
	Joint REA([19])	V/V	V/M	V/V	V/M	M/M	M/M
	Joint Full HTA([6])	V/V	V/V	V/V	V/V	V/V	V/M
Implementation		No EU input	Project based cooperation	EU/MS secretariat	Existing EU agency	Existing EU agency	New EU agency
Financing		None from EU	EU+MS	EU+MS+fees from industry for early dialogues, joint REA and full HTA			
Scope			All medicines, medical and other technologies	Tools: all medicines, medical technologies, other technologies (phasing in), ED: industry submission	Tools and ED see PO 3. REA: certain categories of medicines (e.g. centrally authorised, high value/budget impact, agreement between MS), certain categories of medical technologies(e.g. high risk, high value products) and other technologies (agreement and prioritisation between MS) – phasing in([20])		Tools and ED see PO 3, REA see PO4. For others: ad hoc agreement and prioritisation between MS

([17]) Assuming that 50% of the Member States participate, a mix between high/low income, large/small MS.

([18]) Early Dialogue: Here mandatory uptake means that the MS cannot repeat an ED that was done at EU level. Technology providers initiate Early Dialogues.

([19]) Either at time of market or re-assessment

([20]) A gradual introduction of products during a transitory period that allows to manage the workload while the structures/implementation model are being developed.

Short description of policy options:

Policy Option 1. Baseline scenario - No EU action after 2020:

- Non-regulatory framework
- Participation/uptake entirely voluntary
- No EC action & no EU funding. MS are free to cooperate in any kind

Policy Option 2. Voluntary cooperation supported by the Public Health Programme:

- Non-regulatory framework
- Participation entirely voluntary
- Mandatory uptake of (some of the) common (IT-) tools, templates, methodologies + Early Dialogue + joint REA. EU contribution can only be obtained if contractually agreed by the participants.
- Voluntary uptake of joint Full HTA
- Coordination organised on a project basis
- EU & MS funding: long term commitment of funding, (minimum 4, maximum 7 years), annual budget([21])
- Scope: All medicines, medical and other technologies

Policy Option 3. Legislation covering Common Tools and Early Dialogues:

- Regulatory framework will be established
- Mandatory participation and uptake in common (IT-) tools, templates, methodologies, etc.
- Opt-in (foreseen in legislation) in early dialogues and reassessments, mandatory uptake for those who opted in
- Voluntary participation in and uptake of joint REA + joint Full HTA
- Coordination organised by a secretariat run by EC or MSs
- Funding by EU, MS and by other sources (e.g. company fees for early dialogues or registries for reassessment)
- Scope: for tools: all medicines, medical technologies, other technologies (phasing in), for early dialogue: industry submission

Policy Option 4.1. Opt-in for Joint REA plus option 3:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies – see option 3
- Opt-in (foreseen in legislation) in joint REA and early dialogues and mandatory uptake by those who opted in. It is assumed that 50% of the Member States participate, a mix between high/low income, large/small MS.
- Voluntary participation and uptake of joint Full HTA
- Coordination organised in an existing EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for joint EDs and REAs)
- Scope: Tools and ED see PO 3. REA: certain categories of medicines (e.g. centrally authorised, high value/budget impact, agreement between MS), certain categories of medical technologies (e.g. high risk, high value products) and other technologies (agreement and prioritisation between MS) – phasing in

([21]) Through the Multiannual Financial framework (MFF)

Policy Option 4.2. Mandatory Joint REA plus option 3:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies + early dialogues + joint REA
- Voluntary participation in and uptake of joint Full HTA. It is assumed that 50% of the Member States participate, a mix between high/low income, large/small MS.
- Coordination organised in an existing EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for joint EDs and REAs)
- Scope: Tools and ED see PO 3. REA: certain categories of medicines (e.g. centrally authorised, high value/budget impact, agreement between MS), certain categories of MDs (e.g. high risk, high value products) and other technologies (agreement and prioritisation between MS) – phasing in

Policy Option 5: Option 4.2 and Opt-in for Full HTA:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies + Early Dialogue + joint REA – option 4.2
- Opt-in (foreseen in legislation) participation in joint Full HTA and mandatory uptake for those who opted in
- Coordination organised in a new EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for Full HTA)
- Scope: for tools and ED see policy option 3. For REA see policy option 4. For others: ad hoc agreement and prioritisation between MS.

Part 4: Assessment of policy options

In the following part of the questionnaire, we kindly ask you to assess each of the policy options described above according to their economic and social/health impacts.

Compared to the status quo, how do you estimate the different policy options' may impact on the economic indicators in the table below?

Please indicate for each question on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+) for each policy option.

Example: If you expect that for option 4.2 the total number of HTA submission across Europe will be cut by half, you should put -50.

Costs

Compared to the status quo, how do you estimate the different policy options' may impact on your average ***costs per product****?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+) for each policy option, with the status quo (=the current situation) set at zero (0).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
To what extent do you expect each policy option to impact on the ***costs for horizon scanning*** *(all costs)?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
To what extent do you expect each policy option to impact on the total ***costs for early dialogues?*** (Total costs including costs for staff, administrative costs, etc.)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
To what extent do you expect each policy option to impact on the ***total costs*** *of a* ***REA submission (if applicable)****?* (Total costs including costs for staff, (re)submission costs, administrative cost, costs for including stakeholder etc.)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
To what extent do you expect each policy option to impact on the ***total costs*** *of a full* ***HTA submission****?* (Total costs including costs for staff, (re)submission costs, administrative costs, travel costs, costs for including stakeholder)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on **HTA submission fees**?* (Fees that have to be paid for submitting an HTA/REA to the respective institution)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact on the **costs for additional data** requested by HTA bodies?* (Referring to all studies performed in addition to clinical studies conducted for regulatory approval)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact on the **needs for Human Resource**s (full time equivalents including consultants)?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact on the **costs for HTA re-assessment** (all costs)?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	

Administrative burden

*Compared to the status quo, how do you estimate the different policy options' may impact on your **administrative burden**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+), with the status quo set at zero (0).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **overall administrative burden*** associated with HTA submissions*?*(Administrative burden arising from the information obligations imposed on industry with regard to HTA processes)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact on the **number of HTA submissions** for the same product and indication across* European countries*?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact on **the time needed for an HTA process**?*(The time span of the whole assessment procedure)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact on the **complexity of HTA assessment processes**?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	

Competitiveness of EU health technology sector

*Compared to the status quo, how do you estimate the different policy options' may impact on the following indicators regarding the **competitiveness of EU health technology sector**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+), with the status quo set at zero (0).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **predictability of the HTA system** in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **competitiveness of SME**?* (SME is defined by staff headcount,)<250 and either turnover ≤ 50m or balance sheet total ≤ 43m)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on **your revenues?***	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Innovation and research

*Compared to the status quo, how do you estimate the different policy options' may impact on the following indicators regarding **Innovation and research**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+), with the status quo set at zero (0).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **research** climate in the European market?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact on the actual **innovation** for the European market?* (i.e. focus on predictability and deduction of fragmentation as key factors for favorable business climate for industry facilitating innovation thrive)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	

International Trade

*Compared to the status quo, how do you estimate the different policy options' may impact on **international trade**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+), with the status quo set at zero (0).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on **international trade** related to pharmaceuticals/ medical technologies?* (Possibility to import and/or export)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Functioning of the internal market and competition

*Compared to the status quo, how do you estimate the different policy options' may impact on the following indicators regarding **the functioning of the internal market and competition**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+), with the status quo set at zero (0).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **fragmentation of the HTA** system in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **convergence of HTA methodologies** in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **attractiveness of the EU market** for Industry?* (Reduction of fragmentation of HTA systems)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Consumer and households

*Compared to the status quo, how do you estimate the different policy options' may impact on the following indicators regarding **consumer and households**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+), with the status quo set at zero (0).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **number of health technologies available** (consumer choice – mainly for medical technologies) in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **number of health technologies assessed** in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Macroeconomic environment

*Compared to the status quo, how do you estimate the different policy options' may impact on the following **macroeconomic environment**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+), with the status quo set at zero (0).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **overall economic growth and labor market**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **health technology sector**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on **the health care sector (including providers)**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Assessment of Social/health impacts

In the following part of the questionnaire, we kindly ask you to assess each of the policy option described according to their social/health impacts.

Compared to the status quo, how do you estimate the different policy options' may impact on the social/health indicators in the table below?

Please indicate for each question on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+) for each policy option.

Example: If you expect that for option 4B the total number of HTA submission across Europe will be cut by half, you should put -50.

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
Employment (labor market)							
*To what extent do you expect each policy option to impact on the **number of staff** employed at your company (full time equivalents including consultants)?* (Number of full time equivalents (including consultants), which are involved in HTA and on the payroll of your organization)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
Governance, participation and good administration							
*To what extent do you expect each policy option to impact on the **involvement of stakeholder groups** in HTA processes?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **responsibilities of public institutions and administrations in HTA on MS level**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **uptake of joint outputs (HTA reports, early dialogues, tools, etc.)**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **resource efficiency of HTA processes**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **sustainability of EU HTA cooperation**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
Access to and effects on social protection and health systems							

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **access to innovative treatments**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
Sustainability of health systems							
*To what extent do you expect each policy option to impact on the **financing of expensive treatments** with little or no added value?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **negotiation power** of MS in setting prices?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
Public health							
*To what extent do you expect each policy option to impact on the **availability of health technologies on the market**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact o**verall public health**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Part 4 - Assessment of Preferences

Q.1. Please indicate which relevance/importance you attribute to the impacts on HTA cooperation after 2020 listed below. Please rate the impacts from low priority = 1 to high priority = 10.

Impacts		Importance (0 to 10)
Economic impacts	**Costs**	Range 1/10
	Administrative burden	Range 1/10
	Competitiveness of EU health technology sector	Range 1/10
	Innovation and research	Range 1/10
	International Trade	Range 1/10
	Functioning of the internal market and competition	Range 1/10
	Consumers and households	Range 1/10
	Macroeconomic environment	Range 1/10
Social/health impacts	**Employment (labour market)**	Range 1/10
	Governance, participation and good administration	Range 1/10
	Access to social protection and health systems	Range 1/10
	Sustainability of health systems	Range 1/10
	Public health and safety	Range 1/10

Q.2. *The part on policy options included **an example** of what sub-categories of pharmaceuticals and medical technologies could be included in the **scope** of HTA cooperation.*

Please indicate which sub-categories you would find particularly useful to include in the EU HTA cooperation.

Please be sure you want to submit the questionnaire, once submitted answers cannot be altered!

Thank you very much for participating and filling in the questionnaire!

Annex 4: Industry Questionnaire

Introduction to the survey

Purpose of the survey

The European Commission (EC) is exploring and assessing options for a new and sustainable mechanism for Health Technology Assessment (HTA) in Europe after 2020. Consequently, the Directorate General for Health and Food Safety (DG SANTE) of the European Commission started an impact assessment process.

In the framework of this process, the EC commissioned the consortium of Sogeti, the Austrian Public Health Institute (GÖ FP) and the London School of Economics and Political Science (LSE Health) to provide **data and evidence** to identify the impact of policy options for strengthened EU cooperation on HTA in order to support the Impact Assessment process of the EC**.**

This survey is part of the data collection process, which focuses on the insights of key stakeholders, and is to be completed by industry stakeholders. There is an additional version of the survey for completion by non-industry stakeholders, in particular public bodies.

Aim

We would like you to assess, from your perspective, the potential impacts of different policy options for strengthened EU cooperation on HTA after 2020.

Outline of the questionnaire

The survey is split into four parts:
Part 1: General questions.
Part 2: Questions regarding the costs incurred as a result of the HTA process.
Part 3: Information about the (preliminary) policy options. Assessment of possible impacts of 5 policy options (scenarios) for strengthened EU cooperation on HTA after 2020.
Part 4: Your assessment on how relevant the defined impacts and scope are.

How we will process the information you provide

The results will be gathered and clustered and will finally feed into a Multi-Criteria Decision Analysis (MCDA) model. The MCDA is a method, based on mathematical algorithms, for evaluating individual, often conflicting, criteria. The criteria are then combined into one matrix for general assessment to help decision-makers consider multiple conflicting factors, or "impacts", in a rational and consistent manner. The objective of the MCDA is to identify policy options which take into account the preferences of the involved stakeholders as well as account for the conflicting nature of related impacts.

General instructions

If your company is a subsidiary of another company, we recommend that the questionnaire is transferred to the ultimate parent company for completion of the questionnaire for all subsidiaries.

Confidentiality clause

We would like to assure you that the European Commission's statuary obligation of confidentiality is in place. The final report will only present aggregated or anonymized data.
If you include confidential information/business secrets, please clearly identify/mark the section; non-marked sections are assumed not to be confidential. A non-confidential version is also welcome. According to the framework contract with the consortium, the European Commission may request the data gathered by the contractor.

Deadline for the survey

This online survey will be active until January 22nd 2017.

In case you have questions or need any support please contact:

Gesundheit Österreich Forschungs- und Planungs GmbH (GÖ FP)
Stubenring 6, 1010 Vienna (Austria)
E-Mail: EU.HTA@goeg.at
Phone: 0043 (0)151561285

Part 1: General Questions

Organization

Please fill in the name of the organisation/association and your function within:
Organisation/association:
Role*:*
Your contact details (E-Mail):

Operational level

Please indicate the operational level of your organisation/association (one answer possible):

- International (e.g. representative at EU level)
- National

Country:

Please select the country (if national or regional operational level) or countries (if international operational level) in the EU your organization is represented/working in.

Please note that you will be asked to provide more detailed information regarding the costs for the countries selected.

Size of company

Please indicate the size of the organisation you are working for:

- Large
- Medium
- Small

Product Scope

Please indicate which category of product your organisation specializes in (please tick all that apply):

- Pharmaceuticals
- Medical technologies
- Other technology (please specify)

Personal /organizational capacity:

We kindly ask you to fill out the questionnaire from your organisational point of view. If this is not possible, please state that your answers represent your personal perspective*.*

- Personal perspective
- Organisational perspective

Question regarding the HTA system within a country:

Please indicate whether in your country, HTA / REA reports are performed in-house within your company (preparation by staff or consultants) or if data for assessment (e.g. clinical studies, economic models) is delivered to HTA bodies?

- In-house performance
- Delivering data to HTA agency

Please state whether you are working at a trade association or at a manufacturer:

- Trade association
- Manufacturer

Part 2: Questions regarding the status quo

Please answer the following questions related to the **costs of performing and undergoing a health technology assessment** for the technology developer.

When answering the questions please refer to the timeframe that is stated within the question.

General instructions:

- Please refer to the timeframe that is stated within the question.
- Please use € if available, otherwise use your local currency
- All figures should be in the Continental European format (e.g. 3,4.)
- All dates should be given in the format YYMMDD

Q1: If one or more of your products was a subject of **Horizon Scanning**, were any costs incurred as a result of this process within the last 5 years?

A. Yes
If yes, please specify what costs these were and give an approximate figure (in Euros):

B. No

For this survey, Horizon Scanning is defined as "The systematic identification of health technologies that are new, emerging or becoming obsolete and that have the potential to effect health, health services and/or society".

Q2: Have you participated to an **Early Dialogue** process within the past 5 years?

A. Yes *(fill in Q2_1 till Q2_4)*
B. No *(jump to part Q3_1)*

For this survey early dialogue is defined as follows: Early Dialogues are undertaken with the aim of helping pharmaceutical and MedTech companies to understand the evidence and information needs of the HTA organisations and reimbursement bodies to improve the quality and adequacy of early evidence generation

Q2_1: With which institution did you undergo an Early Dialogue process?

- *European Medicines Agency (EMA)*
- *EUnetHTA*
- *Individual HTA Body*
- *Other*

Q2_2: What was the disease area?

Q2_3: What is the approximate cost (in Euros) of your participation in <u>one</u> ***Early Dialogue process****?*

- User/submission fees
- Administration costs
- Human resources costs
  (*Please indicate in Full Time Equivalents)*
- Other expenses, please specify

Q2_4: *Did Early Dialogue lead to a reduction in the overall costs of a full HTA process within the past 5 years?*

A. Yes
   If yes, please specify by how much (in Euros):

B. No

<u>For this survey full HTA is defined as follows:</u> Full HTA Assessment not only addresses the medical/therapeutic added value of a new technology (assessment of clinical domains) but also covers the assessment of aspects such as cost-effectiveness, budget impact, ethical aspects, legal considerations and impact on patients as well as on the health care systems.

Q3_1: How many of your **staff** work on HTA submissions currently?
Please indicate for your country / all countries applicable.

Q3_2: Is HTA performed centrally in your organisation? If yes, how many staff work on HTA submissions centrally?

Q3_3: If possible, please state how many person months are invested in one HTA submission on average (person month meaning one person working full time for one month).

<u>For this survey HTA submission is defined as follows</u>: HTA submission refers to submitting evidence (report or clinical/economic data and studies) to an HTA Body/regulatory body for assessing the value of a health technology

Q4: What are the average **costs** associated with one HTA submission?

A. Staff costs
B. In-house model (clinical and economic assessment) and evidence generation

C. External model (clinical and economic assessment) and evidence generation
D. Outside consultancy/sub-contracting
E. Dissemination costs (printing, binding, distributing)
F. Other, please specify

Q5: Please insert the information on the submission and re-submission fees paid to HTA bodies in the last year:

HTA Body	Submission fees	Re-submission fees

Q6: Are there any other fees/expenses that have not been included?

A. Yes
If yes, please specify (with figures in Euros):

B. No

Q7: Looking at your HTA submissions over the past five years have you incurred costs related to **additional evidence generation**?

A. Yes *(fill in Q8 – Q13)*
B. No *(jump to part 3)*

Q8: What are the **costs** (on average) for generating **additional clinical evidence** required by the HTA body?

A. Health surveys
B. Supplement to randomised controlled trial:
C. Practical clinical trials:
D. Registry data:
E. Electronic health records/medical chart review:
F. Administrative data:
G. Other please specify:

For the purpose of this survey additional evidence generation is defined as follows: Generation of additional clinical evidence refers to all studies and provision of data in addition to clinical studies performed for marketing authorization within the course of an HTA process

For the purpose of this survey health survey is defined as follows**:** Health surveys are designed to collect descriptions of health status and well-being, health-care utilization, treatment patterns, and health-care expenditures from patients, providers, or individuals in the general population, which are representative of the target population. Health surveys are methodologically rigorous, for example, relying on complex sample survey designs.

For the purpose of this survey supplement to randomised controlled trial is defined as follows: To provide additional data alongside standard clinically focused randomized controlled trials, researchers often gather information on variables such as patient reported outcomes, medical resource use, and costs. Such efforts can add valuable evidence on treatment patterns for common events, e.g., such as the doses of drugs used to treat rejection in kidney transplantation

For the purpose of this survey practical clinical trials is defined as follows**:** practical or pragmatic clinical trials (also called large simple trials) involve prospective, randomized assignment but are aimed at larger, more diverse real world populations. Practical or pragmatic clinical trials have the important strength of randomization, which minimizes bias in the estimation of treatment effects. These trials are by design larger than conventional randomized controlled trials. For this reason, they are more likely to have sufficient power to capture significant differences in key outcomes of interest, such as hospitalizations.

For the purpose of this survey registry data is defined as follows**:** Registries are prospective, observational cohort studies of patients who have a particular disease and/or are receiving a particular treatment or intervention. They can be used for understanding natural history, assessing or monitoring real world safety and effectiveness, assessing quality of care and provider performance, and assessing cost-effectiveness

For the purpose of this survey administrative data is defined as follows**:** administrative data (typically retrospective or real-time, if possible) are collected primarily for reimbursement, but contain some clinical diagnosis and procedure use with detailed information on charges. Claims databases lend themselves to retrospective longitudinal and cross-sectional analyses of clinical and economic outcomes at patient, group, or population level.

For the purpose of this survey electronic health records/medical chart reviews is defined as follows: electronic health records/medical chart reviews**,** such as the UK General Practice Research Database, contain more detailed, longitudinal information including disease-specific symptoms at the personal level and should greatly expand the use of this type of information.

Q.9. What are the costs (on average) for generating additional evidence on non-clinical domains?

Definition Non-clinial domains (Please see EUnetHTA core model): Costs and economic evaluation; Ethical analysis; Organizational aspects; Patients and Social aspects; Legal aspects)

Q10: Please give us an example where additional evidence was required over the past five years and state the associated costs:

A. Health Technology for which additional evidence was required:
B. Indication for which this Health technology is used:
C. Type of additional evidence requested:
D. Costs for this additional evidence:

Q11: Which countries were more likely to request additional evidence? *Please refer to your experience over the past five years*

Q12: Did the additional evidence requested by the country, result in:

A. Supplementary submission
    a. Yes
    b. No

B. Re-submission
    a. Yes
    b. No

C. Withdrawal of submission
    a. Yes
    b. No

D. What was the impact on costs?

    a. Staff

    b. HTA related costs

    c. Real word evidence generation

E. What was the impact on the time until the final HTA report was available?

Q13: Have any of your products undergone a re-assessment?

If yes, please indicate how much extra costs it incurred (in Euros).

a. Yes
b. No

Part 3: Information about the preliminary policy options on HTA cooperation after 2020

In this section, we provide you with key information to assess the impact of the different preliminary policy options.

Please read carefully through the short description of each policy option in order to understand the scope of the questions asked in Section 3.

Please note:

For the purpose of assessing the impacts of the various options and the various implementation mechanisms /business models, fine-tuned options were created within the course of the study. These combine the options with the implementation mechanisms (for details see below).

The fine-tuned options in this section are provisional. They are merely examples of the possible combinations of the IIA options with the IIA implementation mechanisms that were developed in order to facilitate the analysis. In any event, they do not represent the preferred combinations of the European Commission nor the contractor and other combinations are possible. Furthermore, the policy options may need to be revised following the input of Member States and stakeholders through public consultation and discussions. The final policy option does not have to be exactly in line with one that was analysed, but it can combine elements. (E.g. it is possible to have option X, but combine it with the implementation mechanism of option Y.)

Key characteristics

The different **policy options** for cooperation on HTA after 2020 are defined along several **key characteristics** focusing on 1. HTA output, 2. Participation and uptake from Member States' perspectives, 3. Organizational aspects, 4. Funding aspects as well as 5. Timelines. These are explained in the following:

1) The scope of the cooperation is defined by several **outputs**([22]) created by a joint collaboration, comprising of:

- Common tools and procedures, including common submission templates, an IT system with planned and ongoing assessments, common methodologies (e.g EUnetHTA Core Model), a joint prioritization process, and cooperation on data requirements, including Horizon Scanning
- Performing joint Early Dialogues
- Performing joint Relative Effectiveness Assessments (REA can take place at time of market launch, or later (re-assessment))
- Performing joint Full Health Technology Assessments (Full HTA can take place at time of market launch, or later (re-assessment))

2) The engagement in participation and uptake([23]) of jointly produced outputs can be either **voluntary** or **mandatory**:

([22]) The scope of the activities may differ between pharmaceuticals, medical devices and other technologies.

- Voluntary participation/ voluntary uptake (V/V): Member States can decide if they wish to participate in the production of outputs and take up the respective output; cooperation is entirely voluntary.
- Voluntary participation/mandatory uptake (V/M): The participation in the creation of joint work is voluntary, meaning that Member States can decide to opt-in[24] to the joint cooperation. However, once a Member State has opted-in the uptake of the joint work into the national setting is mandatory.
- Mandatory participation/mandatory uptake (M/M): Both participation in the production of outputs and the uptake of these into the national setting are mandatory.

For each of the policy options, different combinations of **voluntary or mandatory** participation and uptake per Output are possible.

3) For organizing the creation of these joint HTA outputs a number of different **organizational mechanisms** are conceivable:

- Project based cooperation: The secretariat is set up by the Member States that participate (similar to EUnetHTA).
- EU/MS secretariat: A permanent Secretariat is established.
- Existing EU agency: A permanent Secretariat is integrated in an already existing EU agency. This Secretariat will coordinate the work of national experts in HTA bodies in carrying out the assessments.
- New EU agency: A permanent Secretariat is integrated in a NEW EU agency. This Secretariat will coordinate the work of national experts in HTA bodies in carrying out the assessments.

4) For financing the joint cooperation several **funding mechanisms** are conceivable:

- EU funding, either through a Public Health program or another financial instrument
- Funding by Member States joining the collaboration
- Funding through industry fees

5) **Timelines**:

Timelines for implementation of the proposed policy options after 2020 range from immediately, without delay, for option 1 (i.e. 2021) to transitional periods for implementing options 4 or 5 in a new legal framework).

Table 1 provides an overview of each policy option and the envisaged implementation/funding mechanism. A short summary for each policy option can be found afterwards.

([23]) Please note that Up-take concerns using or considering the results and findings of the HTA cooperation, reaching from jointly developed submission templates to outcomes in full HTA. The subsequent pricing and reimbursement decision would remain purely on national level. Also providers / developers need to adhere to this process.

([24]) Opt-in by MS is by output, not by individual products e.g. once a MS has opted in for joint REA, they take part in all joint REAs - but not necessarily as an author.

Table 5: Overview of Policy Options

		Baseline	Non-legislative	Legislative			
		PO 1	PO 2	PO 3	PO 4[25]		PO 5
		No EU action after 2020	Voluntary cooperation through Public Health Programme	Legislation covering common tools and early dialogues	Legislation covering Joint work on REA Plus common tools and early dialogues		Legislation covering Joint work on Full HTA (incl. REA) Plus common tools and early dialogues
					4.1 REA V/M	4.2 REA M/M	
Outputs	Common tools, incl. templates, methodology	V/V	V/M	M/M	M/M	M/M	M/M
	Early dialogue([26])	V/V	V/M	V/M	V/M	M/M	M/M
	Joint REA([27])	V/V	V/M	V/V	V/M	M/M	M/M
	Joint Full HTA([6])	V/V	V/V	V/V	V/V	V/V	V/M
Implementation		No EU input	Project based cooperation	EU/MS secretariat	Existing EU agency	Existing EU agency	New EU agency
Financing		None from EU	EU+MS	EU+MS+fees from industry for early dialogues, joint REA and full HTA			
Scope			All medicines, medical and other technologies	Tools: all medicines, medical technologies, other technologies (phasing in), ED: industry submission	Tools and ED see PO 3. REA: certain categories of medicines (e.g. centrally authorised, high value/budget impact, agreement between MS), certain categories of medical technologies(e.g. high risk, high value products) and other technologies (agreement and prioritisation between MS) – phasing in([28])		Tools and ED see PO 3, REA see PO4. For others: ad hoc agreement and prioritisation between MS

([25]) Assuming that 50% of the Member States participate, a mix between high/low income, large/small MS.

([26]) Early Dialogue: Here mandatory uptake means that the MS cannot repeat an ED that was done at EU level. Technology providers initiate Early Dialogues.

([27]) Either at time of market or re-assessment

([28]) A gradual introduction of products during a transitory period that allows to manage the workload while the structures/implementation model are being developed.

Short description of policy options:

Policy Option 1. Baseline scenario - No EU action after 2020:

- Non-regulatory framework
- Participation/uptake entirely voluntary
- No EC action & no EU funding. MS are free to cooperate in any kind

Policy Option 2. Voluntary cooperation supported by the Public Health Programme:

- Non-regulatory framework
- Participation entirely voluntary
- Mandatory uptake of (some of the) common (IT-) tools, templates, methodologies + Early Dialogue + joint REA. EU contribution can only be obtained if contractually agreed by the participants.
- Voluntary uptake of joint Full HTA
- Coordination organised on a project basis
- EU & MS funding: long term commitment of funding, (minimum 4, maximum 7 years), annual budget([29])
- Scope: All medicines, medical and other technologies

Policy Option 3. Legislation covering Common Tools and Early Dialogues:

- Regulatory framework will be established
- Mandatory participation and uptake in common (IT-) tools, templates, methodologies, etc.
- Opt-in (foreseen in legislation) in Early Dialogues and reassessments, mandatory uptake for those who opted in
- Voluntary participation in and uptake of joint REA + joint Full HTA
- Coordination organised by a secretariat run by EC or MSs
- Funding by EU, MS and by other sources (e.g. company fees for Early Dialogues or registries for reassessment)
- Scope: For tools: all medicines, medical technologies, other technologies (phasing in), for Early Dialogue: industry submission

Policy Option 4.1. Opt-in for Joint REA plus option 3:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies – see option 3
- Opt-in (foreseen in legislation) in joint REA and Early Dialogues and mandatory uptake by those who opted in. It is assumed that 50% of the Member States participate, a mix between high/low income, large/small MS.
- Voluntary participation and uptake of joint Full HTA
- Coordination organised in an existing EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for joint EDs and REAs)
- Scope: Tools and ED see PO 3. REA: certain categories of medicines (e.g. centrally authorised, high value/budget impact, agreement between MS), certain categories of medical technologies (e.g. high risk, high value products) and other technologies (agreement and prioritisation between MS) – phasing in

([29]) Through the Multiannual Financial framework (MFF)

Policy Option 4.2. Mandatory Joint REA plus option 3:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies + Early Dialogues + joint REA
- Voluntary participation in and uptake of joint Full HTA. It is assumed that 50% of the Member States participate, a mix between high/low income, large/small MS.
- Coordination organised in an existing EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for joint EDs and REAs)
- Scope: Tools and ED see PO 3. REA: certain categories of medicines (e.g. centrally authorised, high value/budget impact, agreement between MS), certain categories of MDs (e.g. high risk, high value products) and other technologies (agreement and prioritisation between MS) – phasing in

Policy Option 5: Option 4.2 and Opt-in for Full HTA:

- Regulatory framework will be established
- Mandatory participation in and uptake of common (IT-) tools, templates, methodologies + Early Dialogue + joint REA – option 4.2
- Opt-in (foreseen in legislation) participation in joint Full HTA and mandatory uptake for those who opted in
- Coordination organised in a new EU agency
- Funding by EU, MS and other sources (e.g. company fees – including for Full HTA)
- Scope: For tools and ED see policy option 3. For REA see policy option 4. For others: ad hoc agreement and prioritisation between MS.

Part 4: Assessment of policy options

In the following sections of the questionnaire, we kindly ask you to assess each of the policy options described above according to their economic and social/health impacts.

Compared to the status quo, how do you estimate the different policy options' may impact on the economic indicators in the table below*?*

Please indicate for each question on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+) for each policy option.

Example: If you expect that for option 4.2 the total number of HTA submission across Europe will be cut by half, you should put -50.

Costs

Compared to the status quo, how do you estimate the different policy options' may impact on your average ***costs per product****?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+) for each policy option.

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
To what extent do you expect each policy option to impact on the ***costs for Horizon Scanning*** *(all costs)?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
To what extent do you expect each policy option to impact on the total ***costs for Early Dialogues?*** (Total costs including costs for staff, administrative costs, etc.)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
To what extent do you expect each policy option to impact on the ***total costs*** *of a* ***REA submission (if applicable)****?* (Total costs including costs for staff, (re)submission costs, administrative cost, costs for including stakeholder etc.)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
To what extent do you expect each policy option to impact on the ***total costs*** *of a full* ***HTA submission****?* (Total costs including costs for staff,	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
(re)submission costs, administrative costs, travel costs, costs for including stakeholder)							
*To what extent do you expect each policy option to impact on **HTA submission fees**?* (Fees that have to be paid for submitting an HTA/REA to the respective institution)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **costs for additional data** requested by HTA bodies?* (Referring to all studies performed in addition to clinical studies conducted for regulatory approval)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **needs for Human Resource**s (Full time equivalents including consultants)?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **costs for HTA re-assessment** (all costs)?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Administrative burden

*Compared to the status quo, how do you estimate the different policy options' may impact on your **administrative burden**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
To what extent do you expect each policy option to impact on the	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

overall administrative burden associated with HTA submissions*?* (Administrative burden arising from the information obligations imposed on industry with regard to HTA processes)							
To what extent do you expect each policy option to impact on the ***number of HTA submissions*** *for the same product and indication across* European countries*?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
To what extent do you expect each policy option to impact on ***the time needed for an HTA process****?* (The time span of the whole assessment procedure)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
To what extent do you expect each policy option to impact on the ***complexity of HTA assessment processes****?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Competitiveness of EU health technology sector

Compared to the status quo, how do you estimate the different policy options' may impact on the following indicators regarding the ***competitiveness of EU health technology sector****?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+).

Indicator (impact on)	**PO 1**	**PO 2**	**PO 3**	**PO 4.1**	**PO 4.2**	**PO 5**	**Comments**
To what extent do you expect each policy option to impact on the ***predictability of the HTA system*** *in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
To what extent do you expect each policy option to impact on the ***competitiveness of SME****?* (SME is defined by staff headcount<250	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

and either turnover ≤ 50m or balance sheet total ≤ 43m)							
*To what extent do you expect each policy option to impact on **your revenues?***	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Innovation and research

*Compared to the status quo, how do you estimate the different policy options' may impact on the following indicators regarding **Innovation and research**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **research** climate in the European market?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the actual **innovation** for the European market?* (I.e. focus on predictability and deduction of fragmentation as key factors for favorable business climate for industry facilitating innovation thrive)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

International Trade

*Compared to the status quo, how do you estimate the different policy options' may impact on **international trade**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on **international trade** related to pharmaceuticals/ medical technologies?* (Possibility to import and/or export)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Functioning of the internal market and competition

*Compared to the status quo, how do you estimate the different policy options' may impact on the following indicators regarding **the functioning of the internal market and competition**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **fragmentation of the HTA** system in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **convergence of HTA methodologies** in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **attractiveness of the EU market** for Industry?* (Reduction of fragmentation of HTA systems)	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Consumer and households

*Compared to the status quo, how do you estimate the different policy options' may impact on the following indicators regarding **consumer and households**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **number of health technologies available** (Consumer choice – mainly for medical technologies) in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **number of health technologies assessed** in Europe?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Macroeconomic environment

*Compared to the status quo, how do you estimate the different policy options' may impact on the following **macroeconomic environment**?*

Please indicate on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+).

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
*To what extent do you expect each policy option to impact on the **overall economic growth and labor market**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on the **health technology sector**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	
*To what extent do you expect each policy option to impact on **the health care sector (including providers)**?*	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	range - 100/+100	

Assessment of Social/health impacts

In the following section of the questionnaire, we kindly ask you to assess each of the policy option described according to their social/health impacts.

Compared to the status quo, how do you estimate the different policy options' may impact on the social/health indicators in the table below?

Please indicate for each question on a range (from -100 to +100) whether the indicator may decrease (-) or increase (+) for each policy option.

Example: If you expect that for option 4B the total number of HTA submission across Europe will be cut by half, you should put -50.

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
Employment (labor market)							
To what extent do you expect each policy option to impact on the ***number of staff*** *employed at your company (full time equivalents including consultants)?* (Number of full time equivalents (including consultants), which are involved in HTA and on the payroll of your organization)	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
Governance, participation and good administration							
To what extent do you expect each policy option to impact on the ***involvement of stakeholder groups*** *in HTA processes?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
To what extent do you expect each policy option to impact on the ***responsibilities of public institutions and administrations in HTA on MS level****?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
To what extent do you expect each policy option to impact on the ***uptake of joint outputs (HTA reports, Early Dialogues, tools, etc.)****?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
To what extent do you expect each policy option to impact on the ***resource efficiency***	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	

Indicator (impact on)	PO 1	PO 2	PO 3	PO 4.1	PO 4.2	PO 5	Comments
***of HTA processes**?*							
*To what extent do you expect each policy option to impact on the **sustainability of EU HTA cooperation**?*	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range - 100/+100	
Access to and effects on social protection and health systems							
*To what extent do you expect each policy option to impact on the **access to innovative treatments**?*	range - 100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
Sustainability of health systems							
*To what extent do you expect each policy option to impact on the **financing of expensive treatments** with little or no added value?*	range - 100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact on the **negotiation power** of MS in setting prices?*	range - 100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
Public health							
*To what extent do you expect each policy option to impact on the **availability of health technologies on the market**?*	range - 100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	
*To what extent do you expect each policy option to impact o**verall public health**?*	range - 100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	range -100/+100	

Part 4 - Assessment of Preferences

Q.1. Please indicate which relevance/importance you attribute to the impacts on HTA cooperation after 2020 listed below. Please rate the impacts from low priority = 1 to high priority = 10.

Impacts		Importance (0 to 10)
Economic impacts	**Costs**	Range 1/10
	Administrative burden	Range 1/10
	Competitiveness of EU health technology sector	Range 1/10
	Innovation and research	Range 1/10
	International trade	Range 1/10
	Functioning of the internal market and competition	Range 1/10
	Consumers and households	Range 1/10
	Macroeconomic environment	Range 1/10
Social/health impacts	**Employment (labour market)**	Range 1/10
	Governance, participation and good administration	Range 1/10
	Access to social protection and health systems	Range 1/10
	Sustainability of health systems	Range 1/10
	Public health and safety	Range 1/10

Q.2. *The section on policy options included **an example** of what sub-categories of pharmaceuticals and medical technologies could be included in the **scope** of HTA cooperation.*

Please indicate which sub-categories you would find particularly useful to include in the EU HTA cooperation.

Please be sure you want to submit the questionnaire, once submitted answers cannot be altered!

Thank you very much for participating and filling in the questionnaire!

Annex 5: List of agencies performing HTA agencies operating at EU level

Country	HTA Agency	Scope of Recommendations	Technologies Appraised	Role of HTA Body	Publicly Available HTA Reports
Austria	GÖG LBI-HTA Hauptverband	National	Pharmaceuticals, medical devices and other technologies	Advisory	Yes
Belgium	KCE	National	Pharmaceuticals and other technologies	Advisory	Yes
Bulgaria	NCPHA Centre for Health Technology Assessment and Analysis	National	Pharmaceuticals	Advisory	No
Croatia	Azz	National	Pharmaceuticals and medical devices	Advisory	No
Cyprus	MoH	National	Pharmaceuticals	Advisory	No
Czech Republic	MoH	National	Pharmaceuticals	Advisory	No
Estonia	Centre for Health Technology Assessment-University of Tartu Estonian Health Insurance Fund (EHIF)	National	Pharmaceuticals	Advisory	Yes

Country	HTA Agency	Scope of Recommendations	Technologies Appraised	Role of HTA Body	Publicly Available HTA Reports
Finland	FIMEA KELA	National	Pharmaceuticals, medical devices and other technologies	Advisory	Yes
France	HAS	National	Pharmaceuticals, medical devices, hospital medical technologies	Advisory	Yes
Germany	IQWIG G-BA	National	Pharmaceuticals	Advisory (IQWIG) Regulatory (G-BA)	Yes
Hungary	OGYEI	National	Pharmaceuticals, medical devices, hospital medical technologies	Advisory	No
Ireland	NCPE HIQA	National	Pharmaceuticals, medical devices and other technologies	Advisory	Yes partly
Italy	AIFA (national) UVEF (regional) AGENAS (regional) REGIONE EMILIA ROMAGNA (regional)	National and Regional	Pharmaceuticals and medical devices	Regulatory (AIFA) Advisory (UVEF & AGENAS)	Yes
Latvia	ZVA	National	Pharmaceuticals	Regulatory	No
Lithuania	VASPVT	National	Medical Devices	Advisory	Yes

Country	HTA Agency	Scope of Recommendations	Technologies Appraised	Role of HTA Body	Publicly Available HTA Reports
Malta	Directorate of Pharmaceutical Affairs-MoH	National	Pharmaceuticals	Advisory	No
Netherlands	ZiN	National	Pharmaceuticals, medical devices and other technologies	Advisory	Yes partly
Poland	AOTMiT	National	Pharmaceuticals, medical devices and other technologies	Advisory	Yes
Portugal	Infarmed	National	Pharmaceuticals and medical devices	Advisory	Yes
Romania	NAMMD	National	Pharmaceuticals	Regulatory	Yes
Slovakia	MoH	National	Pharmaceuticals and medical devices	Advisory	No
Slovenia	MoH	National	Pharmaceuticals	Advisory	No

Spain	**CADIME (regional)** **AQuAS (regional)** **ISCII (national)** **OSTEBA (regional)** **AETSA (regional)** **SECS (Regional)**	**Regional**	**Pharmaceuticals and medical devices**	**Advisory**	**Yes**
Sweden	TLV	National	Pharmaceuticals and medical devices	Regulatory	Yes
United Kingdom	NICE SMC	National	Pharmaceuticals, medical devices and other technologies	Advisory	Yes
EU level	EUnetHTA	European Level	Pharmaceuticals, medical devices and other technologies		

Legend: NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; GÖG: Gesundheit Österreich GmbH; LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment; KCE: Belgian Health Care Knowledge Centre; NCPHA: The National Center of Public Health and Analyses ; MoH: Ministry of Health; Azz: Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi; FIMEA: Finnish Medicines Agency KELA: Kansaneläkelaitos; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; OGYEI: Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet; NCPE: National Centre for Pharmacoeconomics; HIQA: Health Information and Quality Authority AIFA: Agenzia Italiana del Farmaco UVEF: Unità di valutazione dell'efficacia del farmaco ; AGENAS: Agenzia Nazionale per i servizi sanitari regionali; ZVA: Zalu valsts agentura; VASPVT: Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento; NAMMD: National Agency for Medicines and Medical Devices; CADIME: Centro Andaluz de Documentación e Información de Medicamentos; AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya; ISCII: Instituto de Salud Carlos III OSTEBA: Basque Office for Health Technology Assessment; AETSA: Andalusian Agency for Health Technology Assessment; SECS: Servicio de Evaluacion del Servicio Canario de salud.

Source: The Authors

Annex 6: Minutes Focus Group Pharma

EUROPEAN COMMISSION
DIRECTORATE GENERAL FOR HEALTH AND FOOD SAFETY

Directorate B - Health systems, medical products and innovation
Unit B4 - Medical products: quality, safety, innovation

Pharmaceutical Industry focus group

Date: 02/05/2017

Location: DG SANTE offices

Participants

Pharmaceutical companies: The company representatives that participated in the online survey related to Health Technology Assessment (HTA) ("the survey") were attending in order to provide additional information on the survey results. The survey is part of a "Study on impact analysis of policy options for strengthened EU cooperation on HTA" ("the study") - run by the Austrian Public Health Institute (GO FP) and the London School of Economics on behalf of DG SANTE/CHAFEA. The following companies were represented:

Biogen International GmbH
Johnson & Johnson
Pfizer
Novo Nordisk Region Europe Pharmaceuticals A/S
Eli Lilly & Co
CelgenE
Teva Pharma

DG SANTE: Dominik Schnichels, Head of Unit, Medical products: quality, safety, innovation; F. Giorgio, N.Orsi, C. Larsson Lindqvist, K. Valkova, N. Suleiman

The Austrian Public Health Institute (GO-FP): Anja Laschkolnig
London School of Economic (LSE): Panos Kanavos, Erica Visintin

Purpose of the meeting

Discussion, interpretation and validation of the survey results with industry experts regarding costs and impacts of the policy options.

Discussion

General observations

Industry participants agreed that the results of the survey are useful to understand preferences of the pharma industry regarding the HTA policy options. The survey results should however not be over-interpreted as precise quantifications of the impacts (e.g.

cost increases by x%). The survey results should rather be taken as a general indication of trends. The respondents also noted that exact quantification of certain impacts has been difficult as many factors had to be taken into consideration for one indicator. Also the impacts will depend on how the policy options would be implemented and for some participants this was not defined sufficiently when answering the questionnaire.

To compensate for the above limitations, it was recommended to triangulate the results with additional data sources and complement by the outcome of the focus group discussion. DG SANTE clarified that the online survey is one part of the data gathering exercise to support the analysis of the impacts of the policy options. The survey is further supported by the literature review and a set of case studies. In addition, it was also clarified that the study is one input to the impact assessment process along with the results of the public consultation, the outcome of the ongoing additional stakeholders' consultation and further data gathering which is currently ongoing via additional studies which aim to map processes and procedures of HTA systems across the EU.

Largely, the representatives of pharma companies expressed a preference for policy options 4.1 and 4.2. Both of them having provisions for a centralised REA with a varying degree of uptake – respectively voluntary participation and mandatory uptake; and mandatory participation and uptake. The stated reasoning was that pharmaceutical companies could use the results from an EU-wide REA as supporting the various pricing and reimbursement discussions which normally follow the HTA process and these options would further increase the business predictability across Member States providing for a better investment as well as research and innovation environment.

Participants expressed strong concerns towards policy option 5. As option it is considered to bring the most substantial (structural) changes by moving decisions from the local towards EU level. They agreed that a joint European full HTA is not feasible due to the specificities, e.g. in the organisational care or economic domains and so policy option 5 would lead to a duplication of demands for pharmaceutical companies – first at EU level, and then at national level, in the cases where Member States do not find the EU demands sufficient enough. This leads to duplications and even higher unpredictability, which strongly affects the responses to all indicators.

EC1 Costs

The participants confirmed that the general trend for costs is plausible. Discussing the results for policy option 2 to 4 the industry representatives explained that they do not expect any significant changes in their current costs, yet the overall consistency of HTA processes and outcomes would increase resulting in better business predictability having positive effects on investment as well as research and innovation.

The participants explained that they usually prepare a central/global value dossier for each product. This dossier is then used as a main source of input by the HTA teams across the countries where the products is foreseen to be launched. One estimation was that a joint HTA report could replace 20-25% of the local HTA costs if there is no requirement for translation/adaptation. At the same time, even if there is an EU-centralised REA at the time of market launch, companies would still have to go through national reimbursement procedures. While this could result in a reduction of some costs (see above), the companies would still have significant and possibly increased expenditure for the national requirements, which are outside the EU cooperation (eg "economic evaluation"). That is why industry believes that the increases and decreases in costs would just balance each other out.

Furthermore, it was explained that today there are certain risks when performing evidence generation. Should the company align to the market that requires the highest level of evidence or can a lower standard be sufficient. In that regard, companies take risks when deciding for a lower or medium standard. Following that logic it is perceived likely that a framework for an EU HTA may provide a compromise between data needs.

The key driver for HTA-related costs is the evidence generation. It is mainly in the largest markets that companies perform additional clinical trials requested by HTA bodies. Otherwise, the existing knowledge gaps are often covered with post-marketing studies (investigator-initiated trial). The companies also explained that the requests for evidence by smaller countries might be more difficult to address – taking into account the market size.

Harmonisation of data requirements was perceived positive. It reduces risks but does not necessarily result in overall cost reduction as the data needs at EU level will likely not end up at the level of the lowest denominator.

Comments on the costs reported

The costs for industry (absolute figures) were considered to be realistic, but erring on the conservative side. The actual costs would depend on what is included in the cost factors (such as costs related to RCTs, which were not included by the study team on purpose). It was also noted that many indirect costs may not have been reported and that establishing the costs for additional evidence generation is particularly difficult (different budget lines, data may also serve other – regulatory/pricing and reimbursement - purposes etc.)

Participants agreed to follow up on the issue of additional evidence generation and to provide further information to DG SANTE.

EC2 Administrative Burden

The industry representatives reiterated that the recurrent sharp rise of expected costs between policy option 4 and 5 can be explained with the aforementioned multiplication of national requirements – in addition to the harmonisation achieved at EU level. Industry also argued that option 5 does not appear feasible in practice due to the different economic situations of Member States.

EC 3 Competitiveness of the EU health technology sector

The pharma representatives clarified that, overall, they could expect an increase in competitiveness in the EU with the reduction of the heterogeneity of the markets and the potential shortening of timelines that stronger cooperation in HTA on EU level would achieve. However, less heterogeneity among EU markets would not necessarily translate immediately into higher revenues since the negotiations on the pricing and reimbursement of pharmaceuticals will still take place and the overall budget for pharmaceuticals is not expected to increase.

EC 4 Innovation and Research

The main driver is the improved predictability of the HTA process which could lead to increased efforts to innovate, since operating in an environment with less variability between markets, would lead to less risks and thus, to more investments. Joint REA in parallel with market authorisation should shorten the market access process – at least in certain countries. If the process is shortened, there would cost savings and earlier revenues. Participants also pointed out the value in accessing the first markets quickly. This could be particularly relevant for SMEs.

Meanwhile, additional efforts would be needed from the small and medium enterprises (SMEs) to keep up with new requirements and stay competitive on the market. These trends are reflected in the answers for the respective policy options.

SH 4 Sustainability of health systems and SH 5 Public Health

Most of the participants did not provide input to this question, since they deemed the question out of their reach. According to them, one of the positive aspects of HTA is the value-based approach for treatments and products.

Follow up

DG SANTE thanked the participants of the focus group and asked them to provide clarification on the occasions when they have been performed additional evidence generation by 12th May.

Annex 7: Minutes Focus Group MedTech Minutes

EUROPEAN COMMISSION
DIRECTORATE GENERAL FOR HEALTH AND FOOD SAFETY

Directorate B - Health systems, medical products and innovation
Unit B4 - Medical products: quality, safety, innovation

HTA Focus Group: Medical Technologies (incl. diagnostics)

Date: 02/05/2017

Location: DG SANTE offices

Participants

Medical technologies industry:
Company representatives that participated in the online survey related to Health Technology Assessment (HTA) ("the survey") were attending in order to provide additional information on the survey results. The survey is part of a "Study on impact analysis of policy options for strengthened EU cooperation on HTA" ("the study") - run by the Austrian Public Health Institute (GO FP) and the London School of Economics on behalf of DG SANTE/Chafea. The following companies were represented:

Beckman Coulter
GE Healthcare Europé
Baxter World Trade
Johnson & Johnson Medical
Roche Diagnostics
B.Braun Melsungen AG
Philips Healthcare
Biocartis
Fresenius SE & Co. KGaA

DG SANTE: Dominick Schnichels, Head of Unit, Medical products: quality, safety, innovation; F. Giorgio, N.Orsi, C. Larsson Lindqvist, K. Valkova, N. Suleiman.

The Austrian Public Health Institute (GO-FP): Anja Laschkolnig
London School of Economic (LSE): Panos Kanavos, Erica Visintin

Purpose of the meeting

Discussion,interpretation and validation of the survey results with industry experts regarding costs and impacts of the policy options.

Discussion

The majority of participants to the focus group had relevant HTA experience, either in their current function or in their past professional career.

General observations

Industry participants agreed that the results of the survey are useful to understand preferences of the medtech industry regarding the HTA policy options. The survey results should however not be over-interpreted as precise quantifications of the impacts (e.g. cost increases by x%). Certain values are rather the expression of significant concerns that the market access path for medtech products might change substantially – over and above the new legislation for medical technologies that was just adopted. The survey results should rather be taken as a general indication of trends. The respondents also noted that exact quantification of certain impacts has been difficult as many factors had to be taken into consideration for one indicator. Also the impacts will depend on how the policy options would be implemented and for some participants this was not defined sufficiently when answering the questionnaire.

To compensate for the above limitations, it was recommended to triangulate the results with additional data sources and complement by the outcome of the focus group discussion. DG SANTE clarified that the online survey is one part of the data gathering exercise to support the analysis of the impacts of the policy options. The survey is further supported by the literature review and a set of case studies. In addition, it was also clarified that the study is one input to the impact assessment process along with the results of the public consultation, the outcome of the ongoing additional stakeholders' consultation and further data gathering which is currently ongoing via additional studies which aim to map processes and procedures of HTA systems across the EU.

Many industry participants explained that their responses for Policy Option 2 are based on the assumption that the collaboration is expected to be demand driven, from the 'bottom upwards' and the overall number of HTAs for medical technologies would remain stable. Whilst in options 3 to 5 the collaboration would become more top-down and the number of (joint) HTA reports would increase significantly – leading to additional costs for industry and delays in market launch. Also some participants indicated that in their responses they considered that Option 2 is fully aligned with the proposal of the European medtech association, where clusters of Member States (MS) that are interested in a given technology can agree to cooperate on a voluntary basis.

DG SANTE explained that in its view the main difference between Policy Options 2 and 3 is the cooperation framework for HTA bodies. In Policy Option 2 the cooperation of HTA bodies is based on a contractual arrangement (like EUnetHTA). In Policy Option 3 the cooperation is based on legislation. In this sense the risk of diverging submission templates, diverging data requirements etc. is less pronounced in Policy Option 3. Joint Assessments can be done under both Policy Options alike, in both cases on a voluntary basis. Industry participants had different understanding of Policy Option 3 had been clear to them – they would have replied differently by giving more favourable marks to Policy Option 3.

Participants also clarified that they had interpreted Policy Options 3-5 as legally mandating REA (or full HTA) at the time of launch, and as such they felt it would substantially increase HTA activities in MS for medical technologies. Ultimately it would fundamentally change the current business model, which is based largely on public procurement at local level. In their view the creation of a legal framework, even if it did not impose a legal obligation on REA or Full HTA, would provide a driver for further increase of HTA activities in MS. Some participants also argued that the market access path for medical products typically does not foresee setting prices or reimbursement levels at national level. This would question the value of HTA at time of launch (no impact on "decision making") and could delay market access. For the majority of technologies it might therefore be preferable to allow immediate market access and foresee a demand-driven reassessment based on real world evidence (value based pricing) at a later stage (e.g. on clinical uncertainty after a period of clinical experience). This would also maintain the first mover advantage.

Industry participants also indicated that there is a perceived risk that even though an EU Assessment would be implemented, there would be duplications on national and local level. In the view of the industry it will still be essential to capture the specific elements present at local level which have to be part of the assessment related to the use of the technologies in the local settings. Therefore HTA bodies are considered likely to continue to ask additional information, including for generation of evidence, which are particularly costly for the industry.

The discussion also touched upon the difference between regulatory and HTA requirements; where industry pointed out that they should remain separate. The regulatory framework, currently in transition, aims to ensure that products are safe, and that label claims are correct. HTA, on the other hand, intends to assess the clinical benefit of an intervention. These purposes are complementary but different, and should not be confused. It would instead make more sense to align HTA requirements with needs of market access decision-makers / payers, to increase the relevance of HTAs.

When defining the value of a technology, one particular challenge for medical technologies are the large variability in service delivery models across Member States and the fact that the costs and benefits are often realised in health and social budgets (e.g. less invasive surgeries and other technologies shifting care from hospitals to social settings) and they are not fully captured in the assessment. Moreover, it is particularly dependent on the local specificities and would be impossible to capture it in a single EU full HTA.

EC1 Costs

The participants confirmed that the general trend visible is plausible.

In response to the question how to explain the major differences between Policy Options 2 and 3, participants explained that the main driver for increased costs from policy option 3 to 5 is the legal nature of the cooperation. A described earlier (see "general observations"), participants expect a legal system to significantly increase HTA activities across Member States and between Member States in the field of medical devices and IVDs at the time of the market launch of the product, where currently there are limited activities (if at all).

The key cost factor is the generation of evidence. Companies noted that currently efficacy data is not required (and in the revised regulation it will only be required for a limited number of technologies). The cost of regulatory and HTA data generation differs; HTA evidence generation is estimated to be four times more expensive. It was also discussed that for products requiring additional clinical data, it may be beneficial to align requirements, if possible to maximise the use of data and reduce duplication.

Comments on the costs reported:

- The large variation reported on the costs related to HTA is a good reflection of large variation of real-life costs of different technologies. Costs are considered to be realistic yet slightly conservative, depending on what is included in the cost factors.

- For the number companies involved in early dialogues: of the participants that responded “yes”, they clarified that they only had undergone one ED process respectively (i.e. do not routinely engage in early dialogues for medical devices), so the number overestimates the importance of EDs for medical technologies. This is explained by the short life cycle of medical technologies (including fast development phase) and the limited requirements for clinical evidence, according to the current regulatory framework.

EC2 Administrative Burden

Industry reiterated that they expect a legally mandated REA at the time of launch to substantially increase HTA activities in MS, and so fundamentally change the business model. This explains the sharp increase from policy option 2 to 3. At the same time, once evidence needs to be generated for HTA there is little difference in terms of administrative burden, if this additional data should focus on effectiveness or on economic aspects. This accounts for the relative stability of the curve from policy option 3 to 5.

EC3 and EC4 Innovation, Competitiveness

If HTA is conducted at the time of market launch and the first mover needs to generate comprehensive evidence, which can then be used for the early followers, a situation is created where the first mover has a considerable disadvantage. In the view of participants this explains the sharp expected decline for these impacts form a voluntary cooperation to a mandatory one. More general/academic HTAs, which are not fully recognized by each Member State and hence informing decision making to a less effective extend create extra cost with a less clear link to a potential return. This would be harmful for investment decisions of all companies, but companies with a weaker cash position (i.e. many innovating SMEs) might be forced to change strategic direction away from the riskier/more innovative IVDs.

In addition, if the EU market is not attractive (limited growth opportunities, difficult entry) industry would prioritise other markets. Ultimately all products would arrive on the EU market, but just delayed. It was further emphasised that the growth in the European medical technologies market is already quite low and that any additional burden might jeopardise it further. Additional legislation and slower market access in particularly for first movers/innovators with no clear link to pricing and reimbursement might reduce the attractiveness of the EU market.

Particular challenges for SMEs relate to the fact that increased harmonisation can delay the first revenues, which are particularly challenging due to the higher costs of financing. So even if harmonization means access to more countries, losing the quick access to the first market overrides the advantage of accessing some countries (quicker). This can already be seen today where focus is given to launch products in certain markets with earlier access to provide the first additional revenues. At the same time participants expressed understanding that Member States have a legitimate interest to ensure the sustainability of their national health systems and to favour effective treatments over ineffective treatments.

Furthermore, one participant indicated that an EU system might lead to a higher demand for costly quality evidence, which does not inform decisions and does not improve patients' situations. Moreover, SMEs might not be able to handle such increased costs (extra burden of adapting to any new harmonised tools or assessments). Therefore, private equity investors might be more inclined to find other opportunities for investment and/or larger companies would take over of SMEs. Large companies would probably be able to cope with the additional costs, but SMEs would have a very difficult time in an already competitive market.

EC6 Internal Market

Respondents mentioned a number of factors through which legislation can in fact increase fragmentation and complexity:

- In particular in the first years of the new regulatory framework, due to the exceptions the landscape may paradoxically become more fragmented.

- It was also considered that a joint submission template may even increase complexity if it adds a high number of general fields which are not relevant in local settings.
- Voluntary cooperation on the other hand would still enable HTA bodies and/or decision makers and Industry to work together/ facilitate evidence generation (eg cooperation with different research centres testing the new product). This is perceived to share the risk of evidence generation rather than provide additional hurdles. These reasons would explain the expected positive impact of policy option 2.

SH4 Sustainability

Participants considered that due to the weak link between health technology assessments and pricing and reimbursement decisions for medical technologies, the changes in the HTA processes would not affect the negotiation power or the funding of technologies with little or no added value in this sector.

It was also mentioned that there were difficulties in answering to the indicator on "financing of expencive treatments with little or no added value" (whether a higher score meant more technologies with little or no added value funded or an improved situation i.e. reduced number of technologies with little or no added value funded).

It was also stated by certain participants that they do not necessarily see that financing of medical technologies with little or no added value is a major issue, as the sector is very competitive and having large number of technologies on the market drives price down. But participants conceded that Member States might be concerned for ensuring sustainability.

SH5 Public Health

In general, if the number of medical technologies available decreases as consequence of any changes in the HTA sector, this is expected to translate to lower level of public health. Participants accepted on the other hand that Member States might want to favour those treatments where the added value is particularly high for patients.

Product scope

In certain responses it was assumed that legal cooperation implies a broad scope of medical technologies (potentially all devices), which has been an important factor in the responses relating to policy option 3 to 5. There was a general agreement that currently the topic selection for joint assessment is not defined and would benefit from further input. Also, when defining the product scope, it the purpose of the HTA needs to be clarified. In response to two posed questions on potential product scope and timing of assessments the following was relayed:

Suggestions for product scope in the future:

- Respond to decision-makers' needs and/or feed into access decisions
- Transformative technologies
- High budget impact
- Unmet medical needs

Timing of assessment:

- Anytime when there is a need from decision-makers/ local request
- Should allow for sufficient evidence to be gathered.
- Transformative technologies in need of real-life evidence
- Later, for disinvestment decisions

It was also mentioned that when a common technology is adopted and further comparisons are needed with available alternatives of the technology also known as Multi Technology Assessment; EU cooperation and in particular Joint REA, could provide a

benefit where different health care providers might have adopted different alternatives and would jointly be able to deliver evidence to support comparisons between alternatives.

Follow up

DG SANTE, LSE and GO FP thanked the participants of the focus group and asked them to provide clarification on defining transformative health technologies as well as to provide examples on these by 12th May.

Annex 8: Minutes Focus Group Public Administration and others

EUROPEAN COMMISSION
DIRECTORATE GENERAL FOR HEALTH AND FOOD SAFETY

Directorate B - Health systems, medical products and innovation
Unit B4 - Medical products: quality, safety, innovation

EUnetHTA Joint Action Executive Board Meeting-

Focus group with Public authorities

Summary of discussion results from the online survey for the "Study on impact analysis of policy options for strengthened EU cooperation on HTA"

Date: 03/05/2017

Location: DG SANTE offices

Participants

EUnetHTA Joint Action Executive Board

G-BA - Pharmaceutical Dpt.	**Germany**
Belgian Health Care Knowledge Centre (KCE)	**Belgium**
Onassis Cardiac Surgery Centre (OCSC)	**Greece**
NICE National Institute for Health and Care Excellence	**United Kingdom**
ZIN - Zorginstituut Nederland	**The Netherlands**
AETS - Health Technology Assessment Agency Carlos III Institute for Health	**Spain**
ZIN - Zorginstituut Nederland	**Netherlands**
Health Care Knowledge Centre (KCE)	**Belgium**
Haute Autorité de Sante (HAS)	**France**
Fimea - Finnish Medicines Agency	**Finland**
Health Information and Quality Authority	**Ireland**
Norwegian Institute of Public Health (NIPHNO)	**Norway**
INFARMED (National Authority of Medicines and Health Products)	**Portugal**
Comenius University - Faculty of Pharmacy	**Slovakia**

DG SANTE

Austrian Public Health Institute (GO-FP): Anja Laschkolnig, Katharina Habimana

Purpose of the meeting

Discussion, interpretation and validation of the survey results HTA experts (members of the EUnetHTA executive board) regarding costs and impacts of the policy options.

Discussion

This report only refers to the first part of the Executive Board meeting, which was dedicated to the discussion of the results from the online survey for the "Study on impact analysis of policy options for strengthened EU cooperation on HTA", Anja Laschkolnig and Katharina Habimana (GO-FP) presented the results, which was followed by a discussion.

General observations

It was clarified in advance that the results represent the expectations of the respondents. The results do not allow precise quantification, but should be taken as general indications on the overall trends. The survey results should therefore not be over-interpreted as precise quantifications of the impacts (e.g. cost increases by x%). The respondents also noted that the quantification of the impacts has been difficult as many factors had to be taken into consideration for one indicator and some of these factors would also depend on how the policy options would be implemented.

To compensate for the above limitations, it was recommended to triangulate the results with additional data sources and complement by the outcome of the focus group discussion (as already planned by the study team). DG SANTE clarified that the online survey is one part of the data gathering exercise to support the analysis of the impacts of the policy options. The survey is further supported by the literature review and of the case studies done by London School of Economics. In addition, it was also clarified that the study is one input to the impact assessment process along with the results of the public consultation, the outcome of the ongoing additional stakeholders' consultation and further data gathering which is currently ongoing via additional studies mapping processes and procedures of HTA systems across the EU.

There was a discussion on to which extent and how the different indicators can be interpreted. The interpretation has to be done with caution, as the number of different factors affects the impacts. For example for "costs impact" the answer would depend whether an activity is already done or not in the country responding, whether fees are charged to support a specific activities etc. Therefore it was underlined that the different baselines also affect results, which is however natural since respondents were asked answer the questionnaire from their respective position. The contractor explained that this point was already made by the expert group, which is supporting the study and a number of actions have been put in place to address this issue. An example will be provided during the presentation in relation to costs, where for example a comparison between the estimation on cost development will be displayed separated for HTA institutes that stated experience with Early Dialogues and the ones not performing Early Dialogues.

One additional suggestion aiming at increasing the comparability of data was to distinguish HTA bodies with research focus and the ones which need to give advice for pricing and reimbursement decision as the timelines for their assessments as well as the criteria used may differ.

It was also pointed out that where there is a high variation of responses (high standard deviation), the results are less conclusive and a simple average does not reflect a trend. The contractor was aware of this and will be transparent about this limitation, when this is the case. Grouping respondents according to their functions may address also this issue. It was also clarified that the focus group may help to explain the reasoning behind answers and large variations, when these occur.

EC1 Cost indicators:

In the discussion, there was consensus that stronger EU cooperation would lead to cost decreases per products, rather than increases, as indicated in the online survey. This is mainly due to reduced duplication of efforts and increased efficiency. Current experience suggests that sharing the work lowers the costs for agencies very significantly (in one case where only two agencies agreed to cooperate on clinical guidelines they were able to save 30% respectively). Whilst there are higher overheads, which are particularly important in the beginning, this would be more than compensated by work-sharing arrangements. It was suggested that for smaller agencies, with currently limited HTA activities, cooperation could increase the scope of activities – albeit with a relatively small investment. This could explain some of the answers. In conclusion participants agreed that the results as presented were not in line with their expectations based on their experience in the cooperation.

DG SANTE confirmed that for the calculations of costs within the Impact Assessment, the primary input will be calculations based on the first part of the survey, and the follow up interaction with EUnetHTA Board in subsequent meetings (December 2016 and February 2017). The availability of the data regarding the baseline costs of HTA is not as extensive as it was hoped for. On the other hand, since the first follow up meeting with EUnetHTA Board, availability of data increased and is considered acceptable. In any event it is the best available evidence. It was also noted that for the respondents of the survey it was difficult to estimate the costs per product (considering overheads or the methodology used for assessment). It was noted that the wage difference across MS will also explain some of the differences in the variations of costs declared for national HTA products.

GO-FP presented the costs for HTA processes conducted by LSE. The HTA institutions were categorised in two ways. The first categorisation aimed to reflect the institutional differences. The second categorisation aimed to capture the differences in the costs of REA and single technology full HTAs.

It was agreed that the costs from the Joint Actions on the joint products would be a very important input. Further efforts will be made using data available from Joint Action 2 and Joint Action 3 and work within EU funded project (i.e. SEED for early dialogues). When considering these data the relevant assumptions will be made to reflect the learning curves and the number of countries involved.

EC2 Administrative burden:

It was considered that this is an example in which the overall expected variations of administrative burden may not be significant between the different policy options. Policy option 1 to 4 are all in rather close range, policy option 5 would foresee a more relevant increase, which was considered to be plausible due to the increased complexity of reaching a common agreement on economic aspects of the HTA reports which will be more context specific.

It was however also mentioned that while administrative complexity may increase from policy option 1 to 5, the resources for research may be spent more efficiently, which can ultimately lead to a more neutral effect.

EC3 Competitiveness of the EU health technology sector, EC4 Innovation and research, EC5 Internal market and competition:

These impacts and some of the sub-indicators are more applicable for industries, nevertheless the survey aimed at gathering the expectations of HTA bodies as key players in the HTA sector. It was agreed that the sub-indicator "revenue" is ambiguous in relation to HTA bodies and it was recommended to be discarded.

On other impacts, with the caveat mentioned above, the general trends outlined in the graph were confirmed as plausible. The following comments were made:

- The predictability is an important component also for academic research institutions.

- It was noted and confirmed that stronger cooperation should reduce significantly fragmentation of the HTA.

- Stronger EU cooperation may increase overall evidence needs, which are costly for the industry, in particular for medical technologies. Nevertheless there would be a significant benefit for public health.

SH4 Sustainability of Health Systems

It was agreed that a joint perspective on the added value can improve sustainability. There was consensus that stronger cooperation would improve the negotiation power to achieve lower prices for technologies with limited added value. Nonetheless, it would be more difficult to discontinue the financing of such technologies alltogether. This is mainly due to the fact that final decisions on availability of technologies will remain a national/local decision based on additional considerations than HTA assessments.

SH5 Effect on Public Health

It was noted that the availability of the technologies also depends on other factors, in particular the marketing authorisation and pricing and reimbursement systems. Therefore it is difficult to quantify with precision the impact of HTA cooperation. Nevertheless it was considered that increased convergence of HTA methods would increase the availability of health technologies with added benefits, and as such benefits public health. Variations between expectations reported between PO3 and PO4 were not considered significant.

It was noted that in particular for medical technologies the regulatory framework is less stringent in the EU than in the US.

Follow up

It was agreed that it would be useful to look at the cost structures established for Joint Action 2. DG SANTE encouraged participants to engage with the HTA team if there would be any further comments or information to be sent in relation to costs and perceived impacts in relation to the preliminary identified policy options.

Annex 9: Sample of 20 Pharmaceutical products

TECHNOLOGY GENERIC NAME	TECHNOLOGY BRANDED NAME	INDICATION	M.A Holder
Abiraterone	Zytiga®	Treatment of metastatic castration-resistant prostate cancer in adult men whose disease has progressed on or after a docetaxel- based chemotherapy regimen.	Janssen-Cilag International N.V.
Aclidinium Bromidum	Eklira Genuair®	Genuair is a treatment Bretaris maintenance bronchodilator for relieving symptoms in adults with illness chronic obstructive pulmonary disease (COPD).	AstraZeneca AB
Alemtuzumab	Lemtrada®	For adult patients with relapsing-remitting multiple sclerosis (RRMS) with active disease defined by clinical or imaging features.	Genzyme Therapeutics Ltd
Apremilast	Otezla®	Treating moderate to severe plaque psoriasis	Celgene Europe Limited
Ataluren	Translarna®	Translarna is indicated for the treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 5 years and older	PTC Therapeutics International Limited
Canagliflozin	Invokana®	Treatment of Diabetes Mellitus Type 2	Janssen-Cilag International N.V.
Dapagliflozin	Forxiga®	Forxiga is indicated in Adults aged 18 years and over, diabetes type II, for improve glycemic control in the form of: monotherapy	AstraZeneca AB
Defibrotide	Defitelio®	Defitelio is indicated for the treatment of severe hepatic veno-occlusive disease (VOD) also known as sinusoidal obstructive syndrome (SOS) in haematopoietic stem-cell transplantation (HSCT) therapy. It is indicated in adults and in adolescents, children and infants over 1 month of age.	Gentium S.r.l.
Ivacaftor	Kalydeco®	For the treatment of cystic fibrosis in patients age 6 years and older who have the G551D mutation	Vertex Pharmaceuticals (Europe) Ltd
Mirabegron	Betmiga®	Mirabegron for treating symptoms of overactive bladder	Astellas Pharma Europe B.V.
Nivolumab	Opdivo®	OPDIVO® is indicated as a monotherapy in adults for the treatment of advanced (non-resectable or metastatic) melanoma.	Bristol-Myers Squibb
Nintedanib	Ofev®	Ofev is indicated in adults for the treatment of Idiopathic Pulmonary Fibrosis (IPF).	Boehringer Ingelheim International GmbH
Ocriplasmin	Jetrea®	Jetrea is indicated in adults for the treatment of vitreomacular traction (VMT).	ThromboGenics NV
Ofatumumab	Arzerra®	Arzerra in combination with chlorambucil or bendamustine for the treatment of chronic lymphocytic leukemia (CLL) in patients for these disease not previously treated and which are not eligible eligible for a treatment based on fludarabine.	Novartis Europharm Ltd
Omalizumab	Xolair®	Xolair is indicated in adults, adolescents and children (Aged 6 to <12 years). Xolair treatment should be considered only in patients with asthma-mediated certainty of IgE (immunoglobulin E).	Novartis Europharm Ltd

TECHNOLOGY GENERIC NAME	TECHNOLOGY BRANDED NAME	INDICATION	M.A Holder
Pasireotide	Signifor®	For the treatment of adult patients with Cushing's Disease for whom surgery is not an option or for whom surgery has failed	Novartis Europharm Limited
Ramucirumab	Cyramza®	Treating advanced gastric cancer or gastro–oesophageal junction adenocarcinoma previously treated with chemotherapy	Eli Lilly Nederland B.V.
Rilpivirine in combination with other antiretroviral medicinal	Edurant®	Rilpivirine in combination with other antiretroviral medicinal products, is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-naive adult patients with a viral load ≤ 100,000 HIV-1 RNA copies/ml.	Janssen-Cilag International N.V.
Riociguat	Adempas®	Adempas is indicated for the treatment of adult patients with WHO Functional Class (FC) II to III with inoperable CTEPH, persistent or recurrent CTEPH after surgical treatment, to improve exercise capacity	Bayer Pharma AG
Sofosbuvir	Solvaldi®	In combination with other medicines, indicated in the treatment of Chronic hepatitis C (HCC) in adults	Gilead Sciences International Ltd
Tolvaptan	Jinarc®	Tolvaptan for treating autosomal dominant polycystic kidney disease	Otsuka Pharmaceutical Europe Ltd

Annex 10: Sample of 15 Medical devices

TECHNOLOGY GENERIC NAME	INDICATION	Main companies marketing the MD and specific nomenclature of the Medical device
Endovascular stents	Endovascular repair of aortic aneurysms	Talent stent–graft (Medtronic), Excluder AAA endoprosthesis (WL Gore), Aorfix AAA stent–graft (Lombard Medical), Zenith AAA endovascular graft (Cook Medical) and Endologix Powerlink Systems (Le Maitre).
Home haemodialysis device	Renal replacement therapy in chronic kidney disease	NxStage System One NX1000-1 (NxStage Medical)
Transcatheter implantable devices	Transcatheter implantable devices for mitral valve repair in adults with chronic mitral valve regurgitation	CARILLON® Mitral Contour System® (Cardiac Dimensions, Inc.) and , MitraClip® System (Abbott Vascular)
Balloon Eustachian Tuboplasty	Balloon Eustachian tuboplasty for the treatment of Eustachian tube dysfunction	"Bielefelder Ballonkatheter"/ TubaVent® by Spiggle and Theis, and AERATM by Acclarent Inc. (Johnson and Johnson).
Oscillometric blood pressure monitor	Diagnosis and monitoring of hypertension	Watch BP Home ® Microlife
High intensity focused ultrasound (HIFU)	High intensity focused ultrasound in oncologic indications	Mixed producers depending on country
Gene expression profiling diagnostics	Gene expression profiling and expanded immunohistochemistry tests for guiding adjuvant chemotherapy decisions in early breast cancer management	MammaPrint (Agendia) and Oncotype DX (Genomic Health)
Positron emission tomography (PET)	PET in oncological indications	Mixed producers depending on country
Cochlear implants	Cochlear implants for children and adults with severe to profound hearing loss.	Clarion CII Bionic Ear System and the HiResolution Bionic Ear System (Advanced Bionics UK) Nucleus Freedom cochlear implants (Cochlear Europe) Pulsar CI-100 (MED-EL UK) Digisonic SP (Neurelec)
Left ventricular assist devices	Mechanical pump that's used to support heart function and blood flow in people who have weakened hearts.	Mixed producers depending on country
LASER KTP	Laser treatment for treating benign prostatic hyperplasia	GreenLight XPS (Boston Scientific)
Self-monitoring coagulometers	Self-monitoring system for self-monitoring (self-testing or selfmanaging) coagulation status in people with atrial fibrillation or heart valve disease for whom long-term vitamin K antagonist therapy is intended	CoaguChek XS system and the INRatio2 PT/INR monitor (International Technidyne Corporation and Alere) and other depending by countries.
Nucleic acid amplification tests (NAATs)	Detecting system for Neisseria gonorrhoeae (NG), by a nucleic acid amplification test (NAAT) in symptomatic patients, asymptomatic patients (screening of persons at risk) and in other clinical situations.	Roche's Amplicor (PCR), Becton Dickinson's ProbeTec (SDA), and Gen-Probe's APTIMA Combo 2 (AC2)
Duodenal-jejunal bypass sleeve	Treatment of obesity	GI Dynamics (GI Dynamics, Inc., Lexington, Massachusetts, USA)
Vitro fertilisation (IVF)	Fertilization of Egg in laboratory	Mixed producers depending on country

Annex 11: Sample of 5 'Other technologies'

Name of the intervention	Description of the intervention
HPV Vaccination	Role of vaccination against human papillomavirus in reducing the risk of cervical cancer.
Colorectal cancer screening	Screening program aiming to identify people who appear healthy but may be at increased risk of a colorectal cancer.
Pneoumococcla vaccination	Pneumococcal vaccination in children
Rotavirus vaccination	Rotavirus vaccination is usually part of the childhood vaccination programme for babies aged 8 weeks and 16 weeks.
Cervical cancer Screening programme.	Evaluation of seasonal influenza vaccines practices and programs

Annex 12: Indicators

Indicator / Information	Scope of information to be gathered per technology and MS	Variables	DEFINITIONS
Basic information	Name, active substance/mode of action	Molecules name	Name of the molecules under review
		Branded name	Branded name of the molecules under review
		Clinical pharmacology	Therapeutic class of the drugs considered
	Producer/sponsor of the technology	Manufacturer	The pharmaceutical company presenting the request for the HTA
	Description of the technology	Route of administration	Oral/intravenous etc
		Mechanism of action	How does the active substance act
		Available Dosage	The dosage(s) available on the market
		DDD	Recommended daily dose by WHO (http://www.whocc.no/ddd/definition_and_general_considera/)
	Indication(s) and target population of the marketing authorization	M.A. Indication(s)	Medical condition that a medicine is used for approved by EMA. This can include the treatment, prevention and diagnosis of a disease.
		M.A. Indication(s) for other diseases (if applicable)	List If Other Medical condition that a medicine is used for approved by EMA
	Indication(s) and target population of the HTA body (if appraised)	Exact indication under review of the HTA (e.g. specific stage of a disease such as RRMS)	State indication under assessment (if applicable) or the therapeutic category under review (e.g. Belgium breast-cancer in metastatic setting)
		Dosage under review	Recommended dosage by the manufacturer (SPC leaflet)
		Dosage recommended	The dosage recommended by the HTA body after the assessment
	Therapeutic area(s)	ICD-10 classification	Code
		Disease area	State the disease area identified by the ICD-10 code
	Price (actual price)	Actual price by country based on DDD	Market price weighted on the DDD
Timeliness/ Timing from regulatory approval to market launch	Date of marketing authorization or other form of market approval	Date of M.A	Date of Marketing Authorization retrieved by the EMA website
		Type of Authorisation procedure	Centralized/ Decentralized/mutual-recognition procedure
	Date on which the HTA dossier was submitted including a differentiation between REA and Full HTA and different involved bodies if applicable	HTA body	HTA body performing the assessment
		Date of the submission to the HTA body	(If available)
		HTA body	HTA body performing the REA (if applicable)
		Date of the submission of the REA	(If applicable and available)
	date on which the HTA body issued its report (or reports if different reports are submitted or different bodies involved)	Date of the decision	
		Date of publication of the report	
	if applicable the date on which an application for price and reimbursement status was submitted	Date on which the price application was submitted	
		Date on which the reimbursement application was submitted (if different from the price)	
	date on which the decision on prices and reimbursement status were communicated to the company	If applicable (or calculate based on the guidelines instructions)	
	Date on which the product was launched on the market (1st sale/effective market access)	Availability on the market	When it is available to patient
	the length of the actual HTA process (from first formal submission to final report including stop the clock periods, if applicable) in days	Actual length (days)	Length calculated between the date of the submission of the report and the HTA decision (detracting the stop of the clock)
		Estimated time (days) by the HTA body	
		Number of stop of the clock were given	
		Length of stop of the clock given	How many days were allowed to the company
	Dates of possible reassessment of the technology after the market launch in terms of the date and the outcome	If rejected (or accepted with restrictions)	
		Length of resubmission process (if applicable)	Length calculated between the date of the resubmission of the report and the HTA decision
		If accepted/ restricted	
		Days forecasted for the reassessment of the technology by the HTA	
		Lag time between the first approval and the reassessment (if applicable)	

Indicator / Information	Scope of information to be gathered per technology and MS	Variables	DEFINITIONS
	Date and year of an early dialogue with the HTA body, if applicable	Date and year of an early dialogue with the HTA body, if applicable	Date and year of an early dialogue with the HTA body, if applicable
	Reasons / relevant contributions to the duration of the process		List of legislative delays with records and, if not confidential information, reasons given by the industry or HTA bodies
Type/typology of procedure	Information on the number of clinical and economic studies which need to be submitted to the HTA bodies	Number of clinical studies needed for the submission (If applicable)	Minimum number of clinical studies requested by the HTA body for a complete submission
		Number of economic evaluation needed for the submission (If applicable)	Minimum number of economic evaluation requested by the HTA body for a complete submission
	Information on the number of additional clinical and economic studies/submissions which took place during the process specifically for HTA (if these has been submitted at Market Authorization this will be indicated)	Number of studies submitted by the manufacturer at the first submission	
		Final Number of studies submitted by the manufacturer (accounting for all the stop of the clock information)	
	if applicable information on the number of "stop the clocks"	Documentation requested to the manufacturer once the stop of the clock was granted	e.G.more clinical evidence, different/additional comparators, different Indirect comparisons
	overview on how many different studies were requested across Member states	Differences in the number of studies considered and requested by different HTA bodies	
		Type of clinical study preferred by the HTA body	
		Type of economic study preferred by the HTA body	
		Type of other evidence requested (if applicable)	e.g. RWE
	Stakeholder involvement	Type of stakeholders involved	e.g. patients group, clinicians, health economists
		Level of Involvement	Mandatory or voluntary
	Information's on full HTA		
Outcomes of HTA	Information on recommendation (recommended, not recommended, recommended with restrictions) and where not applicable information on the benefit given (e.g. minor, medium or major)	Decision (if applicable)	Listed /Listed with restrictions/ Rejected
		Benefit Identified (if applicable)	ASMR I-V No proof of added benefit Major added benefit/ Hint of added benefit
	Information on possible restrictions or conditions for each technology classified by macro areas (economic restrictions and clinical restrictions)	Clinical Restrictions	Clinical restrictions are applied. E.g. subgroup or first line therapy
		Economic restrictions	PAS, Improvement of Cost-effectiveness , Lower price, Other financial provisions
	Information on quantitative assessment	Type of Economic evaluation considered	Cost-utility, cost minimization, cost-comparison or cost consequences
		Comparator(s)	Comparator(s) included
		ICER - Base case	ICER submitted by the Manufacturer
		ICER - Accepted	Final ICER calculated by the HTA
		Cost-minimization (saving costs)	Cost saving or final cost for the cost-minimization
		Final cost	Final cost accepted for the cost-comparison.
		Other quantitative results steaming by different type of analysis (e.g. cost-consequences)	If applicable for "other technologies"
	Number of studies	Number of study considered for supporting clinical benefit	
		Number of studies/clinical evidence considered for supporting the economic analysis	
		Type of the clinical evidence submitted	Observational (cross sectional, case series, case-control studies, cohort studies) vs experimental comparative trials (controlled or head to head), randomised trials) or indirect comparison (naive indirect comparison, network meta-analysis
		Number of economic evaluation considered	Number of studies submitted by the Manufacturer to the HTA company
		Clinical benefit	Achieved/ not achieved/ statistically significant/not statistically significant
		Economic results	Cost-effective/Cost-saving/not cost-effective not cost-saving
	Information's on REA (if applicable)		

Indicator / Information	Scope of information to be gathered per technology and MS	Variables	DEFINITIONS
	Information on recommendation (recommended, not recommended, recommended with restrictions) and where not applicable information on the benefit given (e.g. minor, medium or major)	Decision (if applicable)	Listed /Listed with restrictions/ Rejected
		Benefit Identified (if applicable)	ASMR I-V No proof of added benefit Major added benefit/ Hint of added benefit
	Information on possible restrictions or conditions for each technology classified by macro areas (economic restrictions and clinical restrictions)	Clinical Restrictions	Clinical restrictions are applied. E.g. subgroup or first line therapy
		Economic restrictions	PAS, Improvement of Cost-effectiveness , Lower price, Other financial provisions
	Information on quantitative assessment	Type of Economic evaluation considered	Cost-utility, cost minimization, cost-comparison or cost consequences
		Comparator(s)	Comparator(s) included
		ICER - Base case	ICER submitted by the Manufacturer
		ICER - Accepted	Final ICER calculated by the HTA
		Cost-minimization (saving costs)	Cost saving or final cost for the cost-minimization
		Final cost	Final cost accepted for the cost-comparison.
		Other quantitative results steaming by different type of analysis (e.g. cost-consequences or budget impact analysis)	If applicable for "other technologies"
	Number of studies	Number of study considered for supporting clinical benefit	
		Number of studies/clinical evidence considered for supporting the economic analysis	
		Type of the clinical evidence submitted	Observational (cross sectional, case series, case-control studies, cohort studies) vs experimental comparative trials (controlled or head to head), randomised trials) or indirect comparison (naive indirect comparison, network meta-analysis
		Number of economic evaluation considered	Number of studies submitted by the Manufacturer to the HTA company
	information's on the clinical and economic reasons for the recommendations	Clinical benefit	Achieved/ not achieved/ statistically significant/not statistically significant
		Economic results	Cost-effective/Cost-saving/not cost-effective not cost-saving
	Information on special arrangements in place that influence the outcome (e.g. EoL)	Elicited	
		Elicited Social value judgements considered in the guidelines?	EoI, severity and National priority in France
		Considered for the technology under review?	
		Non elicited	
		Severity	High/low
		Rarity	Rare/not rare
		Unmet need for treatments	Yes/no (if no list the other treatments mentioned)
		Special conditions considered	End of life criteria/humanitarian dignity principle solidarity principle/ the human value principle
		Burden on family and carers emotional well being	Yes/no
		Impact on work and everyday life activities	Yes/no
		Wider societal Benefits	Yes/no
		Equality issues	Yes/no
		Small population	Yes/no (for NICE to be considered only if they account for it outside EoL)
		Significant innovation	
		Life expectancy	Short-Life threatening-Chronic disease(for NICE to be considered only if they account for it outside EoL)
Impact of HTA recommendation on market launch	Information on how the HTA recommendation had an impact on the steps towards market launch	If accepted in how many days the reimbursement is implemented.	
		If rejected what was the next step taken by the company?	Resubmission, withdrawal, extension of studies (RCTs phase 4) or appeal
	Information regarding impact on pricing and reimbursement level (e.g. patient access scheme in UK)	Presence of Managed entry agreements or any other provisions implemented for the reimbursement	
	Information on time to market launch	Date on which the Drug was launched in the market (exact date of availability of the drug to suppliers)	

Indicator / Information	Scope of information to be gathered per technology and MS	Variables	DEFINITIONS
	Information on budget impact on the health system as a whole	Percentage of the technology reimbursement cost over country pharmaceutical expenditure	
	Information on eligible population in order to assess the impact regarding patient access	Breakdown of Prevalence data and socio-economics data on the indication under review	

Annex 13: Cost indicators

Indicator	Sub-indicator	Variable*	Definition of the variable
Costs of performing a health technology assessment for the technology developer	Costs for early dialogues (without considering the clinical trials costs)	Travel costs/Locum Costs/ general expenses connected to the procedures / meeting expenses	All the costs incurred for meetings with HTA agencies
		Submission fees	Fees asked by the HTA body to participate to the evaluation process
		Administrative costs	All the expenses incurred in controlling and directing an organization, but not directly identifiable with financing marketing or production operations. This will not include any salary costs.
		Human resource costs	All the costs related to hiring experts/sub-contractors employees or permanent employee
	Costs for clinical studies additional to market authorization	Costs by clinical trial phase	
		Costs by therapeutic area	
		Pre-study costs	
	Costs for human resources to handle the procedure (including fees to consultants)	Permanent Staff costs	
		Consultant costs	
		Sub-contractor costs	
		Travel costs/Locum Costs/ general expenses connected to the procedures -	
	Fees to be paid to the HTA bodies (if applicable)	Submission fees	
		Re-submission fees	
	Nature and cost of additional data requirement requested during the HTA phases of market launch and post market authorization	Costs by clinical trial phase/ type of clinical evidence	Additional cost of studies explicitly requested by the HTA body
		Costs by therapeutic area	
		Pre-study costs	
		Costs associated to perform again the economic analysis	Consultant
		Re-evaluation of the HTA decision costs	Associated costs for further assessment
	In case of early dialogues: did it lead to a reduction of overall costs for performing a HTA for the technology developer and if so how	HTA costs when early dialogue is in place - HTA complete assessment costs. (If applicable)	
Costs of performing a health technology assessment for the HTA body	Operating Costs	Premises & fixed plants/rentals/establishment expenses/Supplies and Services/Education &training/Recruiting costs/Non-cash items (Depreciation, Amortisation, Provisions and profit/loss on disposal)	
	Audit Costs	Auditor's remuneration/ Audit Reports	
	Full time equivalents and expenditure for human resources costs in order to perform the assessments (taking account the differences between a Full HTA and an REA-Report)	**REA**	
		Permanent Staff costs	Salary and wages/ performance-related pay/benefits in kind/severance pay/ pension contributions-social security costs
		Consultant costs/ External contractors costs	e.g.: NICE recruits external contractors for systematic literature searching and quality assurance
		Sub-contractor costs	Associated costs with any external contractors such as academic units, other organisations
		Travel costs/Locum Costs/ general expenses connected to the procedures -	
		FULL HTA	
		Permanent Staff costs	Salary and wages/ performance-related pay/benefits in kind/severance pay/ pension contributions-social security costs
		Consultant costs	e.g.: NICE recruits external contractors for systematic literature searching and quality assurance
		Sub-contractor costs	Associated costs with any external contractors such as academic units, other organisations
		Travel costs/Locum Costs/ general expenses connected to the procedures -	

		Stakeholders involvement	Interview costs(Including Staff, experts in the health and care system, industry representatives, patients and c charitable groups, and international bodies)/Workshop expenses/ Costs for Programs engaging stakeholders
	Horizon Scanning Associated Costs	Costs associated with the process of horizon scanning, identifying and recording new technologies	e.g.: NICE uses UK PharmaScan database as a primary-source of horizon scanning information
	Other costs (specify)	Iterative approach-other costs that maybe HTA bodies will highlight as important	
	Information on to which extent they cover the costs	Fees charged - Overall expenditure per drug for the process per drug	
	Cost of involvement of stakeholders	Fees for participation	HTA to set up stakeholders groups
		Travel costs/Locum Costs/ general expenses connected to the procedures	
	Dissemination costs	Publication costs such as reports/ Digital services' costs such as web development and maintenance	
	Implementation Costs	Enforce implementation/ monitoring implementation associated costs	

Annex 14: Ten concrete examples

Ten concrete examples indicators			
Influence of the regulatory framework on technology developer investment behavior / decision **(Information on the underlying motivations of the developers)**	**Country setting**	The scope of the recommendations of the HTA body.	If the recommendation has national or regional or local applicability
		Did the scope of the recommendations of the HTA body have an influence on business strategy of the company?	It will be asked to the Manufacturer if the level of scope of the HTA have a clear influence in shaping their business strategy, and if yes if they can give an example.
		Legal status of the HTA advice	Are recommendations by the HTA body legally binding in its country?
		Did Legal status of the HTA body have an influence on business strategy of the company? If yes how?	It will be asked to the Manufacturer if the legal status of the HTA have a clear influence in shaping their business strategy, and if yes if they can give an example.
		Role of the HTA body	Advisory vs. regulatory vs. co-ordinatroy
		Did the role of the HTA body have an influence on business strategy of the company? If yes how?	It will be asked to the Manufacturer if the role of the HTA have a clear influence in shaping their business strategy, and if yes if they can give an example.
		Allowed to resubmit/re-evaluate	Yes/No
		Did the Possibility of re-submission/re-evaluation have an influence on business strategy of the company? If yes how?	It will be asked to the Manufacturer if possibility of re-submission/re-evaluation have a clear influence in shaping their business strategy, and if yes if they can give an example.
		Presence of an appeal process	Yes/No
		Did the appeal process have an influence on business strategy of the company? If yes how?	It will be asked to the Manufacturer if the presence of an appeal process have a clear influence in shaping their business strategy, and if yes if they can give an example.
		Special arrangements	
		Did the any special arrangements have an influence on business strategy of the company? If yes how?	It will be asked to the Manufacturer if the presence of a specific special arrangements have a clear influence in shaping their business strategy, and if yes if they can give an example.
	REA	Presence of a REA process	Yes/No
		Did presence of REA process had an influence on business strategy of the company?	It will be asked to the Manufacturer if the presence of the possibility of REA have a clear influence in shaping their business strategy, and if yes if they can give an example.
	Time-frame	Did the time length of the process to assess the technology have an influence on the company business decisions? If yes, how?	It will be asked to the Manufacturer if the length of the full HTA assessment had an influence in the business strategy, investment decisions (country/therapeutic area).
	Costs	Did the costs of the process to assess the technology have an influence on the company business decisions?	It will be asked to the Manufacturer if the costs
	* All the costs in different currency than Euro will be converted at the historic rate of the data retrieved.		

Annex 15: Semi-structured interview guide

EUROPEAN COMMISSION DG SANTE - HTA PROJECT

Semi-structured interview questions for industry participants

<u>Topic 1: Impact of HTA setting</u>

Aim: *To understand if and how HTA settings affect the decision-making process of manufacturers. How do the legal status, the scope and the role of HTA bodies influence investment behaviours and which are the HTA best practices from an industry perspective?*

Legal status of HTA bodies

- Did the legal status (if it is legally binding or not) of the HTA bodies have an influence on the business strategy of your company so far?
    - If yes, how did you shape your market access strategy?
    - Did you prioritize settings where HTA has a legally binding status?
- Is it possible to give us a concrete example of whether your business strategy was affected positively or negatively by the HTA legal framework?

Scope and role of HTA bodies

- Did the scope (national, regional or local) of the recommendations of HTA bodies have an influence on business strategy of the company?
    - How did you deal with the presence of a regional HTA body (e.g. in Spain)?
    - Could you give us a concrete example of how your company shaped its market strategy based on the different scope of an HTA body?
    - How did you handle HTA submissions for different HTA bodies (NICE and SMC) in the UK?
    - Did you have a single department that coordinated both submissions?
- Did the role (advisory vs. regulatory vs. co-ordination) of HTA bodies have an influence on the company's business strategy?
    - If yes, in what way?
    - How did you deal differently with an advisory HTA body rather than a regulatory one?
    - Would you prioritise a submission to a regulatory HTA body rather than a submission to an advisory one?

Resubmission and re-evaluation

- Did the possibility of resubmission/re-evaluation have an influence on the company's business strategy? Did you shape your submission strategy differently knowing that you have the possibility of re-submission or re-evaluation?
        - If yes, in what way?

Appeal process

- Did the existence of an appeal process have an influence on business strategy of your company?
    - If yes, how did this shape your company's strategy?
    - Did you prioritise launch in settings with a well-established appeal process?

Costs

- Did the costs of the product's assessment process have an influence on the company's business decisions?

- For instance, did the submission fees charged by HTA bodies affect the company's strategy?
- To what extent the cost of the generation of additional evidence required by the HTA body affected the company's market strategy?

Product-specific questions

- Did the product (referring to the product(s) listed in our case study) face specific issues related to the HTA processes across the member states?
  - Is it possible to give us some examples?
- How did the company deal with these issues?
  - Did your company change marketing decisions after facing these issues?
- If this is not applied to the product(s) selected in our case study, is it possible to give us another product-specific example?

Topic 2: Delays related to full HTA submissions

Aim: *To understand to what extent the timelines of HTA bodies might affect the manufacturer's market strategy. Could a shorter review period have a positive impact? How do manufacturers deal with delays related to the submission of further evidence (clock stop) and any other delays caused by administrative issues (legislative delays)? Are there any best practices worth noting in this context?*

Standard length of full HTA submission

- Did the time length of the process to assess the technology have an influence on the company's business decisions (country/therapeutic area)?
  - If yes, in what way?
  - Did you prioritise submissions due to a faster process?

Common delays

- What are the common delays that your company is facing when submitting an HTA dossier (e.g. clock stop, request of additional evidence, or other legislative delays)?
- How has your company overcome issues stemming from HTA-related delays?
  - For instance, if the delay was due to a legislative issue, how did your company change its strategy?
- Has your company faced any legislative delays during the HTA process in the last three years?
  - If yes, could you please specify what kind of legislative issues emerged and how did these affect your market strategy?

Product-specific questions

- Did the product have a clock stop or a request of submission of further evidence?
  - If not, can you give us another product-specific example?

Topic 3: Early dialogue/rapid assessment

Aim: *To understand if and how the possibility of having engaged in early dialogue or undergone a rapid evaluation assessment (REA) has influenced the manufacturer's decisions and market strategy. Were there any best practices worth noting in this context?*

Early dialogue

- Did the possibility of engaging in early dialogue influence your market strategy positively?
  - If yes, was your market strategy shaped accordingly?

- Could you give us a country-specific example?
- If you engaged in an early dialogue in the past, how did it influence the HTA submission?
  - Did it lead to a reduction of overall costs?
  - Did it lead to a shortening of the timeline for the full HTA submission?

Rapid evaluation assessment (REA)

- Did the possibility to undergo a REA have any impact on or shape your market strategy?
  - If yes, in what way?
  - Did you prioritise launch in settings where a REA was present?
- In the last three years, did a REA process lead to a change in your market strategy?
  - If yes, in what way?
  - Could you give a specific example?

Special arrangements

- Did any specific special arrangements influence the business strategy of the company?
  - If yes, in what way?
  - Could you give a specific example?

Product-specific questions

- Were you involved in an early dialogue with any HTA body in Europe?
  - If yes, could you give us an example?
    - How did this affect your business strategy?
    - Did the early dialogue have any effect on the company's submission/market strategy?
  - If not, could you give us another example related to any other product?

<u>Topic 4: Specific product information</u>

In the table below, please provide any available information related to the selected case study product(s).

Country	Launch date	HTA submission date	Reimbursement and pricing decision date	Number of clock stops (if applicable)	Time length of clock stop	Legislative delays	HTA submission-related costs
France (HAS)							
UK (NICE)							
UK (SMC)							
Ireland (NCPE)							
Germany (IQWIG)							
Germany (G-BA)							
Spain (ISCII)							
Portugal (INFRAMED)							
Sweden (TLV)							
The Netherlands (ZIN)							
Belgium (KCE)							
Poland (AOTM)							
Lithuania							
Estonia							
Latvia							
Hungary							

Annex 16: Availability of data Pharmaceuticals products – Kappa score

Kappa scores [Standard error (SE); 95% confidence intervals]	UK-NICE	UK-SMC	Ireland-NCPE	France-HAS	Belgium-KCE*	Italy- UVEF	Sweden- TLV	Germany-IQWIG	Germany-G-BA	Croatia-Azz	Finland- Fimea	Spain-AEMPS	Spain-AQuAs	Austria-LBI-HTA	EUnetHTA	NetherIdans-ZIN	Romania-NAMMD	Portugal- Infarmed	Poland-AOTMiT	Italy-AIFA**
UK-NICE		0 [0.3416; 0-0.6695]	0 [0.3416; 0-0.6695]	0 [0.3416; 0-0.6695]	**0.0441 [0.1568 ;0-0.3515]**	0.0909 [0.166; 0-0.4162]	0.3056 [0.269; 0-0.8327]	0.16 [0.2222 ;0-0.4683]	0 [0.3416 ; 0-0.6695]	0.0441 [0.1568 ;0-0.3515]	0.0909 [0.166; 0-0.4162]	0.1304 [0.2181 ;0-0.5871]	N/A	N/A	0.0909 [0.166; 0-0.4162]	0.4769 [0.2568 ;0-0.5802]	0.3045 [0.2424 ;0-0.5796]	0.0741 [0.207; 0-0.4769]	0.1176 [0.2014 ;0-0.7083]	0 [0.3416; 0-0.6695]
UK-SMC	0 [0.3416; 0-0.6695]		0 [0.3416; 0-0.6695]	0 [0.3416; 0-0.6695]	0 [0.5323 ; 0-1.000]	0 [0.0745 ; 0-0.1461]	0 [0.5323 ; 0-1]	0 [0.3416 ; 0-0.6695]	0 [0.3416 ; 0-0.6695]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.2739 ; 0-0.5368]	0 [0.1826 ; 0-0.3578]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.4472 ; 0-0.8764]	0 [0.3047 ; 0-0.5972]	0 [0.1826 ; 0-0.3578]	0 [0.6708 ; 0-1]	0 [0.3416; 0-0.6695]
Ireland-NCPE	0 [0.3416; 0-0.6695]	0 [0.3416; 0-0.6695]		0 [0.3416; 0-0.6695]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.5323 ; 0-1]	0 [0.5323 ; 0-1]	0 [0.6708 ; 0-1]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.2739 ; 0-0.5368]	0 [0.1826 ; 0-0.3578]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.4472 ; 0-0.8765]	0 [0.3047 ; 0-0.5972]	0 [0.1826 ; 0-0.3578]	0 [0.6708 ; 0-1]	0 [0.3416; 0-0.6695]
France-HAS	0 [0.3416; 0-0.6695]	0 [0.3416; 0-0.6695]	0 [0.3416; 0-0.6695]		0 [0.5323 ; 0-1.000]	0 [0.0745 ; 0-0.1461]	0 [0.5323 ; 0-1]	0 [0.3416 ; 0-0.6695]	0 [0.3416 ; 0-0.6695]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.2739 ; 0-0.5368]	0 [0.1826 ; 0-0.3578]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.4472 ; 0-0.8765]	0 [0.3047 ; 0-0.5972]	0 [0.1826 ; 0-0.3578]	0 [0.6708 ; 0-1]	0 [0.3416; 0-0.6695]
Belgium-KCE*	**0.0441 [0.1568;0-0.3515]**	0 [0.5323 ; 0-1.000]	0 [0.0513 ; 0-0.1005]	0 [0.5323 ; 0-1.000]		N/A	0.0184 [0.1097 ; 0-0.2335]	0.0184 [0.1097 ; 0-0.2335]	0.0135 [0.0928 ; 0-0.1936]	**1**	**0 [0.0745 , 0-0.1461]**	0.0678 [0.1885 ; 0-0.4973]	N/A	N/A	N/A	**0.026 [0.1257 ; 0-0.2725]**	0.0551 [0.1725 ;0-0.3932]	**0.1463 [0.2601 ;0-0.6561]**	0.0116 [0.0828 ; 0-0.1996]	0 [0.0513 ; 0-0.1005]
Italy- UVEF	0.0909 [0.166; 0-0.4162]	0 [0.0745; 0-0.1461]	0 [0.0745; 0-0.1461]	0 [0.0745; 0-0.1461]	N/A		0.0385 [0.1241 ;0-0.2818]	N/A	N/A	N/A	N/A	N/A	0.0476 [0.1608 ; 0-0.5588]	N/A	N/A	0.0541 [0.1365 ;0-0.3255]	N/A	**0.2857 [0.244; 0-0.7639]**	0.0244 [0.1092 ;0-0.2362]	0 [0.6708; 0-1]
Sweden-TLV	0.3056 [0.269; 0-0.8327]	0 [0.5323; 0-1]	0 [0.5323; 0-1]	0 [0.5323; 0-1]	0.0184 [0.1097 ; 0-0.2335]	0.0385 [0.1241 ;0-0.2818]		0.2157 [0.3508 ; 0-0.9032]	0.2157 [0.3508 ; 0-0.9032]	**0.0184 [0.1097 ;0-0.2335]**	**0.0385 [0.1241 ;0-0.2818]**	**0.186 [0.248; 0-0.6721]**	0.2105 [0.1952 ;0-0.593]	N/A	**0.0385 [0.1241 ;0-0.2818]**	**0.4828 [0.2753 ;0-1]**	0.1064 [0.2486 ; 0-0.5015]	0.2105 [0.1952 ;0-0.593]	N/A	0 [0.5323; 0-1]
Germany-IQWIG	0.16 [0.2592; 0-0.6811]	0 [0.3416; 0-0.6695]	0 [0.5323; 0-1]	0 [0.3416; 0-0.6695]	0.0184 [0.1097 ; 0-0.2335]	N/A	0.2157 [0.3508 ; 0-0.9032]		0.3182 [0.3629 ;0-1]	**0.0184 [0.1097 ;0-0.2335]**	**0.0385 [0.1241 ; 0-0.2818]**	0.186 [0.248; 0-0.6721]	0.0551 [0.1952 ;0-0.4176]	N/A	**0.0385 [0.1241 ; 0-0.2818]**	0.1379 [0.3339 ; 0-0.7932]	**0.2405 [0.2594 ;0-0.7489]**	N/A	N/A	0 [0.5323; 0-1]

Kappa scores [Standard error (SE); 95% confidence intervals]	UK-NICE	UK-SMC	Ireland-NCPE	France-HAS	Belgium-KCE*	Italy- UVEF	Sweden- TLV	Germany-IQWIG	Germany-G-BA	Croatia-Azz	Finland- Fimea	Spain-AEMPS	Spain-AQuAs	Austria-LBI-HTA	EUnetHTA	Netherldans-ZIN	Romania-NAMMD	Portugal- Infarmed	Poland-AOTMiT	Italy-AIFA**
Germany-G-BA	0 [0.341 6; 0-0.6695]	0 [0.341 6; 0-0.669 5]	0 [0.670 8; 0-1]	0 [0.341 6; 0-0.669 5]	0.0116 [0.0528 ; 0-0.1936]	N/A	0.2157 [0.3508 ; 0-0.9032]	0.3182 [0.3629 ;0-1]		**0.0184 [0.1097 ;0-0.2335]**	**0.0385 [0.1241 ; 0-0.2818]**	0.186 [0.248; 0-0.6721]	0.0351 [0.1952 ;0-0.4176]	N/A	**0.0385 [0.1241 ; 0-0.2818]**	0.1379 [0.3339 ; 0-0.7923]	**0.2405 [0.2594 ;0-0.7489]**	N/A	N/A	0 [0.532 3; 0-1]
Croatia-Azz	0.0841 [0.136 8;0-0.3573]	0 [0.051 3; 0-0.100 5]	0 [0.051 3; 0-0.100 5]	0 [0.051 3; 0-0.100 5]	**1**	N/A	**0.0184 [0.1097 ;0-0.2335]**	**0.0184 [0.1097 ;0-0.2335]**	**0.0184 [0.1097 ;0-0.2335]**		N/A	**0.0678 [0.1885 ; 0-0.4373]**	N/A	N/A	N/A	0.026 [0.1257 ;0-0.2725]	**0.0551 [0.1725 ;0-0.3932]**	**0.1463 [0.2601 ; 0-0.6561]**	0.0116 [0.0928 ; 0-0.1936]	0 [0.051 3; 0-0.100 5]
Finland-Fimea	0.0969 [0.165; 0-0.4152]	0 [0.074 5; 0-0.146 1]	0 [0.074 5; 0-0.146 1]	0 [0.074 5; 0-0.146 1]	**0 [0.0745 , 0-0.1461]**	N/A	**0.0385 [0.1241 ;0-0.2818]**	**0.0385 [0.1241 ; 0-0.2818]**	**0.0385 [0.1241 ; 0-0.2818]**	N/A		0.1379 [0.1928 ; 0-0.5157]	N/A	N/A	**0.4444 [0.3727 ;0-1]**	N/A	0.1129 [0.1794 ; 0-0.4646]	N/A	0.0244 [0.1091 ;0-0.2382]	0 [0.074 5; 0-0.146 1]
Spain-AEMPS	0.1304 [0.228 1;0-0.5971]	0 [0.273 9; 0-0.536 8]	0 [0.273 5; 0-0.536 8]	0 [0.273 9; 0-0.536 8]	0.0678 [0.1885 ; 0-0.4373]	N/A	**0.186 [0.248; 0-0.6721]**	0.186 [0.248; 0-0.6721]	0.186 [0.248; 0-0.6721]	**0.0678 [0.1885 ; 0-0.4373]**	0.1379 [0.1928 ; 0-0.5157]		0.2308 [0.2107 ; 0-0.6437]	N/A	**0.1379 [0.1928 ; 0-0.5157]**	0.0909 [0.249; 0-0.5789]	0.2553 [0.2269 ;0-0.7001]	N/A	0.0476 [0.2608 ;0-0.5588]	0 [0.273 5; 0-0.536 8]
Spain-AQuAs	N/A	0 [0.182 6; 0-0.357 8]	0 [0.182 6; 0-0.357 8]	0 [0.182 6; 0-0.357 8]	N/A	0.0876 [0.2408 ; 0-0.5588]	0.2105 [0.1952 ;0-0.593]	0.0351 [0.1952 ;0-0.4176]	0.0351 [0.1952 ;0-0.4176]	N/A	N/A	0.2308 [0.2107 ; 0-0.6437]		N/A	**0.0476 [0.2608 ; 0-0.5588]**	0.2857 [0.1956 ; 0 0.6691}	N/A	N/A	N/A	0 [0.182 6; 0-0.357 8]
Austria-LBI-HTA	N/A	0 [0.532 3; 0-0.100 5]	0 [0.051 3; 0-0.100 5]	0 [0.532 3; 0-0.100 5]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A		N/A	0.026 [0.1257 ; 0-0.2725]	N/A	N/A	0.0116 [0.0928 ;0-0.1936]	0 [0.051 3; 0-0.100 5]
EUnetHTA	0.0969 [0.165; 0-0.4152]	0 [0.074 5; 0-0.146 1]	0 [0.074 5; 0-0.146 1]	0 [0.074 5; 0-0.146 1]	N/A	N/A	**0.0385 [0.1241 ;0-0.2818]**	**0.0385 [0.1241 ; 0-0.2818]**	**0.0385 [0.1241 ; 0-0.2818]**	N/A	**0.4444 [0.3727 ;0-1]**	**0.1379 [0.1928 ; 0-0.5157]**	**0.0476 [0.2608 ; 0-0.5588]**	N/A		**0.0541 [0.1385 ;0-0.3255]**	0.1129 [0.1794 ; 0-0.4646]	N/A	0.0244 [0.1091 ; 0-0.2382]	0 [0.074 5; 0-0.146 1]
Netherlda ns-ZIN	0.0769 [0.256 8;0-0.5891]	0 [0.447 2; 0-0.876 5]	0 [0.447 2; 0-0.876 5]	0 [0.447 2; 0-0.876 5]	**0.026 [0.1257 ; 0-0.2725]**	0.0541 [0.1385 ;0-0.3255]	**0.4828 [0.2753 ;0-1]**	0.1379 [0.3339 ; 0-0.7923]	0.1379 [0.3339 ; 0-0.7923]	0.026 [0.1257 ;0-0.2725]	N/A	0.0909 [0.249; 0-0.5789]	0.2857 [0.1956 ; 0 0.6691}	0.026 [0.1257 ; 0-0.2725]	**0.0541 [0.1385 ;0-0.3255]**		N/A	0.1071 [0.1996 ;0-0.4084]	N/A	0 [0.447 2; 0-0.876 5]
Romania-NAMMD	0.3846 [0.242 4;0-0.6796]	0 [0.304 7; 0-0.597]	0 [0.304 7; 0-0.597]	0 [0.304 7; 0-0.597]	0.0551 [0.1725 ;0-0.3932]	N/A	0.1064 [0.2486 ; 0-0.5015]	**0.2405 [0.2594 ;0-0.7489]**	**0.2405 [0.2594 ;0-0.7489]**	**0.0551 [0.1725 ;0-0.3932]**	0.1129 [0.1794 ; 0-0.4646]	0.2553 [0.2269 ;0-0.7001]	N/A	N/A	0.1129 [0.1794 ; 0-0.4646]	N/A		N/A	0.0788 [0.2807 ;0-0.628]	0 [0.304 7; 0-0.597]

Kappa scores [Standard error (SE); 95% confidence intervals]	UK-NICE	UK-SMC	Ireland-NCPE	France-HAS	Belgium-KCE*	Italy- UVEF	Sweden- TLV	Germany-IQWIG	Germany-G-BA	Croatia-Azz	Finland- Fimea	Spain-AEMPS	Spain-AQuAs	Austria-LBI-HTA	EUnetHTA	Netherlands-ZIN	Romania-NAMMD	Portugal- Infarmed	Poland-AOTMiT	Italy-AIFA**
	1	2]	2]	2]																2]
Portugal-Infarmed	0.0741 [0.207; 0-0.4799]	0 [0.182 6; 0-0.357 8]	0 [0.182 6; 0-0.357 8]	0 [0.182 6; 0-0.357 8]	**0.1463 [0.2601 ;0-0.6561]**	**0.2857 [0.244; 0-0.7639]**	0.2105 [0.1952 ;0-0.593]	N/A	N/A	**0.1463 [0.2601 ; 0-0.6561]**	N/A	N/A	N/A	N/A	N/A	0.1071 [0.1996 ;0-0.4984]	N/A		N/A	0 [0.182 6; 0-0.357 8]
Poland-AOTMiT	0.1176 [0.301 4;0-0.7083]	0 [0.670 8; 0-1]	0 [0.670 8; 0-1]	0 [0.670 8; 0-1]	0.0116 [0.0928 ; 0-0.1936]	0.0244 [0.1091 ;0-0.2382]	N/A	N/A	N/A	0.0116 [0.0928 ; 0-0.1936]	0.0244 [0.1091 ;0-0.2382]	0.0476 [0.2608 ;0-0.5568]	N/A	0.0116 [0.0928 ;0-0.1936]	0.0244 [0.1091 ; 0-0.2382]	N/A	0.0769 [0.2807 ;0-0.629]	N/A		0 [0.670 8; 0-1]
Italy-AIFA**	0 [0.341 6; 0-0.6695]	0 [0.341 6; 0-0.669 5]	0 [0.341 6; 0-0.669 5]	0 [0.341 6; 0-0.669 5]	0 [0.0519 ; 0-0.1005]	0 [0.6708 ; 0-1]	0 [0.5323 ; 0-1]	0 [0.5323 ; 0-1]	0 [0.5323 ; 0-1]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.2739 ; 0-0.5368]	0 [0.1826 ; 0-0.3578]	0 [0.0513 ; 0-0.1005]	0 [0.0745 ; 0-0.1461]	0 [0.4472 ; 0-0.8765]	0 [0.2887 ; 0-0.5572]	0 [0.1826 ; 0-0.3578]	0 [0.6708 ; 0-1]	

Legend: NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; GÖG: Gesundheit Österreich GmbH; LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment; KCE: Belgian Health Care Knowledge Centre; NCPHA: The National Center of Public Health and Analyses ; MoH: Ministry of Health; Azz: Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi; FIMEA: Finnish Medicines Agency KELA: Kansaneläkelaitos; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; OGYEI: Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet; NCPE: National Centre for Pharmacoeconomics; HIQA: Health Information and Quality Authority AIFA: Agenzia Italiana del Farmaco UVEF: Unità di valutazione dell'efficacia del farmaco ; AGENAS: Agenzia Nazionale per i servizi sanitari regionali; ZVA: Zalu valsts agentura; VASPVT: Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento; NAMMD: National Agency for Medicines and Medical Devices; CADIME: Centro Andaluz de Documentación e Información de Medicamentos; AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya; ISCII: Instituto de Salud Carlos III OSTEBA: Basque Office for Health Technology Assessment; AETSA: Andalusian Agency for Health Technology Assessment; SECS: Servicio de Evaluacion del Servicio Canario de salud. *****KCE does not have a mandate for Pharmaceuticals but it performed an economic evaluation of the Hepatitis C treatments comprising also Sofusbuvir ** For AIFA the reports were not publicly available but the decision was published in Gazzetta Ufficiale

Note: Countries with no HTA reports publically available have been excluded from this table (e.g. Hungary, Bulgaria, Cyprus, Slovenia, Latvia, etc.) *The confidence level, 1 – α, has the following interpretation. If thousands of samples of N items are drawn from a population using simple random sampling and a confidence interval is calculated for each sample, the proportion of those intervals that will include the true value of kappa is 1 – α*

Source: The Authors

Annex 17: Availability of data – Medical devices– Kappa score

Kappa scores [Standard error (SE); 95% confidence intervals]	UK-NICE	UK- SHTG	Ireland-NCPE	France-HAS	Belgium-KCE	Italy-AGENAS	Sweden-TLV	Germany-IQWIG	Croatia-Azz	Finland-Fimea	Spain-AQuAs	Spain-Avalia	Spain-OSTEBA	Estonia-University of Tartu and EHIF	Lithuania-VASPVT	Austria-LBI	Austria- GÖG	EUnetHTA	Netherlands-ZiN
UK-NICE		N/A	0.0351 [0.1502; 0-0.3296]	0.1667 [0.3568; 0-0.866]	0.3333 [0.2854; 0-0.8928]	0.1667 [0.2635; 0-0.6832]	N/A	N/A	0.1176 [0.186; 0-0.4822]	N/A	N/A	0.1176 [0.186; 0-0.4822]	N/A	N/A	0.0741 [0.1691; 0-0.4054]	N/A	0.1176 [0.186;0-0.4822]	N/A	N/A
UK- SHTG	N/A		N/A	0.0741 [0.1691; 0-0.4054]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.4231 [0.3798; 0-1]	0.2857 [0.3689; 0-1]	N/A	0.2857 [0.3689; 0-1]	0.2857 [0.3689; 0-1]	0.2857 [0.3689; 0-1]	N/A
Ireland-NCPE	0.0351 [0.1502; 0-0.3296]	N/A		N/A	0.069 [0.1963; 0-0.4537]	N/A	N/A	0.25 [0.3211; 0-0.8794]	N/A	0.3284 [0.3468; 0-1]	N/A	N/A	N/A	N/A	N/A	N/A	0.4444 [0.3657; 0-1]		0.0909 [0.2196; 0-0.5212]
France-HAS	0.1667 [0.3568; 0-0.866]	0.0741 [0.1691; 0-0.4054]	N/A		0 [0.3162; 0-0.6198]	N/A	0.1176 [0.186; 0-0.4822]	N/A	N/A	N/A	N/A	0.1176 [0.186; 0-0.4822]	N/A	0.1176 [0.186; 0-0.4822]	0.0741 [0.1691; 0-0.4054]	0.1176 [0.186; 0-0.4822]	N/A	N/A	0.2424 [0.2766; 0-0.7846]
Belgium-KCE	0.3333 [0.2854; 0-0.8928]	N/A	0.069 [0.1963; 0-0.4537]	0 [0.3162; 0-0.6198]		N/A	N/A	0.16 [0.2319; 0-0.6144]	N/A	0.3077 [0.2189; 0-0.7368]	0.1429 [0.207; 0-0.5487]	0.2222 [0.2147; 0-0.643]	N/A	0 [0.2108; 0-0.4132]	0.1429 [0.207; 0-0.5487]	0 [0.2108; 0-0.4132]	0 [0.2108; 0-0.4132]	N/A	0 [0.276; 0-0.541]
Italy-AGENAS	0.1667 [0.2635; 0-0.6832]	N/A	N/A	N/A	N/A		N/A	N/A	0.1026 [0.2477; 0-0.5881]	N/A	N/A	N/A	N/A	0.1026 [0.2477; 0-0.5881]	N/A	N/A	0.1026 [0.2477; 0-0.5881]	N/A	N/A
Sweden-TLV	N/A	N/A	N/A	0.1176 [0.186; 0-0.4822]	N/A	N/A		0 [0.3162; 0-0.6198]	N/A	0.0741 [0.3381; 0-0.7368]	0.2857 [0.3689; 0-1]	N/A	N/A	0.1667 [0.3568; 0-0.866]	0.2857 [0.3689; 0-1]	N/A	N/A	N/A	0.0476 [0.23; 0-0.4984]

Kappa scores [Standard error (SE); 95% confidence intervals]	UK-NICE	UK- SHTG	Ireland-NCPE	France-HAS	Belgium-KCE	Italy-AGENAS	Sweden-TLV	Germany-IQWIG	Croatia-Azz	Finland-Fimea	Spain-AQuAs	Spain-Avalia	Spain-OSTEBA	Estonia-University of Tartu and EHIF	Lithuania-VASPVT	Austria-LBI	Austria- GÖG	EUnetHTA	Netherlands-ZiN
Germany-IQWIG	N/A	N/A	0.25 [0.3211; 0-0.8794]	N/A	0.16 [0.2319; 0-0.6144]	N/A	0 [0.3162; 0-0.6198]		N/A	0.5263 [0.2446; 0.0469-1]	0.1176 [0.3222; 0-0.7491]	0 [0.3162; 0-0.6198]	0.1176 [0.3222; 0-0.7491]	0 [0.3162; 0-0.6198]	0.1176 [0.3222; 0-0.7491]	0.3333 [0.2854; 0-0.8928]	0 [0.3162; 0-0.6198]	N/A	0.25 [0.2372; 0-0.7148]
Croatia-Azz	0.1176 [0.186; 0-0.4822]	N/A	N/A	N/A	N/A	0.1026 [0.2477; 0-0.5881]	N/A	N/A		N/A	N/A	0.1667 [0.3568; 0-0.866]	N/A	N/A	N/A	N/A	0.1667 [0.3568; 0-0.866]	0.5833 [0.2743; 0.0457-1]	0.0476 [0.23; 0-0.4984]
Finland-Fimea	N/A	N/A	0.3284 [0.3468; 0-1]	N/A	0.3077 [0.2189; 0-0.7368]	N/A	0.0741 [0.3381; 0-0.7368]	0.5263 [0.2446; 0.0469-1]	N/A		0.5946 [0.2669; 0.0715-1]	0.0741 [0.3381; 0-0.7368]	0.1892 [0.3472; 0-0.8696]	N/A	0.1892 [0.3472; 0-0.8696]	0.0741 [0.3381; 0-0.7368]	0.0741 [0.3381; 0-0.7368]	N/A	0.1463 [0.2356; 0-0.6081]
Spain-AQuAs	N/A	N/A	N/A	N/A	0.1429 [0.207; 0-0.5487]	N/A	0.2857 [0.3689; 0-1]	0.1176 [0.3222; 0-0.7491]	N/A	0.5946 [0.2669; 0.0715-1]		N/A	0.4231 [0.3798; 0-1]	N/A	0.4231 [0.3798; 0-1]	N/A	N/A	N/A	N/A
Spain-Avalia	0.1176 [0.186; 0-0.4822]	N/A	N/A	0.1176 [0.186; 0-0.4822]	0.2222 [0.2147; 0-0.643]	N/A	N/A	0 [0.3162; 0-0.6198]	0.1667 [0.3568; 0-0.866]	0.0741 [0.3381; 0-0.7368]	N/A		N/A	N/A	N/A	0.1667 [0.3568; 0-0.866]	N/A	0.1667 [0.3568; 0-0.866]	0.0476 [0.23; 0-0.4984]
Spain-OSTEBA	N/A	0.4231 [0.3798; 0-1]	N/A	N/A	N/A	N/A	N/A	0.1176 [0.3222; 0-0.7491]	N/A	0.1892 [0.3472; 0-0.8696]	0.4231 [0.3798; 0-1]	N/A		N/A	N/A	0.2857 [0.3689; 0-1]	N/A	0.2857 [0.3689; 0-1]	N/A
Estonia-University of Tartu and EHIF	N/A	0.2857 [0.3689; 0-1]	N/A	0.1176 [0.186; 0-0.4822]	0 [0.2108; 0-0.4132]	0.1026 [0.2477; 0-0.5881]	0.1667 [0.3568; 0-0.866]	0 [0.3162; 0-0.6198]	N/A	N/A	N/A	N/A	N/A		N/A	N/A	0.1667 [0.3568; 0-0.866]	N/A	0.0476 [0.23;0-0.4984]
Lithuania-VASPVT	0.0741 [0.1691; 0-0.4054]	N/A	N/A	0.0741 [0.1691; 0-0.4054]	0.1429 [0.207; 0-0.5487]	N/A	0.2857 [0.3689; 0-1]	0.1176 [0.3222; 0-0.7491]	N/A	0.1892 [0.3472; 0-0.8696]	0.4231 [0.3798; 0-1]	N/A	N/A	N/A		0.2857 [0.3689; 0-1]	N/A	N/A	0.186 [0.2247; 0-

Kappa scores [Standard error (SE); 95% confidence intervals]	UK-NICE	UK- SHTG	Ireland-NCPE	France-HAS	Belgium-KCE	Italy-AGENAS	Sweden-TLV	Germany-IQWIG	Croatia-Azz	Finland-Fimea	Spain-AQuAs	Spain-Avalia	Spain-OSTEBA	Estonia-University of Tartu and EHIF	Lithuania-VASPVT	Austria-LBI	Austria- GÖG	EUnetHTA	Netherlands-ZiN
																			0.6263]
Austria-LBI	N/A	0.2857 [0.3689; 0-1]	N/A	0.1176 [0.186; 0-0.4822]	0 [0.2108; 0-0.4132]	N/A	N/A	0.3333 [0.2854; 0-0.8928]	N/A	0.0741 [0.3381; 0-0.7368]	N/A	0.1667 [0.3568; 0-0.866]	0.2857 [0.3689; 0-1]	0.2857 [0.3689; 0-1]		N/A	0.1667 [0.3568; 0-0.866]	0.2857 [0.3689; 0-1]
Austria-GÖG	0.1176 [0.186; 0-0.4822]	0.2857 [0.3689; 0-1]	0.4444 [0.3657; 0-1]	N/A	0 [0.2108; 0-0.4132]	0.1026 [0.2477; 0-0.5881]	N/A	0 [0.3162; 0-0.6198]	0.1667 [0.3568; 0-0.866]	0.0741 [0.3381; 0-0.7368]	N/A	N/A	N/A	0.1667 [0.3568; 0-0.866]	N/A	N/A		N/A	0.0476 [0.23;0-0.4984]
EUnetHTA	N/A	0.2857 [0.3689; 0-1]		N/A	N/A	N/A	N/A	N/A	0.5833 [0.2743; 0.0457-1]	N/A	N/A	0.1667 [0.3568; 0-0.866]	0.2857 [0.3689; 0-1]	N/A	N/A	0.1667 [0.3568; 0-0.866]	N/A		0.0476 [0.23;0-0.4984]
Netherlands-ZiN	N/A	N/A	0.0909 [0.2196; 0-0.5212]	0.2424 [0.2766; 0-0.7846]	0 [0.276; 0-0.541]	N/A	0.0476 [0.23; 0-0.4984]	0.25 [0.2372; 0-0.7148]	0.0476 [0.23; 0-0.4984]	0.1463 [0.2356; 0-0.6081]	N/A	0.0476 [0.23; 0-0.4984]	N/A	0.0476 [0.23;0-0.4984]	0.186 [0.2247; 0-0.6263]	0.2857 [0.3689; 0-1]	0.0476 [0.23;0-0.4984]	0.0476 [0.23;0-0.4984]	

Legend: NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; GÖG: Gesundheit Österreich GmbH; LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment; KCE: Belgian Health Care Knowledge Centre; NCPHA: The National Center of Public Health and Analyses ; MoH: Ministry of Health; Azz: Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi; FIMEA: Finnish Medicines Agency KELA: Kansaneläkelaitos; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; OGYEI: Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet; NCPE: National Centre for Pharmacoeconomics; HIQA: Health Information and Quality Authority AIFA: Agenzia Italiana del Farmaco UVEF: Unità di valutazione dell'efficacia del farmaco ; AGENAS: Agenzia Nazionale per i servizi sanitari regionali; ZVA: Zalu valsts agentura; VASPVT: Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento; NAMMD: National Agency for Medicines and Medical Devices; CADIME: Centro Andaluz de Documentación e Información de Medicamentos; AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya; ISCII: Instituto de Salud Carlos III OSTEBA: Basque Office for Health Technology Assessment; AETSA: Andalusian Agency for Health Technology Assessment; SECS: Servicio de Evaluacion del Servicio Canario de salud. *Note:* Countries with no HTA reports publically available have been excluded from this table. *The confidence level, 1 – α, has the following interpretation. If thousands of samples of N items are drawn from a population using simple random sampling and a confidence interval is calculated for each sample, the proportion of those intervals that will include the true value of kappa is 1 – Source: The Authors*

Annex 18: Availability of data- Other technologies – Kappa score

Kappa scores [Standard error (SE); 95% confidence intervals]	**Ireland****	**France-HAS**	**Belgium-KCE**	**Germany-IQWIG**	**Germany-G-BA**	**Finland-Fimea**	**Spain-ISCII**	**Spain- AQuAs**	**Spain-Avalia**	**Estonia-University of Tartu**	**Austria-LBI-HTA**	**Austria-Hauptverband**	**EUnetHTA**	**Portugal - Infarmed and SNS*****
Ireland**		N/A	0 (0.8944;0-1)	0 (0.3651; 0-0.7157)	0 (0.2236; 0-0.4383)	0.1176 (0.3222; 0-0.7491)	0.2857 (0.3912; 0-1)	N/A	N/A	0.5455 (0.4066; 0-1)	N/A	0.2857 (0.3912; 0-1)	0 (0.2236; 0-1)	0.1176 (0.3222; 0-0.7491)
France-HAS	N/A		0 (0.5477;0-1)	0.4 (0.3464; 0-1)	0.5 (0.433; 0-1)	0.2857 (0.3912; 0-1)	N/A	0.2857 (0.3912; 0-1)	N/A	N/A	1 (0; 0-1)	0.6154 (0.344; 0-1)	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)
Belgium-KCE	0 (0.8944;0-1)	0 (0.5477;0-1)		0 (0.5; 0-0.95)	0 (0.2236; 0-0.4383)	0 (0.2236; 0-0.4383)	0 (0.3651; 0-0.7157)	0 (0.2236; 0-0.4383)	0 (0.3651; 0-0.7157)	0 (0.5477; 0-1)	0 (0.5477; 0-1)	0 (0.3651; 0-0.7157)	0 (0.2236; 0-0.4383)	0 (0.2236; 0-0.4383)
Germany-IQWIG	0 (0.3651; 0-0.7157)	0.4 (0.3464; 0-1)	0 (0.5; 0-0.95)		0.5455 (0.4066; 0-1)	0.5455 (0.4066; 0-1)	N/A	0.5455 (0.4066; 0-1)	0.1667 (0.4564; 0-1)	N/A	0.6154 (0.344; 0-1)	0.1667 (0.4564; 0-1)	0.5455 (0.4066; 0-1)	N/A
Germany-G-BA	0 (0.2236; 0-0.4383)	0.5 (0.433; 0-1)	0 (0.2236; 0-0.4383)	0.5455 (0.4066; 0-1)		1 (0; 0-1)	N/A	N/A	N/A	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)	0.5455 (0.4066; 0-1)	1 (0; 0-1)	N/A
Finland-Fimea	0.1176 (0.3222; 0-0.7491)	0.2857 (0.3912; 0-1)	0 (0.2236; 0-0.4383)	0.5455 (0.4066; 0-1)	1 (0; 0-1)		N/A	N/A	N/A	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)	0.5455 (0.4066; 0-1)	1 (0; 0-1)	N/A
Spain-ISCII	0.2857 (0.3912; 0-1)	N/A	0 (0.3651; 0-0.7157)	N/A	N/A	N/A		N/A	N/A	N/A	N/A	0.1667 (0.4564; 0-1)	N/A	0.5455 (0.4066; 0-1)
Spain- AQuAs	N/A	0.2857 (0.3912; 0-1)	0 (0.2236; 0-0.4383)	0.5455 (0.4066; 0-1)	N/A	N/A	N/A		0.5455 (0.4066; 0-1)	N/A	0.2857 (0.3912; 0-1)	N/A	N/A	N/A
Spain-Avalia	N/A	N/A	0 (0.3651;	0.1667 (0.4564;	N/A	N/A	N/A	0.5455 (0.4066;		N/A	N/A	N/A	N/A	N/A

Kappa scores [Standard error (SE); 95% confidence intervals]	**Ireland****	**France-HAS**	**Belgium-KCE**	**Germany-IQWIG**	**Germany-G-BA**	**Finland-Fimea**	**Spain-ISCII**	**Spain- AQuAs**	**Spain-Avalia**	**Estonia-University of Tartu**	**Austria-LBI-HTA**	**Austria-Hauptverband**	**EUnetHTA**	**Portugal - Infarmed and SNS*****
			0-0.7157)	0-1)				0-1)						
Estonia-University of Tartu	0.5455 (0.4066; 0-1)	N/A	0 (0.5477; 0-1)	N/A	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)	N/A	N/A	N/A		0.1667 (0.4564; 0-1)	0.6154 (0.344; 0-1)	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)
Austria-LBI-HTA	N/A	1 (0; 0-1)	0 (0.5477; 0-1)	0.6154 (0.344; 0-1)	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)	N/A	0.2857 (0.3912; 0-1)	N/A	0.1667 (0.4564; 0-1)		0.6154 (0.344; 0-1)	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)
Austria-Hauptverband	0.2857 (0.3912; 0-1)	0.6154 (0.344; 0-1)	0 (0.3651; 0-0.7157)	0.1667 (0.4564; 0-1)	0.5455 (0.4066; 0-1)	0.5455 (0.4066; 0-1)	0.1667 (0.4564; 0-1)	N/A	N/A	0.6154 (0.344; 0-1)	0.6154 (0.344; 0-1)		0.5455 (0.4066; 0-1)	0.5455 (0.4066; 0-1)
EUnetHTA	0 (0.2236; 0-1)	0.2857 (0.3912; 0-1)	0 (0.2236; 0-0.4383)	0.5455 (0.4066; 0-1)	1 (0; 0-1)	1 (0; 0-1)	N/A	N/A	N/A	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)	0.5455 (0.4066; 0-1)		N/A
Portugal - Infarmed and SNS***	0.1176 (0.3222; 0-0.7491)	0.2857 (0.3912; 0-1)	0 (0.2236; 0-0.4383)	N/A	N/A	N/A	0.5455 (0.4066; 0-1)	N/A	N/A	0.2857 (0.3912; 0-1)	0.2857 (0.3912; 0-1)	0.5455 (0.4066; 0-1)	N/A	

Legend: NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; GÖG: Gesundheit Österreich GmbH; LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment; KCE: Belgian Health Care Knowledge Centre; NCPHA: The National Center of Public Health and Analyses ; MoH: Ministry of Health; Azz: Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi; FIMEA: Finnish Medicines Agency KELA: Kansaneläkelaitos; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; OGYEI: Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet; NCPE: National Centre for Pharmacoeconomics; HIQA: Health Information and Quality Authority AIFA: Agenzia Italiana del Farmaco UVEF: Unità di valutazione dell'efficacia del farmaco ; AGENAS: Agenzia Nazionale per i servizi sanitari regionali; ZVA: Zalu valsts agentura; VASPVT: Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento; NAMMD: National Agency for Medicines and Medical Devices; CADIME: Centro Andaluz de Documentación e Información de Medicamentos; AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya; ISCII: Instituto de Salud Carlos III OSTEBA: Basque Office for Health Technology Assessment; AETSA: Andalusian Agency for Health Technology Assessment; SECS: Servicio de Evaluacion del Servicio Canario de salud. * shows available reports before 2006-thus, not included in the analysis. ** Different bodies are performing/requesting the assessment. (National Cancer Registry Ireland, Health Information and Quality Authority,National Immunisation Advisory Committee) *** In Poland, HTA assessments are also performed at county level. However, we considere only the national programmes *Note:* Countries with no HTA reports publically available have been excluded from this table. *The confidence level, 1 – α, has the following interpretation. If thousands of samples of N items are drawn from a population using simple random sampling and a confidence interval is calculated for each sample, the proportion of those intervals that will include the true value of kappa is 1 – α.* *Source: The Authors*

Annex 19: Outcomes

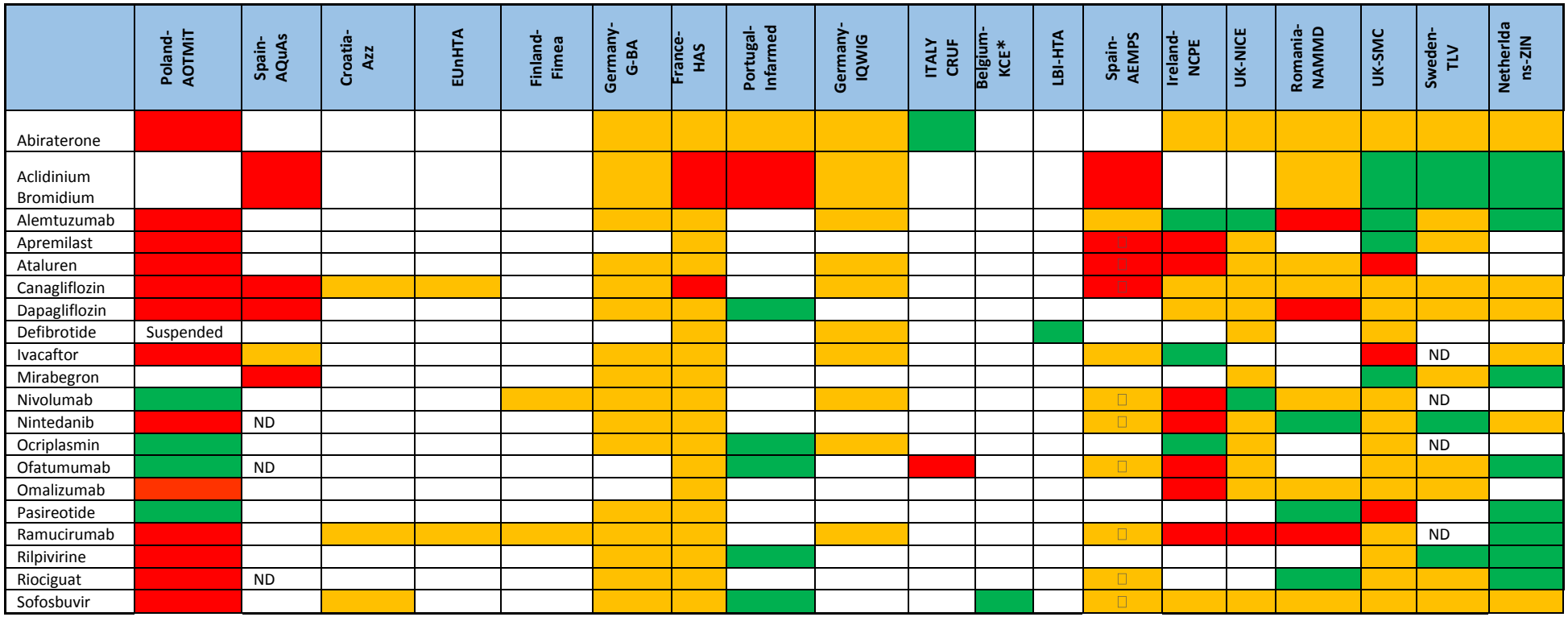


Figure 1- Pharmaceutical products outcomes

Legend: NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; GÖG: Gesundheit Österreich GmbH; LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment; KCE: Belgian Health Care Knowledge Centre; NCPHA: The National Center of Public Health and Analyses ; MoH: Ministry of Health; Azz: Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi; FIMEA: Finnish Medicines Agency KELA: Kansaneläkelaitos; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; OGYEI: Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet; NCPE: National Centre for Pharmacoeconomics; HIQA: Health Information and Quality Authority AIFA: Agenzia Italiana del Farmaco UVEF: Unità di valutazione dell'efficacia del farmaco ; AGENAS: Agenzia Nazionale per i servizi sanitari regionali; ZVA: Zalu valsts agentura; VASPVT: Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento; NAMMD: National Agency for Medicines and Medical Devices; CADIME: Centro Andaluz de Documentación e Información de Medicamentos; AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya; ISCII: Instituto de Salud Carlos III OSTEBA: Basque Office for Health Technology Assessment; AETSA: Andalusian Agency for Health Technology Assessment; SECS: Servicio de Evaluacion del Servicio Canario de salud. ND : No decision. Source: The Authors

Figure 2- Pharamaceuticals products- Outcomes

Molecules name	Branded name	IQWIG	HAS	ZIN
Abiraterone	**Zytiga®**	**Best supportive care population** Mortality: There is an indication of an added benefit of abiraterone acetate/prednisone/BSC over prednisone/BSC for this outcome. Morbidity: There is an indication of an added benefit of abiraterone acetate/prednisone/BSC over prednisone/BSC for both outcomes. **Docetaxel retreatment population:** An added benefit for the docetaxel retreatment population is not proven.	SMR Important ASMR III (moderate)	Included in the list 1B
Aclidinium bromide	**Eklira Genuair®**	**1:** Grade II: added benefit not proven;Grade III with < 2 exacerbations per year: Proof of considerable added benefit;Grade IV with < 2 exacerbations per year: Added benefit not proven;an added benefit for all-cause mortality is therefore not proven. ; an added benefit for the outcome "TDI responder" is therefore not proven.; an added benefit for the outcome "E-RS responder" is therefore not proven. **2:** no hint of an added benefit of aclidinium in comparison with the ACT for adult patients with COPD grades III and IV with 2 or more exacerbations per year; an added benefit is therefore not proven.	Insufficient	Included in the list 1A
Alemtuzumab	**Lemtrada®**	N/A	Moderate SMR (In patients with severe MS-RR, defined by the occurrence of two or more disabling sprays in one year associated with cerebral MRI inflammatory activity (one or more lesions enhanced after injection Of Gadolinium), despite treatment of 1st line or 2nd line) Insufficient SMR (other forms of MS) ASMR IV	Intramural drug
Apremilast	**Otezla®**	an added benefit of apremilast in comparison with the ACT (adalimumab or infliximab or ustekinumab) is not proven for patients with plaque psoriasis.	Moderate SMR ASMR V	N/A
Ataluren	**Translarna®**	no added benefit	Moderate SMR ASMR IV	N/A
Canagliflozin	**Invokana®**	N/A	Insufficient SMR	mural drug, included in the list 1A + list 2

Molecules name	Branded name	IQWIG	HAS	ZIN
Dapagliflozin	**Forxiga®**	Dapagliflozin monotherapy: no added benefit Combination therapy of dapagliflozin and metformin: no added benefit Combination therapy of dapagliflozin and sulfonylureas: no added benefit Combination therapy of dapagliflozin and insulin: no added benefit	Moderate The actual benefit of FORXIGA is : - moderate as dual therapy in combination with metformin or a sulfonylurea - moderate as triple therapy in combination with insulin and metformin Insufficient - insufficient as monotherapy for reimbursement by National Health Insurance Improvement in actual benefit V (absence) In the dual therapy indications, in combination with metformin or a sulfonylurea and triple therapy, in combination with insulin and metformin : Given the very modest glycaemic control observed compared with the placebo, doubts about the safety profile, particularly on an infectious, cardiovascular and carcinogenic level, and the difficulty in defining the therapeutic use, the Committee cannot recognise any improvement for FORXIGA. In addition, the Transparency Committee considers that FORXIGA does not provide any improvement in actual benefit (level V, non-existent) in the management of patients with type 2 diabetes in dual oral therapy, in combination with metformin or a sulfonylurea and in triple therapy, in combination with insulin and metformin. Sans objet In the monotherapy and dual therapy indications, in combination with insulin : not applicable	Extramural drug, included in the list 1B + list 2
Defibrotide	**Defitelio®**	N/A	Moderate SMR ASMR IV	N/A
Ivacaftor	**Kalydeco®**	N/A	Major SMR ASMR II	Included in the list 1B + list 2
Mirabregon	**Betmiga®**	No added benefit of mirabegron can be derived in the overall assessment of morbidity outcomes. Moreover, there were no data on the outcomes “incontinence” and “urge incontinence” for the total population.	Weak SMR (temporary in waiting for study versus solifenacin results) ASMR V	Included in the list 1A
Nintedanib	**Ofev®**		Moderate SMR ASMR IV	Included in the list 1A + list 2
Nivolumab	**Opdivo®**	Subgroup 1: no proven added benefit Subgroup 2: Nivolumab treatment resulted in a statistically significant prolongation of overall survival in comparison with dacarbazine. For morbidity and HQoL: no hint of an added benefit.Men: Indication of considerable added benefit. Women: Hint of minor added benefit Subgroup 3: no proven added benefit	Major SMR ASMR III	N/A
Ocriplasmin	**Jetrea®**	VMT population with mild symptoms:For patients with mild visual impairment (> 60 ETDRS letters), there is an indication of a major added benefit of ocriplasmin in comparison with watchful waiting. For patients with moderate visual impairment (35	Major SMR ASMR IV	N/A

Molecules name	Branded name	IQWIG	HAS	ZIN
		to 60 ETDRS letters), there is an indication of a considerable added benefit of ocriplasmin in comparison with watchful waiting. In summary, for patients with mild visual impairment (> 60 ETDRS letters) there is an indication of a major added benefit of ocriplasmin compared with watchful waiting.In summary, for patients with moderate visual impairment (35 to 60 ETDRS letters) there is an indication of a considerable added benefit of ocriplasmin compared with watchful waiting. Subpopulation with asymptomatic VMT: not proven added benefit Subpopulation with asymptomatic VMT: not proven added benefit VMT population with severe symptoms: not proven added benefit		
Ofatumumab	**Arzerra®**	N/A	Major SMR ASMR V	Intramural drug
Omalizumab	**Xolair®**		Moderate SMR ASMR IV	N/A
Pasireotide	**Signifor®**	N/A	Moderate SMR ASMR V	Included in the list 1B
Ramucirumab	**Cyramza®**	1. no evidence for an additional benefit of ramucirumab + paclitaxel compared to the appropriate comparative therapy 2.no evidence for an additional benefit of ramucirumab compared to the appropriate comparative therapy	Combination with pactlixel: Moderate SMR ASMR V Monotherapy: No SMR	Intramural drug
Rilpivirine	**Edurant®**	N/A	Important SMR (In combination with other antiretroviral in the restricted MA population to patients for whom efavirenz treatment is not appropriate.) Insufficient SMR (all the other category of patients) ASMR V	Included in the list 1B
Riociguat	**Adempas®**	N/A	CTEPH: Moderate SMR ASMR V PAH: Moderate SMR ASMR IV	Included in the list 1A + list 2
Sofosbuvir	**Sovaldi®**	no added benefit proven	SMR Important ASMR II (In combination with pegylated interferon alfa and / or ribavirin In the management of all adult patients infected with HCV, except for patients of genotype 3 naïve antiviral treatment.) ASMR III (In combination with pegylated interferon alfa and / or ribavirin in the management of adult patients infected with HCV genotype 3 naïve antiviral treatment)	Included in the list 1B

HAS: Haute Autorité de Santé; IQWIG: Institute for Quality and Efficiency in Healthcare N/A: not applicable, not appraised; SMR: Service Médical Rendu; ASMR: Amélioration du Service Médical Rendu; ZiN: Zorginstituut Nederland.

Figure 3- Medical device outcomes

Medical Devices Included	Branded name	NICE	TLV	SHGT	HAS	KCE	AGENAS	IQWIG	Croatia	OSTEBA	FinOHTA	AQuAs	AVALIA	Estonia	Lithuania	boltzman institut	EUnetHTA	ZiN
Endovascular stent–grafts	Not specified																	
	TALENT LPS																	
	Aorfix AAA stent–graft																	
	Zenith AAA endovascular graft																	
	Endologix Powerlink Systems																	
Haemodialysis devices		ND																
Transcatheter implantable devices	CARILLON® Mitral Contour System®																	
	MitraClip® System																	
	NeoChord DS1000																	
Balloon Eustachian Tuboplasty	TubaVent® and AERATM®																	
Oscillometric blood pressure monitor	Not specified																	
High intensity focused ultrasound (HIFU)	Sonablate®																	
	Ablatherm®																	
	Focal One																	
	JC/JC200																	
	UroLift system																	
Self-monitoring coagulometers	INRatio2 PT/INR monitor																	
	CoaguChek XS system																	
	Protime®																	
Positron emission tomography (PET)	Not specified																	
Cochlear implants	Not specified																	

Medical Devices Included	Branded name	NICE	TLV	SHGT	HAS	KCE	AGENAS	IQWIG	Croatia	OSTEBA	FinOHTA	AQuAs	AVALIA	Estonia	Lithuania	boltzman institut	EUnetHTA	ZiN
	Clarion CII Bionic Ear System and the HiResolution Bionic Ear System ®																	
	Nucleus 24® and Nucleus Freedom® cochlear implants																	
	Pulsar CI-100 ®																	
	Digisonic SP®																	
Left ventricular assist devices	HeartMate II®																	
LASER KTP	GreenLight XPS®																	
Gene expression profiling diagnostics	uPA/PAI-1®																	
	MammaPrint®																	
	Oncotype DX®																	
	EndoPredict®																	
Nucleic acid amplification tests (NAATs)																		
Duodenal-jejunal bypass sleeve	Not specified																	
	EndoBarrier®																	
In-vitro fertilisation (IVF)	Not specified																	

Legend: NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; GÖG: Gesundheit Österreich GmbH; LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment; KCE: Belgian Health Care Knowledge Centre; NCPHA: The National Center of Public Health and Analyses ; MoH: Ministry of Health; Azz: Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi; FIMEA: Finnish Medicines Agency KELA: Kansaneläkelaitos; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; OGYEI: Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet; NCPE: National Centre for Pharmacoeconomics; HIQA: Health Information and Quality Authority AIFA: Agenzia Italiana del Farmaco UVEF: Unità di valutazione dell'efficacia del farmaco ; AGENAS: Agenzia Nazionale per i servizi sanitari regionali; ZVA: Zalu valsts agentura; VASPVT: Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento; NAMMD: National Agency for Medicines and Medical Devices; CADIME: Centro Andaluz de Documentación e Información de Medicamentos; AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya; ISCII: Instituto de Salud Carlos III OSTEBA: Basque Office for Health Technology Assessment; AETSA: Andalusian Agency for Health Technology Assessment; SECS: Servicio de Evaluacion del Servicio Canario de salud. ND : No decision

Source: The Authors

Figure 4- Other technologies outcomes

Other Technologies Included	Ireland	HAS	KCE	IQWIG	G-BA	Fimea	ISCII	AQuAs	Avalia	Estonia-University of Tartu	Austria-Ludwig boltzman institute	Austria-Hauptverband	EUnetHTA	Portugal
HPV Vaccination				N/A	N/A	N/A	ND	N/A	N/A			ND	N/A	
Colorectal Cancer Screening				ND			N/A	N/A	N/A			ND		N/A
Pneumococcal Vaccination		N/A		N/A	N/A	N/A	N/A	N/A			N/A	N/A	N/A	N/A
Rotavirus Vaccination		N/A		N/A	N/A	N/A		N/A	N/A	N/A	N/A	N/A	N/A	N/A
Cervical cancer screening	N/A	*		ND	N/A	N/A	N/A		**	N/A		N/A	N/A	N/A

Legend: NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; GÖG: Gesundheit Österreich GmbH; LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment; KCE: Belgian Health Care Knowledge Centre; NCPHA: The National Center of Public Health and Analyses ; MoH: Ministry of Health; Azz: Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi; FIMEA: Finnish Medicines Agency KELA: Kansaneläkelaitos; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; OGYEI: Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet; NCPE: National Centre for Pharmacoeconomics; HIQA: Health Information and Quality Authority AIFA: Agenzia Italiana del Farmaco UVEF: Unità di valutazione dell'efficacia del farmaco ; AGENAS: Agenzia Nazionale per i servizi sanitari regionali; ZVA: Zalu valsts agentura; VASPVT: Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento; NAMMD: National Agency for Medicines and Medical Devices; CADIME: Centro Andaluz de Documentación e Información de Medicamentos; AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya; ISCII: Instituto de Salud Carlos III OSTEBA: Basque Office for Health Technology Assessment; AETSA: Andalusian Agency for Health Technology Assessment; SECS: Servicio de Evaluacion del Servicio Canario de salud. ND : No decision ; N/A : not assessed * 1. Smear Test:Listed 2. HPV Test: Rejected ; **mRNA test rejected due to insufficient evidence.

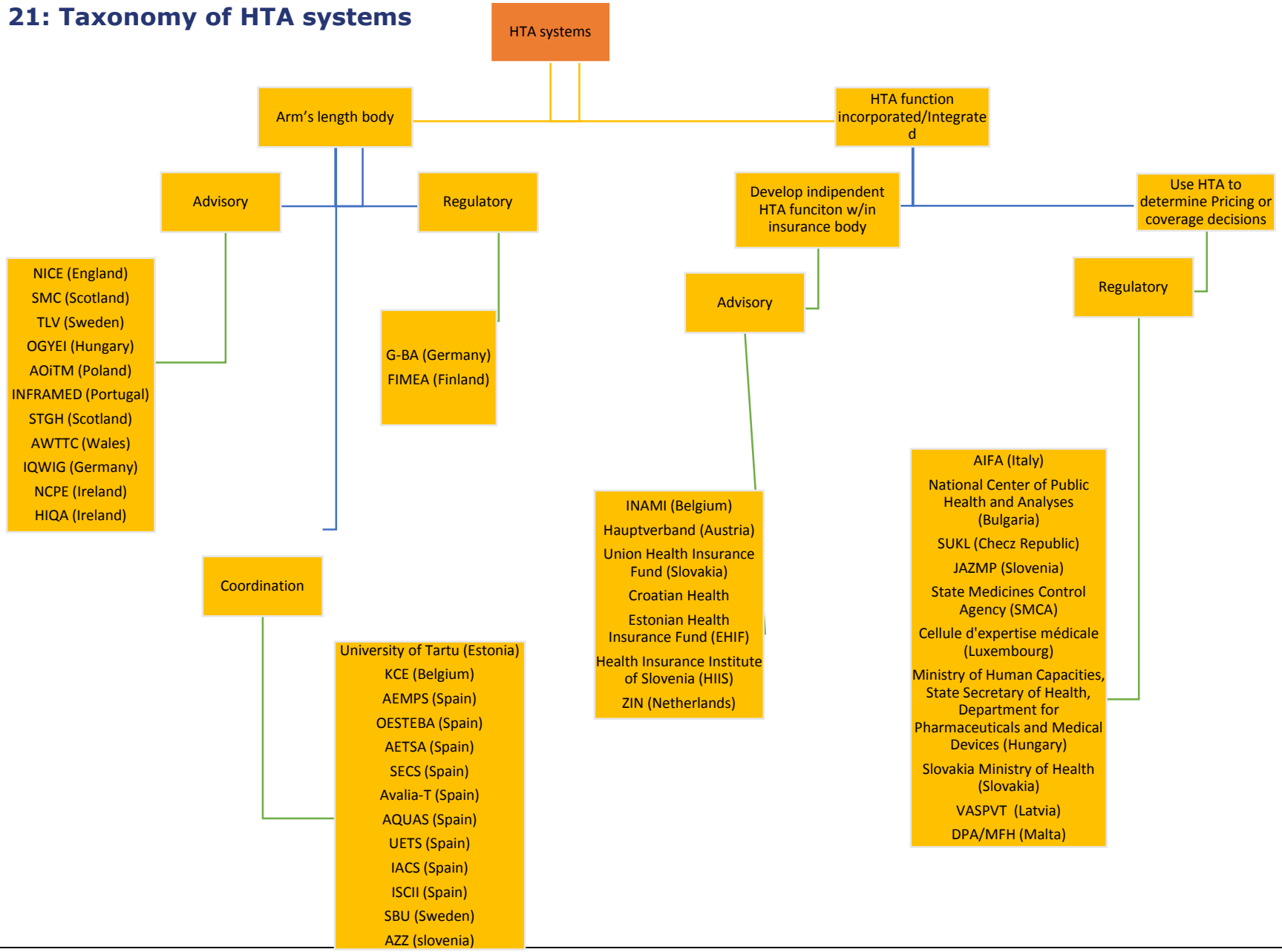
Source: The Authors

Annex 20: Economic restrictions- pharmaceutical sample

	AOTM	AQUAS	CROATIA	HAS*	EUnHTA	FINoHTA	INFRAMED	ITALY CRUF	KCE	LBI-HTA	NCPE	NICE	MoH Romania	SMC	TLV	ZIN
Abiraterone				100%				RSA			Price negotion	RSA		RSA	RSA	RSA
Aclidinium Bromidium				NS												
Alemtuzumab				NS											RSA	RSA
Apremilast				30%								RSA				
Ataluren				NS												
Canagliflozin				65%							Price negotion					
Dapagliflozin				30%							Price negotion					
Defibrotide				NS												
Ivacaftor				65%										RSA		
Mirabegron				15%												RSA
Nivolumab	RSA			100%									RSA	RSA		
Nintedanib	RSA			30%								RSA		RSA		RSA
Ocriplasmin				NS			Price negotiation									
Ofatumumab	RSA			NS								RSA				
Omalizumab	RSA			30%								RSA				
Pasireotide				30%												
Ramucirumab				NS												
Rilpivirine				100%			Price negotiation									RSA
Riociguat				NS										RSA		
Sofosbuvir				NS			Price negotiation							RSA		RSA

Legend: NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; GÖG: Gesundheit Österreich GmbH; LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment; KCE: Belgian Health Care Knowledge Centre; NCPHA: The National Center of Public Health and Analyses ; MoH: Ministry of Health; Azz: Agencija za kvalitetu i akreditaciju u zdravstvu i socijalnoj skrbi; FIMEA: Finnish Medicines Agency KELA: Kansaneläkelaitos; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; OGYEI: Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet; NCPE: National Centre for Pharmacoeconomics; HIQA: Health Information and Quality Authority AIFA: Agenzia Italiana del Farmaco UVEF: Unità di valutazione dell'efficacia del farmaco ; AGENAS: Agenzia Nazionale per i servizi sanitari regionali; ZVA: Zalu valsts agentura; VASPVT: Valstybinė akreditavimo sveikatos priežiūros veiklai tarnyba; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento; NAMMD: National Agency for Medicines and Medical Devices; CADIME: Centro Andaluz de Documentación e Información de Medicamentos; AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya; ISCII: Instituto de Salud Carlos III OSTEBA: Basque Office for Health Technology Assessment; AETSA: Andalusian Agency for Health Technology Assessment; SECS: Servicio de Evaluacion del Servicio Canario de salud. NS: Not stated * HAS decided on the level of reimbursement to apply for each Pharmaceutical product.

Annex 21: Taxonomy of HTA systems



Annex 22: Average percentage of usage of mode

	Pharma Industry	MedTech Industry	Public Administration
EC1	70%	73%	26%
EC2	76%	63%	28%
EC3	51%	41%	34%
EC4	69%	37%	31%
EC5	82%	42%	38%
EC6	72%	59%	31%
EC7	79%	48%	43%
EC8	28%	38%	35%
SH1	60%	33%	43%
SH2	81%	36%	34%
SH3	75%	35%	39%
SH4	84%	60%	36%
SH5	74%	54%	33%
all impacts	69%	52%	32%

Source: GÖ FP / LSE survey 2017

Annex 23: Follow-up questionnaire regarding costs of HTA bodies

Study on impact analysis of
policy options for strengthened EU cooperation on HTA

Costs of the current HTA system in Europe (Baseline costs)

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Forschungs- und Planungs GmbH

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SOGETI

To complete the data gathering exercise and in line with the discussions of the last EUnetHTA Executive Board meeting , **we would kindly ask you to provide the main costs factors for your body in performing HTA activities** as stated in the table below This information is needed to maximize the completeness and the reliability of the results and to cover as many European countries as possible regarding the costs of HTA processes.

Nota bene:

HTA bodies that submitted cost information in response to the online survey do not need to respond to the questions contained in this document. The information previously provided will be used.

Background

In the course of the study a detailed case study covering 40 health technologies including pharmaceuticals, medical devices and other technologies (such as screening programs) has been conducted to assess the status quo of HTA in Europe. Data for this case study have been retrieved by literature review and an additional survey process to complement information retrieved.

Additionally, this study aims to provide an overview about the **costs of HTA assessment processes in Europe for different stakeholder groups**. Therefore, different cost components of performing HTA were requested through an online survey.

The information which will be provided in response to the attached questions will be used in a strictly confidential manner. Only aggregated data will be presented in the report including an indication of the countries and HTA bodies whose information was used. The costs submitted by individual HTA bodies won´t be presented alone and no comparison across different bodies/countries is intended.

Please send the information **by 18th April to EU.HTA@goeg.at.**

Many thanks for your kind cooperation.

Comments:

- **Please fill in if relevant. If not relevant (=not done) please fill in NR. If not available please fill in NA.**
- If data are available for separate product categories (pharmaceuticals, medical technologies and other technologies), please provide information separately
- Include information for 2016 or latest year available (please indicate)
- Please report cost data in Euro and indicate where applicable the exchange rate used.
- Total unit cost should ideally include variable and fixed costs/overheads. The data can be provided as an average or as a range. If the information on total costs is not available provide an estimate or indicate to the extent possible what your cost data includes.

Total budget spent annually on HTA activities (approx.) in 2016 or latest available YEAR	

ITEM	*Total unit costs: please give an average and/or range per item below in Euro*		*Current annual number of products / assessments done by your agency for the years 2014 / 2015 / 2016*	
	Full Cost for HTA body in 2016 (please state if overhead costs are included or not)	**If relevant: Costs for industry** (submission fees) **2016**		
Early Dialogue (ED)[1] (see definition below)			2014:	
			2015:	
			2016:	
REA / Rapid Assessment[2] see definition below			2014:	
			2015:	
			2016:	
REA / Rapid Assessment incl. economic evaluation[3] see definition below			2014:	
			2015:	
			2016:	
Full HTA[4] see definition below			2014:	
			2015:	
			2016:	
[5]**National adaptation** of a joint **REA:** (Please give an estimation for the average costs when a national adaptation is done and specify what was done) 1. Summarizing; 2. Update of searches; 3. Adapting; 4.Translation to own language;			2014:	
			2015:	
			2016:	
[5]**National adaptation** of a joint **full HTA:** (Please give an estimation for the average costs when a national adaptation is done and specify what was done)			2014:	
			2015:	
			2016:	

[1]**Early Dialogue (ED):** Early Dialogues is the process offered by HTA bodies with the aim of helping pharmaceutical and medtech companies to understand the evidence and information needs of the HTA organizations and reimbursement bodies to improve the quality and adequacy of early evidence generation.

[2]**REA / rapid assessment** is the process to assess the medical/therapeutic added value of a new technology (assessment of clinical domains). Broadly speaking two forms exist: a) a Rapid Assessment produced (mainly) by an HTA-body (with no or some evidence/data submission provided by industry) or b) a Rapid Assessment produced mainly by industry and reviewed by an HTA body (please indicate). Please do not include EUnetHTA Joint Assessments.

[3]**REA / rapid Assessment incl. economic evaluations** is the process to assess (1) the medical/therapeutic added value of a new technology (assessment of clinical domains) and (2) the cost-effectiveness / budget impact. Again it may take two forms (see above, please indicate which form corresponds best to your assessments). Please do not include EUnetHTA Joint Assessments.

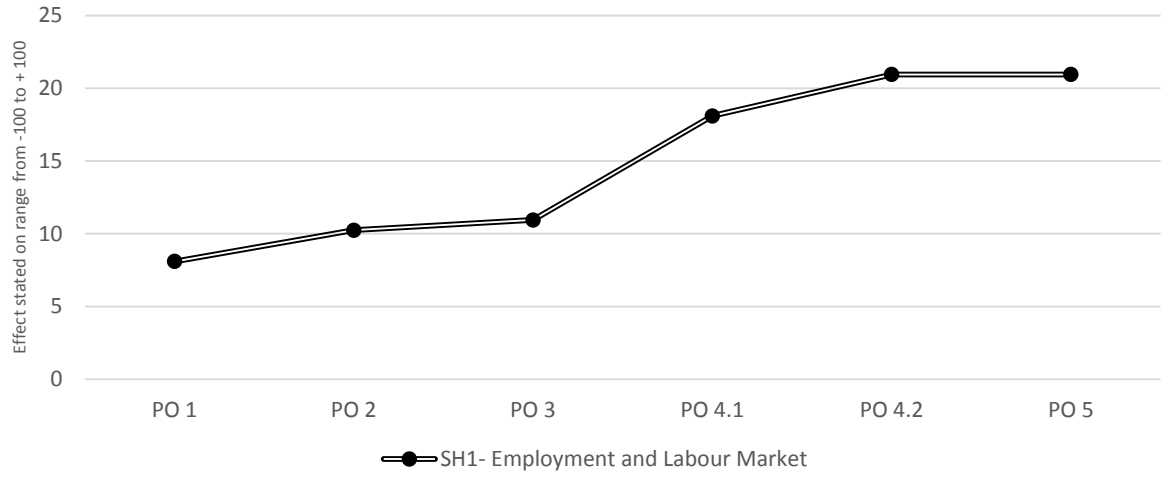
[4]**Full HTA is the process to** assess (1) the medical/therapeutic added value of a new technology (assessment of clinical domains), (2) the cost-effectiveness / budget impact,

and (3) other aspects, e.g. ethical aspects, legal considerations and impact on patients as well as on the health care systems. Please do not include EUnetHTA Joint Assessments.

[5]**National adaptation of a joint REA or a joint full HTA**: includes a range of options; please indicate for your estimates on costs and annual numbers the most suitable option (according to EUnetHTA definition): 1) Summarizing: translate the summary and use this for background information, 2) Updating searches: using the original search strategy to identify any more recent evidence or adding to the search strategy and extending it. 3) Adapting: the systematic extraction of relevant HTA information from an existing report (from a whole report or from part of a report). 4) Adopting: making use of the report without making any changes at all (except perhaps translation into your own language).

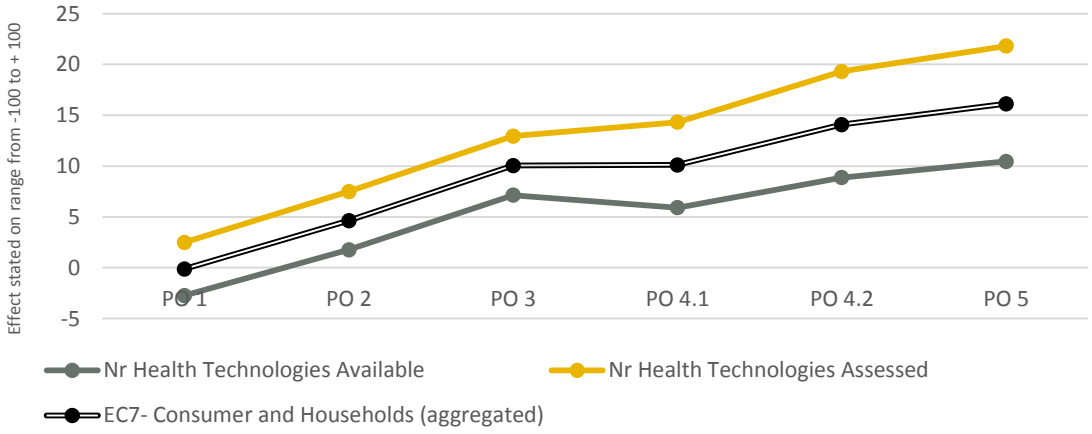
Annex 24: Further impacts for Public Administration - Graphs of survey results

Public Administration – perceived average effect of Policy Options on employment ([30])



Source: GÖ FP / LSE survey 2017

Public Administration – perceived average effect of Policy Options on consumers and households (31)



Source: GÖ FP / LSE survey 2017

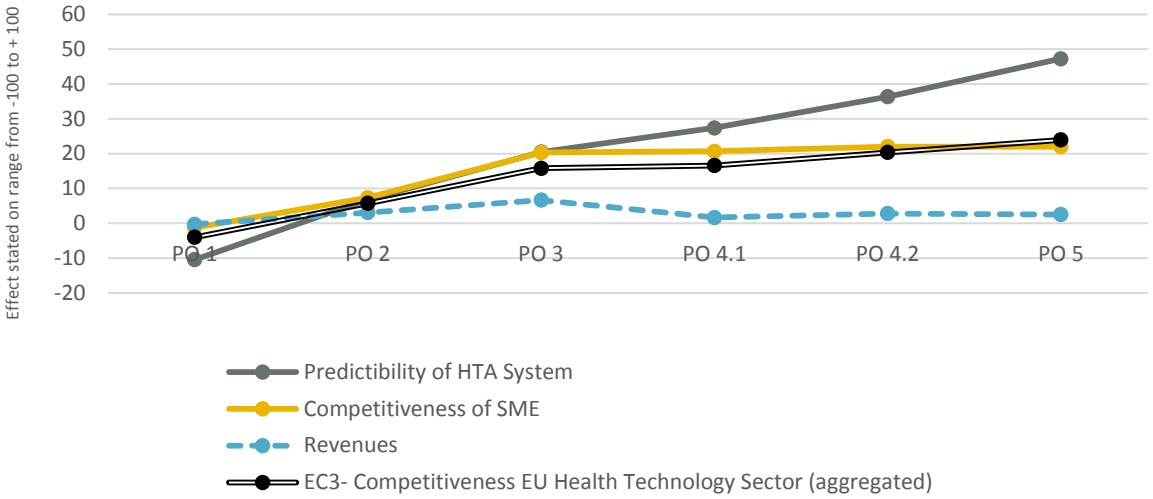
([30])

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Nr of Staff	21,0	91%	22,2	33%	14%	52%

([31])

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Nr Health Technologies Available	22,0	96%	17,0	41%	14%	45%
Nr Health Technologies Assessed	22,0	96%	20,1	18%	9%	73%

Public Administration - perceived average effect of Policy Options on competitiveness of EU health technology sector (32)

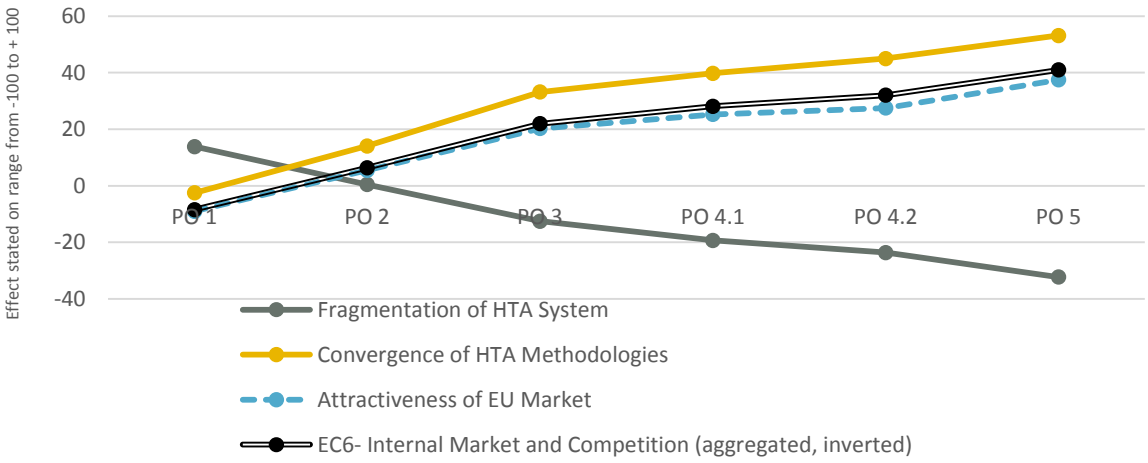


Source: GÖ FP / LSE survey 2017

([32])

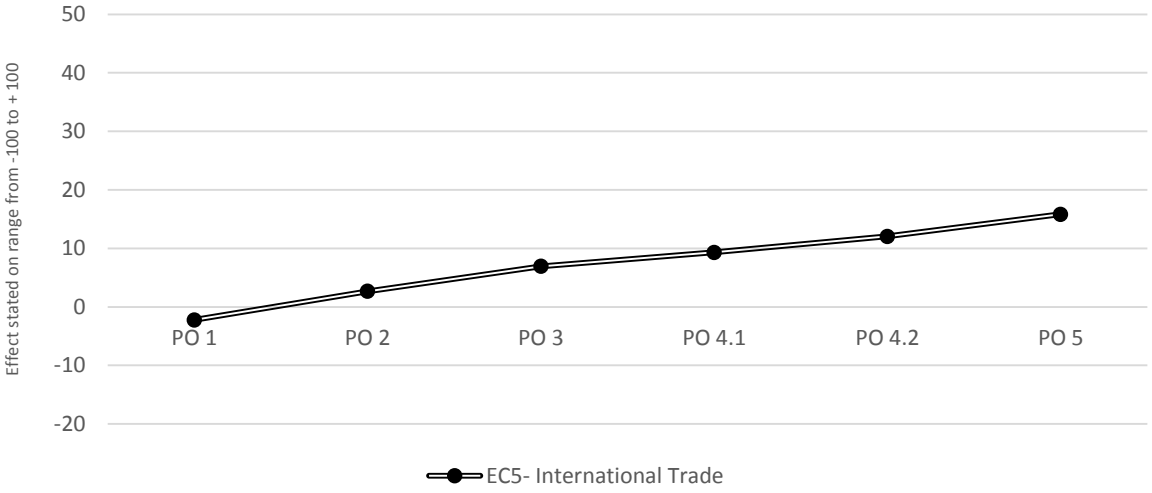
additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Predictibility of HTA System	22,0	96%	28,1	5%	9%	86%
Competitiveness of SME	15,2	66%	23,2	7%	20%	73%
Revenues	18,0	78%	18,3	44%	17%	39%

Public Administration – perceived average effect of Policy Options on internal market and competition (33)



Source: GÖ FP / LSE survey 2017

Public Administration – perceived average effect of Policy Options on International Trade ([34])



Source: GÖ FP / LSE survey 2017

([33])

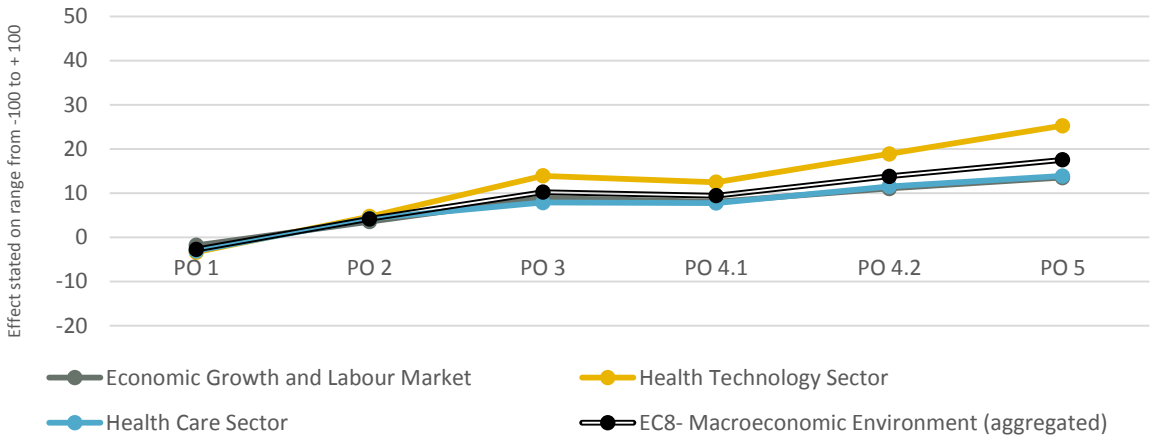
Aggregation: inverted for fragmentation of HTA system

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Fragmentation of HTA System	22,0	96%	33,6	5%	77%	18%
Convergence of HTA	22,0	96%	32,9	5%	9%	86%
Attractiveness of EU Market	20,0	87%	29,3	5%	5%	90%

([34])

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
International Trade	18,0	78%	15,7	27%	6%	67%

Public Administration – perceived average effect of Policy Options on macroeconomic environment ([35])



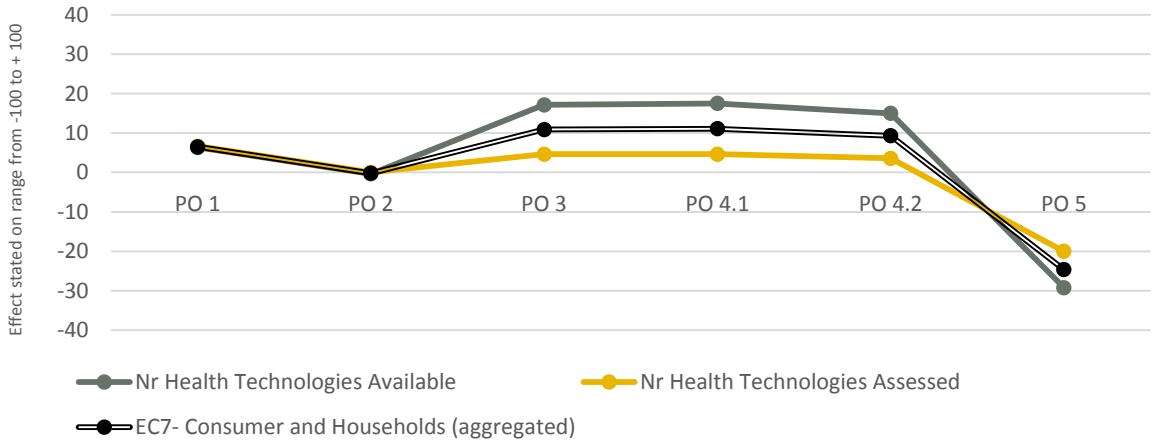
Source: GÖ FP / LSE survey 2017

([35])

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Economic Growth and Labour	17,0	74%	20,0	35%	12%	53%
Health Technology Sector	18,0	78%	23,9	17%	11%	72%
Health Care Sector	18,0	78%	16,8	33%	6%	61%

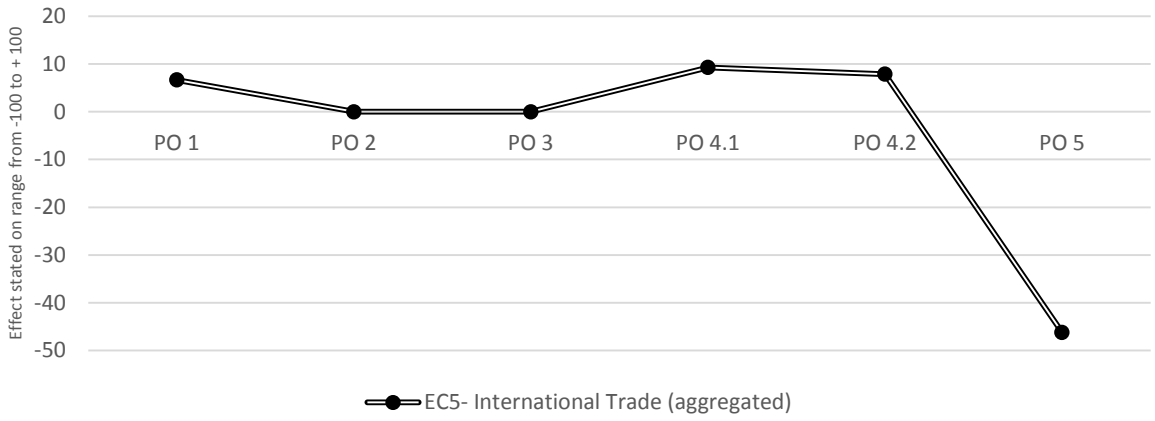
Annex 25: Further impacts for Pharmaceutical Industry - Graphs of survey results

Pharma Industry – perceived average effect of Policy Options on consumers and households (36)



Source: GÖ FP / LSE survey 2017

Pharma Industry – perceived average effect of Policy Options on international trade (37)



Source: GÖ FP / LSE survey 2017

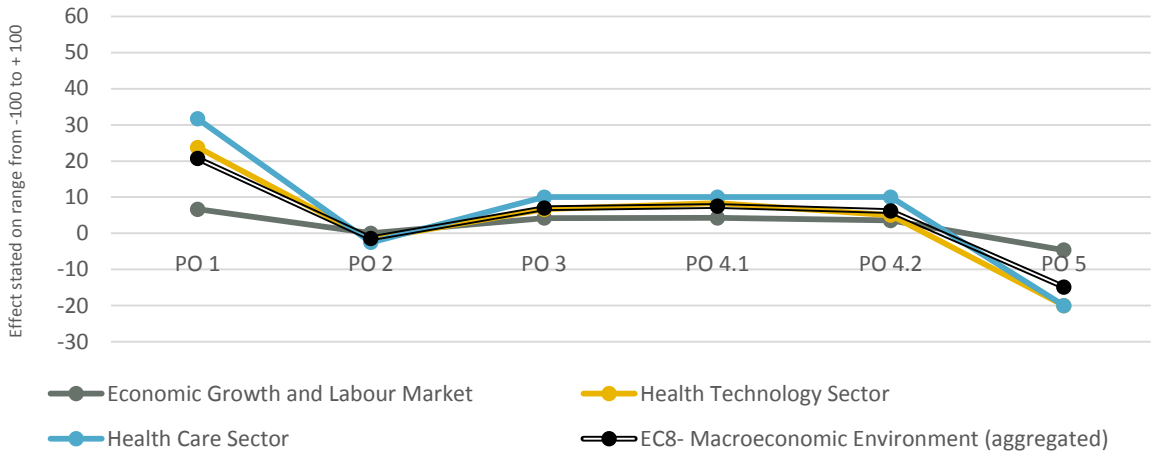
(36)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Nr Health Technologies Available	14,0	88%	9,2	0%	100%	0%
Nr Health Technologies Assessed	14,0	88%	5,4	0%	100%	0%

(37)

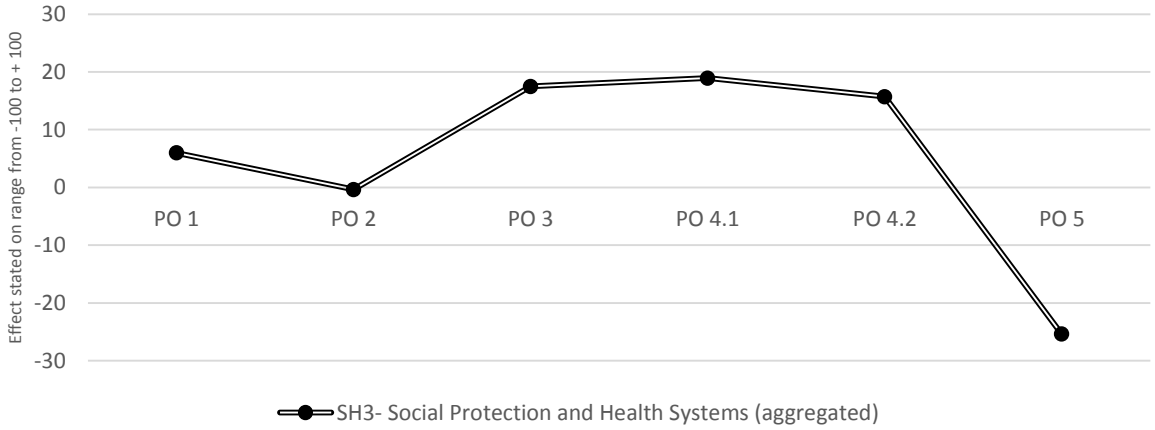
additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
International Trade	14,0	88%	8,0	8%	92%	0%

Pharma Industry – perceived average effect of Policy Options on macroeconomic environment(38)



Source: GÖ FP / LSE survey 2017

Pharma Industry – perceived average effect of Policy Options on access to social protection and health systems(39)



Source: GÖ FP / LSE survey 2017

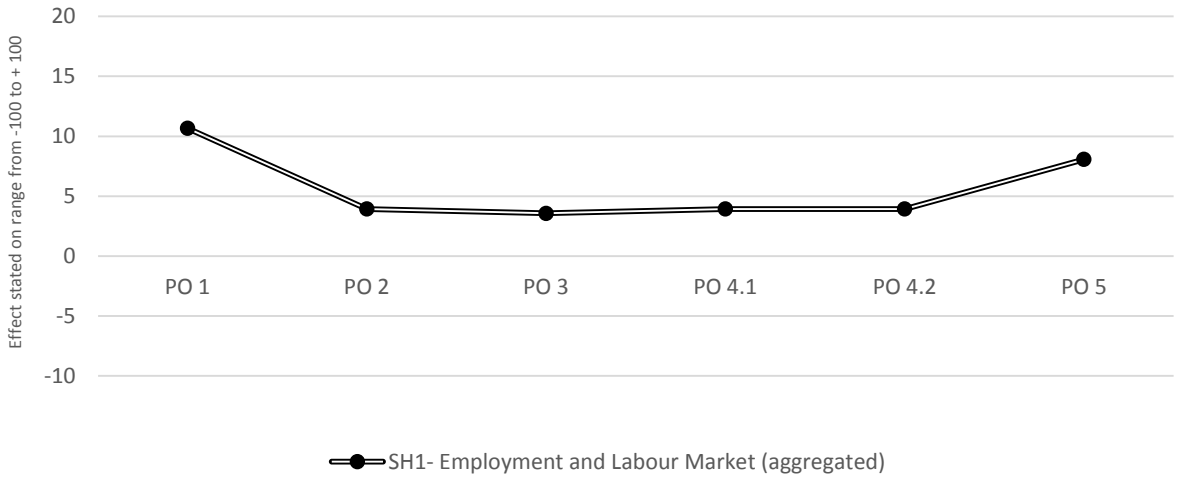
(38)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Economic Growth and Labour	13,8	86%	6,0	0%	92%	8%
Health Technology Sector	3,0	19%	15,1	0%	100%	0%
Health Care Sector	2,0	13%	21,0	0%	100%	0%

(39)

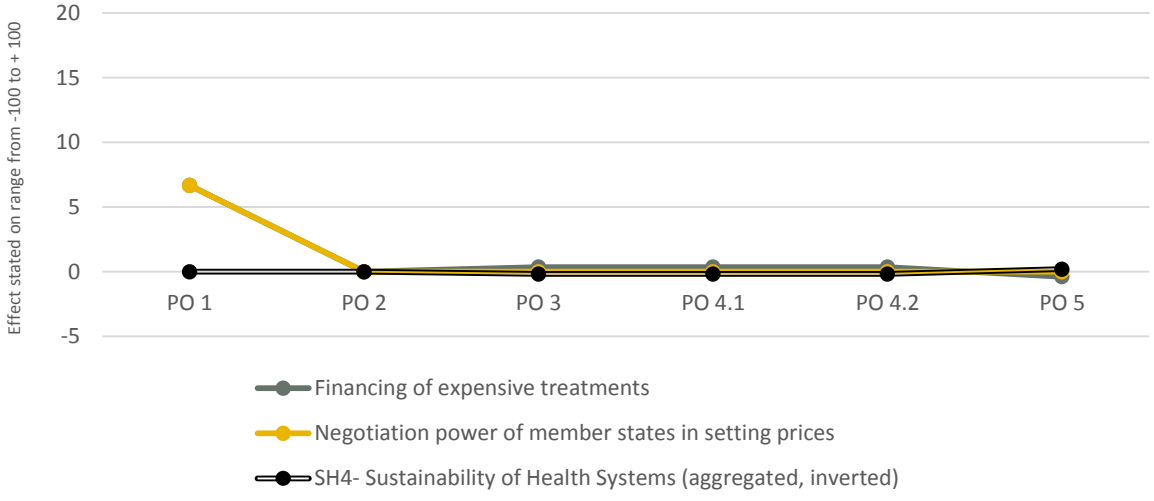
additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Access to Innovative Treatments	14,0	88%	11,2	0%	92%	8%

Pharma Industry – perceived average effect of Policy Options on employment (40)



Source: GÖ FP / LSE survey 2017

Pharma Industry - perceived average effect of Policy Options on sustainability of health systems (41)



Source: GÖ FP / LSE survey 2017

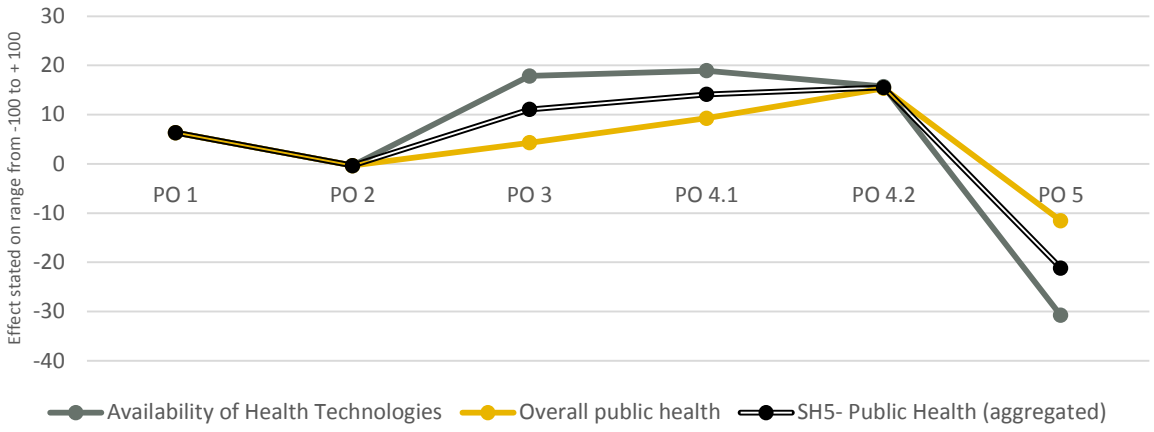
(40)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Nr of Staff	14,0	88%	6,7	23%	0%	77%

(41)

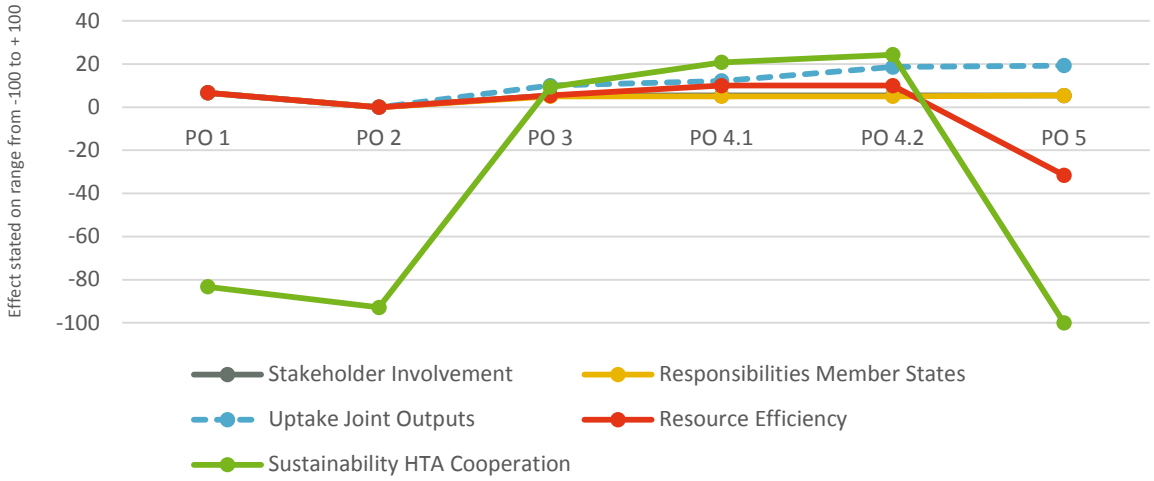
additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Financing of expensive treatments	14,0	88%	5,2	92%	8%	0%
Negotiation power of member	14,0	88%	4,3	100%	0%	0%

Pharma Industry – perceived average effect of Policy Options on Public Health (42)



Source: GÖ FP / LSE survey 2017

Pharma Industry – perceived average effect of Policy Options on indicators for governance, participation and good administration (unaggregated) (43)



Source: GÖ FP / LSE survey 2017

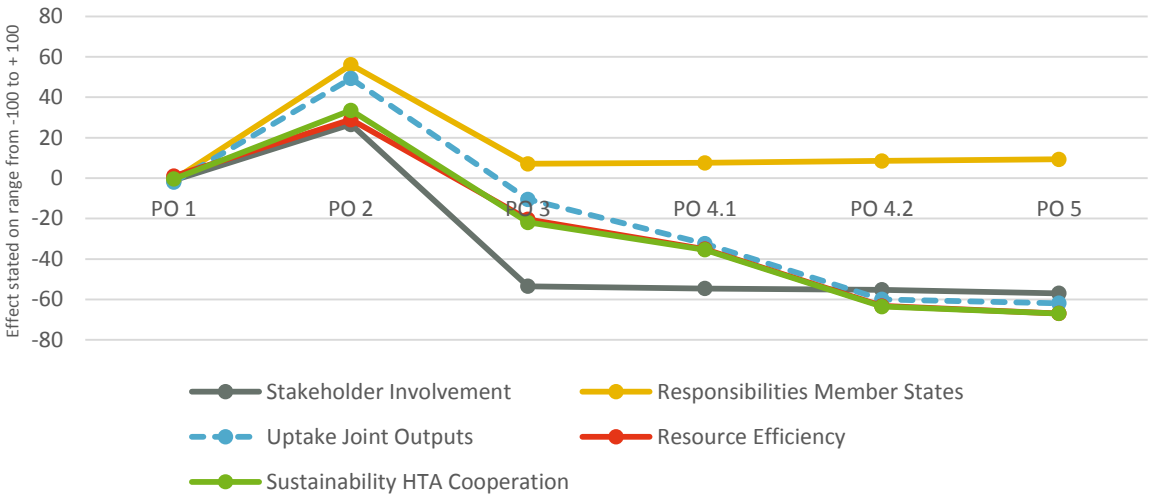
(42)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Availability of Health Technologies	14,0	88%	8,7	0%	100%	0%
Overall public health	14,0	88%	7,3	0%	100%	0%

(43)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Stakeholder Involvement	14,0	88%	5,2	0%	0%	100%
Responsibilities Member States	14,0	88%	5,5	0%	0%	100%
Uptake Joint Outputs	14,0	88%	7,2	8%	0%	92%
Resource Efficiency	14,0	88%	6,1	0%	100%	0%
Sustainability HTA Cooperation	14,0	88%	16,8	92%	8%	0%

MedTech Industry – perceived average effect of Policy Options on indicators for governance, participation and good administration (unaggregated) (44)



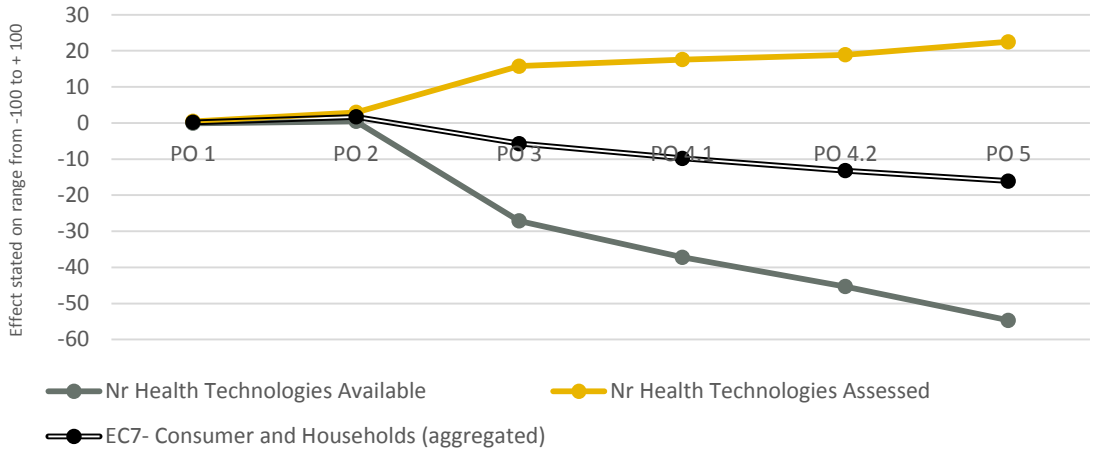
Source: GÖ FP / LSE survey 2017

(44)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Stakeholder Involvement	86,5	87%	37,0	7%	82%	11%
Responsibilities Member States	85,7	87%	24,5	20%	4%	76%
Uptake Joint Outputs	85,5	86%	35,4	2%	82%	15%
Resource Efficiency	85,5	86%	33,6	4%	86%	11%
Sustainability HTA Cooperation	86,5	87%	32,6	1%	85%	14%

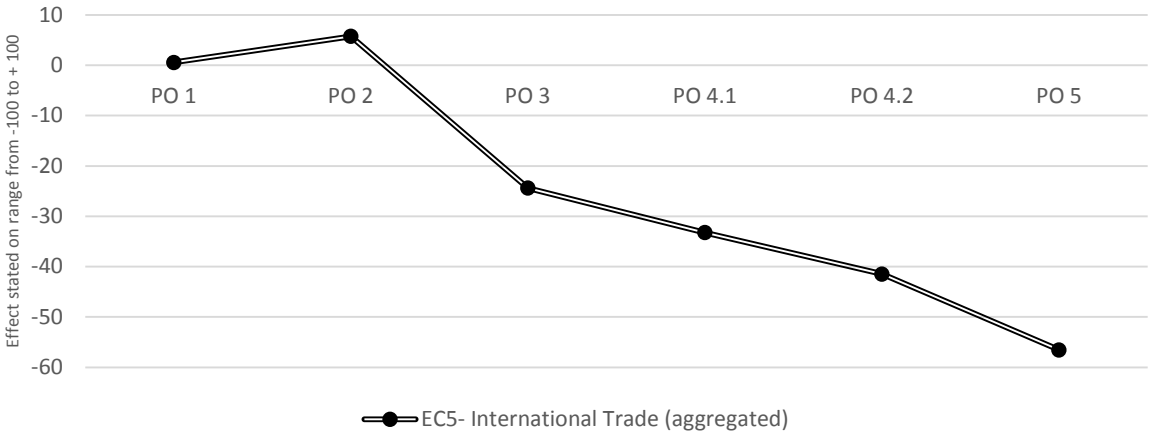
Annex 26: Further impacts for MedTech Industry - Graphs of survey results

MedTech Industry – perceived average effect of Policy Options on consumers and households (45)



Source: GÖ FP / LSE survey 2017

MedTech Industry – perceived average effect of Policy Options on international trade (46)



Source: GÖ FP / LSE survey 2017

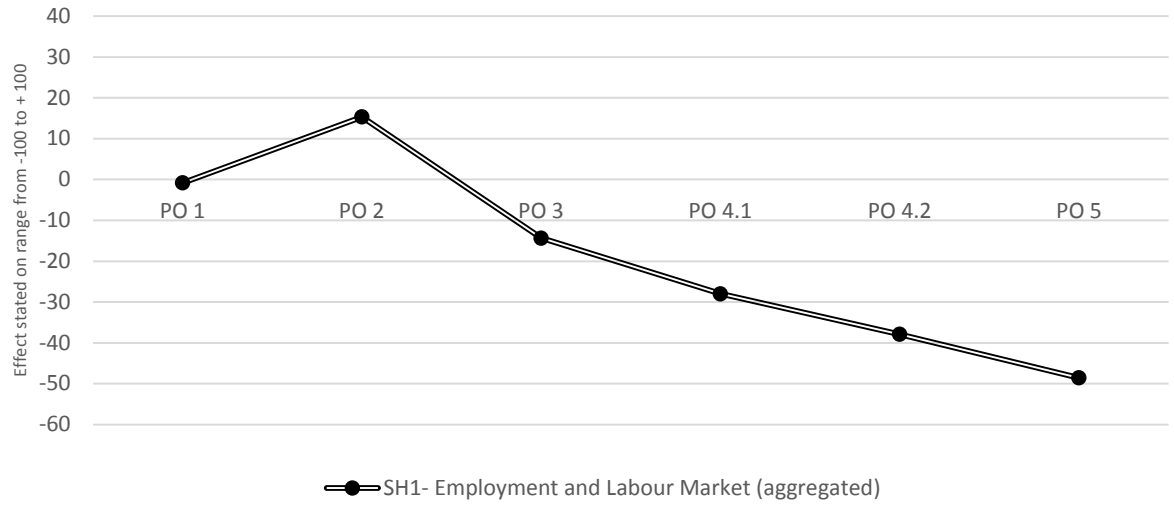
(45)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Nr Health Technologies Available	90,2	91%	23,4	2%	94%	3%
Nr Health Technologies Assessed	87,8	89%	20,4	8%	4%	88%

(46)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
International Trade	90,2	91%	26,2	6%	86%	8%

MedTech Industry – perceived average effect of Policy Options on employment (47)

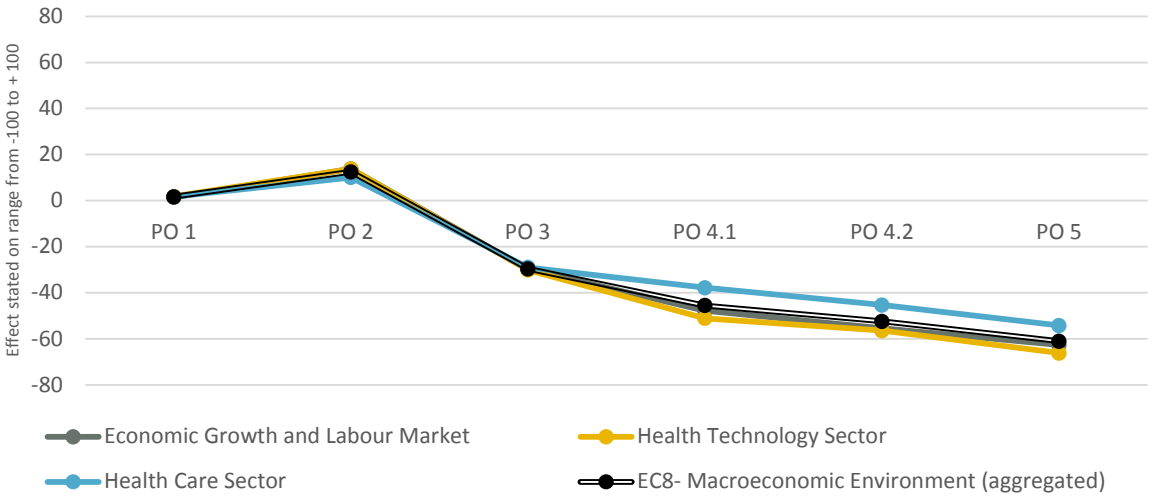


Source: GÖ FP / LSE survey 2017

(47)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Nr of Staff	86,8	88%	29,6	7%	80%	13%

MedTech Industry – perceived average effect of Policy Options on macroeconomic environment (48)

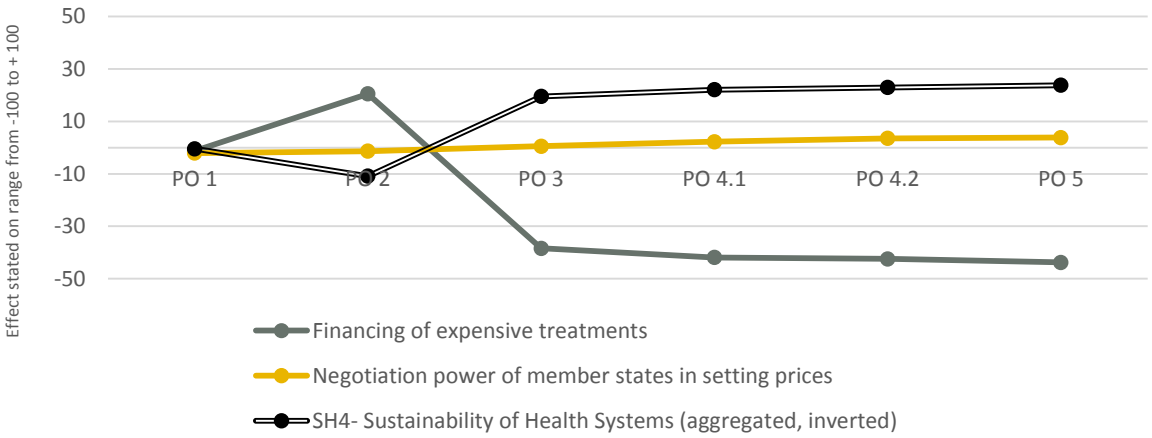


Source: GÖ FP / LSE survey 2017

([48])

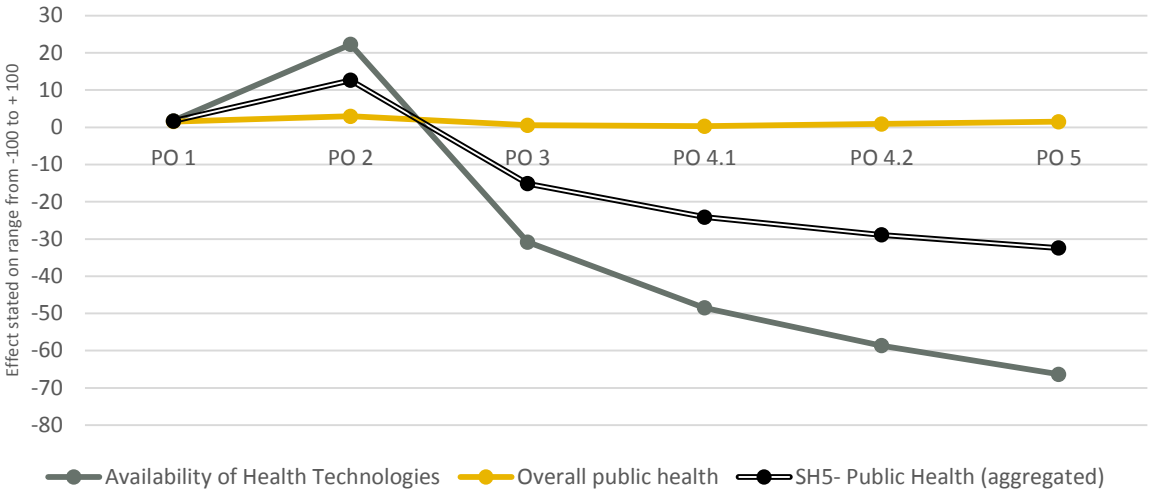
additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Economic Growth and Labour	89,8	91%	29,3	5%	89%	7%
Health Technology Sector	90,0	91%	28,9	5%	91%	5%
Health Care Sector	89,8	91%	28,7	5%	87%	8%

MedTech Industry – perceived average effect of Policy Options on sustainability of health systems (49)



Source: GÖ FP / LSE survey 2017

MedTech Industry – perceived average effect of Policy Options on Public Health (50)



Source: GÖ FP / LSE survey 2017

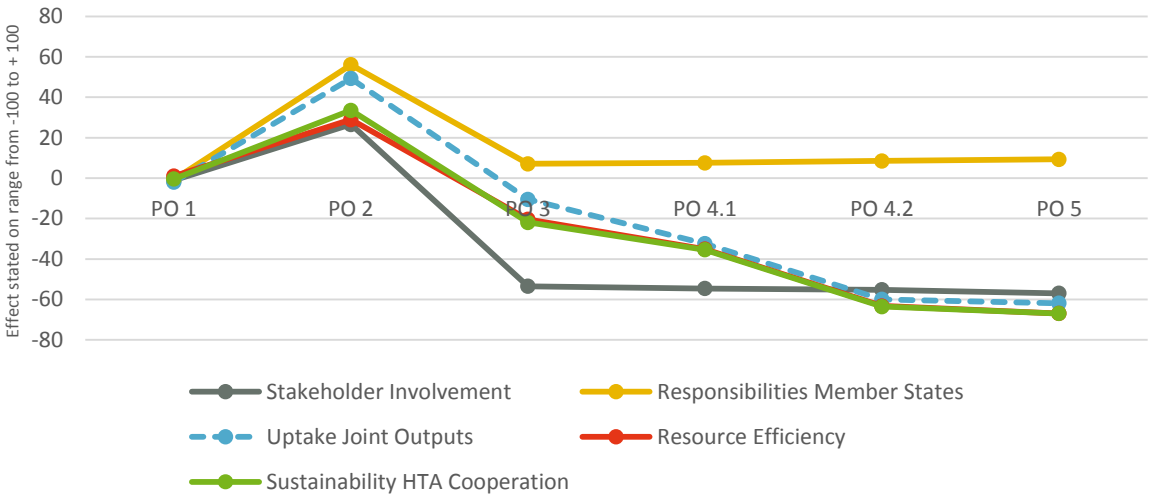
(49)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Financing of expensive treatments	87,5	88%	25,7	6%	88%	6%
Negotiation power of member	85,8	87%	18,2	82%	6%	12%

(50)

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Availability of Health Technologies	87,2	88%	26,7	4%	94%	2%
Overall public health	85,8	87%	18,7	84%	8%	8%

MedTech Industry – perceived average effect of Policy Options on indicators for governance, participation and good administration (unaggregated)(51)

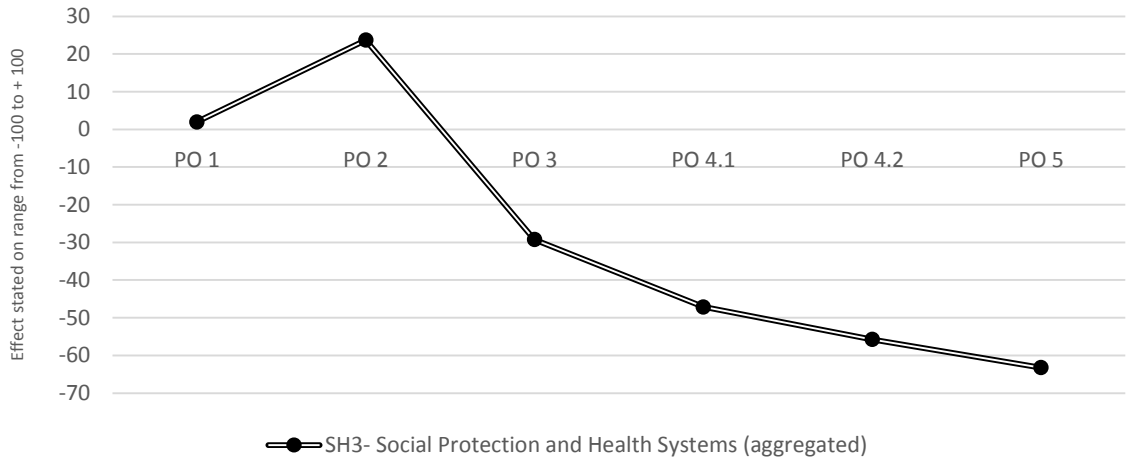


Source: GÖ FP / LSE survey 2017

51

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Stakeholder Involvement	86,5	87%	37,0	7%	82%	11%
Responsibilities Member States	85,7	87%	24,5	20%	4%	76%
Uptake Joint Outputs	85,5	86%	35,4	2%	82%	15%
Resource Efficiency	85,5	86%	33,6	4%	86%	11%
Sustainability HTA Cooperation	86,5	87%	32,6	1%	85%	14%

MedTech Industry – perceived average effect of Policy Options on access to social protection and health systems (52)



Source: GÖ FP / LSE survey 2017

([52])

additional information	av. responses	response rate	av. std. dev	no trend	negative trend	positive trend
Access to Innovative Treatments	87,0	88%	26,3	0%	94%	6%

Annex 27: Medical technology example

The product selected received EMA marketing authorization for two different indications for treating a chronic disease through the centralized procedure.

The product underwent HTA assessments in 11 countries by 12 agencies. In Germany, we considered both the evaluation from IQWIG and G-BA, even if they do not differ in terms of outcome, in order to assess differences, if any, between the two agencies in the way they perceive and assess the submitted evidence. Indeed, the procedure for arriving at the overall conclusion on the extent of added benefit is a proposal from IQWiG in the first instance; G-BA is taking the final decision and also conducts its own evaluation; in some cases, the opinions of the two agencies may differ. In this case, for example, G-BA extended the benefit to Level two also to the other sub-population, rated at Level V by IQWIG.

Table 6- Overview of HTA recommendations

Country (Agency)	Ireland (NCPE)	England (NICE)	Sweden (TLV)	France (HAS)	Scotland (SMC)	The Netherlands (ZIN)	Poland (AOTM)	Germany (IQWIG)	Germany (G-BA)	Portugal (INFARMED)	Romania (MoH)	Italy (CRUF)
M.A. Date:	XX/XX/XXXX											
Type of M.A.	Centralized											
Decision date	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX	XX/XX/XXXX
Decision	LWC	LWC	LWC	ASMR III SMR: Important	LWC	LWC	LWC	Sub-population 1: Level 2 Sub-population 2: Level 5	L (Level 2)	L	L	LWC
Clinical restrictions	Not stated			✓	✓							✓
Economic restrictions	Not stated	✓	✓		✓	✓						✓
Severity	✓		✓	✓								
Rarity												✓
Unmet need for treatments		✓	✓	✓	✓	✓	✓					✓

Country (Agency)	Ireland (NCPE)	England (NICE)	Sweden (TLV)	France (HAS)	Scotland (SMC)	The Netherlands (ZIN)	Poland (AOTM)	Germany (IQWIG)	Germany (G-BA)	Portugal (INFARMED)	Romania (MoH)	Italy (CRUF)
Special conditions considered		✓ End of life criteria	✓ Humanitarian aspect and solidarity principle		✓ SMC Modifiers							
Burden on family and carers emotional well being												
Impact on work and everyday life activities		✓		✓								
Wider societal Benefits				✓								
Equality issues		✓										
Small population		✓										
Significant innovation		✓		✓		✓				✓		

Legend: ✓ : presence of the variables; NICE: National Institute for Health and Clinical Excellence (NICE); SMC: Scottish Medicines Consortium; TLV: Dental and Pharmaceutical Benefits Board; HAS: Haute Autorité de Santé; IQWIG: Institute for Quality and Efficiency in Healthcare; G-BA: Gemeinsame Bundesausschuss; UVEF: Unità di valutazione dell'efficacia del farmaco ; ZiN: Zorginstituut Nederland AOTMiT: Agencja Oceny Technologii Medycznych i Taryfikacji; Infarmed: Instituto Nacional da Farmácia e do Medicamento;.MoH; Minsitry of Health; NCPE: National Centre for Pharmacoeconomics.

The primary evidence for the clinical benefit stemmed by the same randomised, double-blind phase-III study comparing the efficacy and tolerability of the product with placebo. The total number of studies submitted and evaluated by HTA agencies differed widely. In three cases (IQWIG, G-BA and ZIN) an indirect comparison was also included in order to compare the product with a direct comparator whereas NICE, TLV, AOTM and ZIN also included another Phase III trial in order to support the clinical effectiveness arguments. Finally, TLV included an observational study to support the clinical benefit and ZIN included the results of the EPAR report, while AOTMiT included three studies assessing the drug with a direct comparator.

Considering the submission of the economic evidence, HTA agencies considered at least one cost-utility analysis. The comparators included in the analysis differed is some cases, which might lead to a different outcome. For Instance, TLV considered an analysis that compared the cost-effectiveness of the product against the direct comparator and partly against no treatment, that is, only symptomatic treatment, whereas ZIN, NICE, UVEF considered only comparison with the same direct comparator. INFRAMED considered the comparison with a direct comparator, that for example is not licensed in the UK. It is important to highlight also, that most of the agencies (e.g. SMC, AOTMiT and ZIN) considered a budget impact analysis, which, in some cases (ZIN), had a negative influence on the final decision. For instance, ZIN highlighted that the budget impact on pharmaceutical expenditure was calculated between €9 and €13 million per year, leading to a higher cost than the use of the comparator currently used in clinical practice.

A number of elicited and non-elicited social value judgments were identified in the reports, some of which helped shape or influence the final HTA recommendation. These values, comprising clinical, social, and ethical parameters, have increasingly been included in HTA decisions in order fully assess the value of healthcare technologies when making judgments regarding clinical and cost effectiveness. In some cases (e.g. End of life criteria by NICE in England; and SMC modifiers in Scotland), HTA agencies state these values explicitly in the guidelines and are captured in a consistent manner across all the relevant reports. In other cases, some types of value (e.g. Degree of innovation or administration benefit) are taken into consideration in addition to the cost per unit of health gain but in a less standardized manner.

Considering non-elicited social value judgments, seven out of 13 agencies considered important to include a treatment in this area because of unmet medical need. Specifically, TLV, ZIN and HAS highlighted the national importance of having a treatment for this chronic disease in late stage disease whereas SMC specifically stated an unmet need in this treatment category. Whereas most of the agencies consider the product as palliative care treatment, HAS considered that product as a 'curative' treatment and commented it could provide an additional response to public health need compared to the therapeutic strategy currently in place. NICE, ZIN and AOTM pointed out the innovativeness of the treatment in terms of its mode of administration because it is an oral drug taken by patients at home. This advantage is highlighted also by SMC and HAS, the latter stating in its report that the product under review offers an alternative, orally administered to other treatments, and is better tolerated with a different safety profile. SMC highlighted the unmet need in this area with very limited treatment options in this stage of the disease. The most common alternative treatment was cited by HAS and NICE. NICE also suggested another product considered as main treatment an alternative in other countries has not been licensed in UK.

Looking at the management of the disease, HAS pointed out that the method of administration could have a positive impact on the organization of patient care, having a clear influence on the final decision.

For all HTA agencies, the most important "other consideration" in the decision was the improvement in the quality of life of patients using the product.

Looking at the elicited social value judgments, their consideration by three agencies (NICE, SMC and TLV) had a considerable impact on the outcome, leading the agencies to accept an ICER higher than their notional threshold. Specifically, elicited social value judgments played a key role in the assessment by NICE. Initially, NICE rejected the product because it was not considered to be cost-effective stating that the End of life criteria were not applicable due to the absence of the prerequisite of a no small population and the ICER (XX,XXX/QALY) was significantly over what it would consider acceptable even with the application of EoL criteria (which is in the region of XX,XXX /QALY). However, in February 2012 the product underwent a re-evaluation and it was accepted with restrictions, stating that the eligible patient population was actually small and the drug was suitable for the consideration of the end-of-life criteria. Interestingly, NICE reversed its initial decision within one month, whereas it took nearly three years for TLV to decide to reimburse the drug with restrictions.

Table 7: Medical technology example: Conclusions

HTA body	England (NICE)	Scotland (SMC)	Sweden (TLV)	France (HAS)	Ireland (NCPE)	The Netherland (ZIN)	Poland (AOTM)	Germany (IQWIG)	Germany (G-BA)	Portugal (INFARMED)	Romania (MoH)	Italy (CRUF)
Clinical effectiveness	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Economic analysis	×*	✓	×*	N/A	×*	×*	×*	N/A	N/A	✓	N/A	✓
Social value judgments with an influence on decision	End of life criteria	SMC modifiers	Human dignity and solidarity principle	Administration advantage	N/A	N/A	N/A	N/A	N/A		N/A	N/A
Risk sharing agreement/ Pricing agreements	Commercial access arrangement	Patient Access Scheme (PAS)	Yes	N/A	Price negotiation	Annex 1b	Yes-Confidential	N/A	N/A	N/A	the list comprising DCI	Cost Sharing in accordance with the contractual condition. List H

Legend: ×*: clinical effectiveness uncertain and not demonstrated; ✓: improved or positively assessed clinical effective

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