



An analysis of HTA and reimbursement procedures in EUnetHTA partner countries: final report

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Abbreviations

AAZ: Agency for Quality and Accreditation in Health Care and Social Welfare
AEMPS: Agencia Española De Medicamentos Y Productos Sanitarios
AETSA: Andalusian Agency for Health Technology Assessment
Agenas: Agenzia Nazionale Per I Servizi Sanitari Regionali
AIFA: Agenzia Italiana Del Farmaco
AOTMiT: Agency for Health Technology Assessment and Tariff System
AQuAS: Agency for Health Quality and Assessment of Catalonia
ASSR-RER: Agenzia sanitaria e sociale regionale - Regione Emilia-Romagna
ATC: Anatomical Therapeutic Chemical Classification
ATMP: Advanced therapy medicinal products
Avalia-t: Scientific Advice Unit of the Galician Agency for Knowledge Management
AWTTC: All Wales Therapeutics and Toxicology Centre
CADTH: Canadian Agency for Drugs and Technologies in Health
CHIF: Croatian Health Insurance Fund
CHMP: Committee for Medicinal Products for Human Use
CIRS: Centre for Innovation in Regulatory Science
CSR: clinical study report
CT: Computerised tomography
DGCBSF: Directorate-General for NHS Basic Services Portfolio and Pharmacy
DMA: Danish Medicines Agency (Lægemiddelstyrelsen)
DMC: Danish Medicines Council (Medicinraadet)
DPA/MFH: Directorate Pharmaceutical Affairs, Ministry for Health
ECRI: Economic Cycle Research Institute
EHIF: Estonian Health Insurance Fund
EMA: European Medicines Agency
EPAR: European public assessment reports
ESSENTIAL: Low-value clinical practices recommendations project
EU: European Union
EUnetHTA: European network for Health Technology Assessment
EVIDENT: Evidence database on new technologies
FIMEA: Finnish Medicines Agency
FOPH: Federal Office of Public Health, Switzerland
G-BA: Federal Joint Committee (Gemeinsamer Bundesausschuss)
GCPT: Co-ordination Group for Therapeutic Positioning
GOEG: Gesundheit Österreich GmbH
HAS: Haute Autorité de Santé
HIIS: Health Insurance Institute of Slovenia
HILA: Pharmaceuticals Pricing Board
HIQA: Health Information and Quality Authority
HiT: Healthcare in Transition
HST: NICE highly specialised technologies programme
HTA: Health technology assessment

HVB: Hauptverband der Österreichischen Sozialversicherungsträger
INAHTA: International Network of Agencies for Health Technology Assessment
INFARMED: National Authority of Medicines and Health Products
IP: NICE interventional procedures programme
IQWIG: Institute for Quality and Efficiency in Health Care
ISCIII: Instituto De Salud Carlos III
IRP: Institute of Rational Pharmacotherapy
JA: Joint Action
JAZMP: Agency for Medicinal Products and Medical Devices of the Republic of Slovenia
KCE: Belgian Health Care Knowledge Centre
LBI-HTA: Ludwig Boltzmann Institute for Health Technology Assessment
MIB: NICE MedTech innovations briefings programme
MoH: Ministry of Health
MRI: Magnetic resonance imaging
MS: Member States
MTA: Multiple Technology Assessment
MTEP: Medical Technologies Evaluation Pathway
NCPE: National Centre for Pharmacoeconomics
NCPHA: National Center of Public Health and Analyses
NHIF: National Health Insurance Fund, Hungary
NICE: National Institute for Health & Care Excellence
NIHR: National Institute for Health Research
NIHRIO: National Institute for Health Research Innovation Observatory
NIPHNO: Norwegian Institute of Public Health
NIPN: National Institute of Pharmacy and Nutrition
NOMA: Norwegian Medicines Agency
NVD: The National Health Service , Latvia
OSTEBA: Basque Office for Health Technology Assessment
PBS: Pharmaceutical Benefit Scheme
PET: positron emission tomography
PICO: population, intervention, comparator, outcomes
POP: Planned and Ongoing Projects database
PPRI: Pharmaceutical Pricing and Reimbursement
REA: Relative Effectiveness Assessment
RIHTA: La Rete Italiana di HTA, Italian HTA Network,
RIZIV: Rijksinstituut voor Ziekte- en Invaliditeitsverzekering
SBU: Swedish Agency for Health Technology Assessment and Assessment of Social Care
SCS: Canary Islands Unit for Health Technology Assessment
SHTG: Scottish Health Technologies Group
SMC: Scottish Medicines Consortium
STA: Single Technology Assessment
SUKL: State Institute for Drug control, Czech Republic
TA: NICE technology appraisals programme

TLV: The Dental and Pharmaceutical Benefits Agency

UETS Madrid: Health Technology Assessment Unit, Madrid

UK: United Kingdom

UT: University of Tartu

VASPVT: Valstybinė Akreditavimo Sveikatos Priežiūros Veiklai Tarnyba /

State Health Care Accreditation Agency, Lithuania

VVKT: Valstybinė vaistų kontrolės tarnyba/ State Medicine Control Agency
Lithuania

WHO: World Health Organisation

WP: Work package

ZIN: Zorginstituut Nederland

Executive Summary

Background

Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health technologies. HTA aims to respond to decision-makers' information needs regarding the introduction, coverage, use or disinvestment of health technologies. Information needs of decision makers often arise at similar times across Member States (MS) or in close succession leading to duplication of efforts within HTA agencies. While there are differences in information needs across MS because of differences in decision making structures, timing, information requirements and level of HTA implementation, there are also similarities that should be capitalised on so as to make best use of resources.

HTA cooperation and use of joint work is likely to be most successful if it fits as far as possible within MS procedural requirements and reflects HTA products that meet decision-makers' information needs. From an understanding of existing working practices, mechanisms of engagement that complement working practices can be identified and products that MS value and are able to use, created. Identifying flexibilities and restrictions in procedures supports EUnetHTA to have an understanding of the changes required in specific MS. An understanding of existing procedures can also identify areas where MS need support so that implementation challenges can be resolved and are not barriers to HTA cooperation.

Aims

This study analyses existing HTA and reimbursement procedures within EUnetHTA partner countries. It identifies how within their existing procedures agencies in these countries can:

1. engage in HTA cooperation,
2. use jointly produced HTA information, and
3. re-use national, regional and local HTA information from other jurisdictions.

The study includes procedures for assessing pharmaceuticals and non-pharmaceutical health technologies in inpatient and outpatient settings. It includes agencies that produce HTAs and also agencies using HTA type information provided by other parties to support decision-making.

Methods

Agencies were asked to provide documents that described their HTA and reimbursement procedures. Information from these documents was then abstracted into a standardised template. Where information was missing or was not available agencies were asked to complete the template directly. The similarities and differences in the procedures were then analysed. Separately, WP7 asked agencies to take part in case studies to discuss their working practices and use of EUnetHTA assessments to illustrate the report and help develop recommendations.

Results

Data were received from 59 agencies in 31 EUnetHTA partner countries. Data included national procedures as well as regional procedures in Spain and Italy. Twenty-one agencies in 9 countries took part in case studies.

29 out of 31 of countries (94%) reported having procedures for the assessment of pharmaceuticals and 22 out of 31 countries (71%) reported having procedures for the assessment of non-pharmaceutical health technologies. A smaller number of assessments are carried out of non-pharmaceutical health technologies than of pharmaceuticals, 10 countries (45%) complete less than 30 assessments per year for non-pharmaceutical health technologies compared to 4 countries (14%) for pharmaceuticals. For pharmaceuticals, a smaller number of countries assess inpatient than outpatient technologies (22 (76%) and 29 (100%) countries, respectively). However, for non-pharmaceutical health technology assessment most countries (20 out of 22 (91%)) do not differentiate between settings.

Horizon scanning and topic selection

A minority of countries (34% and 45% for pharmaceuticals and non-pharmaceutical health technologies, respectively) currently use horizon scanning procedures to support topic selection, but a number of other countries are currently developing or considering developing horizon scanning systems. In approximately 50% of countries, the HTA agency does not have a role in topic selection. Organisations involved in the topic selection procedure include: Industry (by choosing to submit an application for reimbursement), Ministries of Health and payers. For non-pharmaceutical health technologies, providers, medical and clinical societies and regional authorities also have a role in topic selection. Among countries who select from eligible topics, topic selection criteria are most frequently based on: economic or resource impact, potential health benefits, severity or burden of disease, population size, importance to healthcare and innovativeness. Currently, agencies often do not know far in advance whether a topic will need to be assessed.

Assessment and evaluation procedures

In the majority of countries (55% and 77% for pharmaceuticals and non-pharmaceutical health technologies, respectively) there is a procedure to define the scope or decision problem of the assessment before the procedure formally starts. However, this is not normally undertaken significantly in advance of the assessment starting and the responsibility for defining the scope often includes not only the HTA agency but also the initiator of the assessment, clinical experts or stakeholders.

In the majority of countries (76%) the HTA for pharmaceutical assessment is provided by industry and evaluated by the agency. In contrast, in 82% of countries the assessment of non-pharmaceutical health technologies is completed by the HTA agency which produces its own assessment either using evidence from industry or by identifying the evidence itself. For pharmaceuticals in the majority of countries

(79%) the timelines for completion are not defined by the regulatory timetable, rather the assessment is initiated by an application for assessment and then follows timelines governed by the Transparency directive (89/105/EEC). For pharmaceuticals the amount of time to carry out an assessment was most frequently 2-3 months, and the predominant approach was single technology assessment including an assessment of relative effectiveness and some kind of assessment of economic impact. For non-pharmaceutical health technologies the point in the product lifecycle when an assessment will be initiated in a national setting is less clearly defined, there is a longer timeframe for assessment (3-6 months was most frequent) and no single approach to assessment dominates.

Use of HTA from other jurisdictions

Twenty-one countries (72%) used information from other jurisdictions to support the assessment or evaluation of pharmaceuticals and 18 countries (82%) used information from other jurisdictions to support the assessment or evaluation of non-pharmaceutical health technologies. Documents used tended to be HTA reports and recommendations published in English language. However, documents written in French and German were also referred to. Information tended to be used as supporting information, to support detailed insight, or as background information.

Conclusions

The study identifies differences in working practices for the assessment of pharmaceuticals and non-pharmaceutical health technologies. These differences affect how within their existing working practices MS may engage in HTA cooperation and be able to use jointly produced HTA information. In addition, in some countries HTA is still in the process of becoming established, a sustainable mode of HTA collaboration will need to support agencies to develop their HTA systems and capability to use and produce HTA.

For many countries there is little predictability as to which assessments will be required and when. Agencies may be requested to carry out assessments at short notice and with short timeframes for completion. Implementation of and engagement in collaborative HTA would be facilitated by a system of HTA cooperation that is predictable and supports early awareness among MS of new and emerging technologies and planned collaborative HTA activities.

Within existing procedures some agencies will mainly use collaborative HTA to support the evaluation procedure (e.g. to help the agency validate the case put forward by the company in their submission of evidence). For agencies evaluating company submissions collaborative HTA could be an alternative to a national REA submission, an addition to the national REA submission or incorporated into the national REA submission. The changes required to national procedures to implement these scenarios vary and a model of HTA cooperation needs to identify which scenarios agencies are working towards and support necessary.

For pharmaceuticals the assessment procedure commonly fits into a larger pricing and/or reimbursement decision-making procedure governed by the Transparency directive (89/105/EEC) with associated timelines and requirements for transparency and accountability. To support implementation, collaborative HTA must be available at or before marketing authorisation to enable maximum use by agencies. Collaborative HTA must also adopt appropriate quality assurance, stakeholder engagement and governance procedures such as those that are in place to support the rigour and accountability of national procedures. The procedures and documentation behind the assessment must be fully transparent and robust to ensure that collaborative HTA is seen as a legitimate alternative to national HTA.

The study identifies that agencies frequently use HTA from other jurisdictions to support their assessment. Therefore the issue of implementation does not appear to be agencies not wanting to use or being unable procedurally to use HTA from other sources, rather it is how meaningfully they are able to use collaborative HTA and the amount of value it adds by going beyond that which they can achieve as an individual agency. Dialogue with users of the collaborative HTA and with decision makers will help ensure that collaborative assessment products provide additional value and agencies want to and are motivated to use the assessment.

Introduction

Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health technologies. It is a multidisciplinary procedure to evaluate the social, economic, organisational and ethical issues of a health intervention or health technology¹. HTA aims to respond to decision-makers' information needs regarding the introduction, coverage, use or disinvestment of health technologies. These information needs often arise at similar times across Member States (MS) or in close succession leading to duplication of efforts. There are differences in information needs across MS that arise because of differences in decision making structures, timing, information requirements and level of HTA implementation. However, there are also similarities that should be capitalised on so as to make best use of resources.

A sustainable mechanism of HTA cooperation within Europe that meets the information needs of decision makers would decrease the duplication of efforts and result in increased efficiency within national HTA agencies and across MS. The European Network for Health Technology Assessment (EUnetHTA) Joint Action (JA) 1 2010-2012 refined the collaboration structure and tools with attention to global developments in the field². EUnetHTA JA2 (2012-2015) extended this by strengthening the practical application of tools and approaches to cross-border HTA collaboration, further supporting and refining a system of collaboration in HTA. These experiences have proven the ability of national HTA organisations to work together and produce valuable products.

There are 2 overarching objectives of EUnetHTA JA3:

- (1) To increase the use, quality and efficiency of joint HTA work at European level to support evidence-based, sustainable and equitable choices in healthcare and health technologies and ensure re-use in regional and national HTA reports and activities, in order notably to avoid duplication of assessments.
- (2) To support voluntary cooperation at scientific and technical level between HTA agencies by providing a sustainable model for the scientific and technical mechanism of a permanent European cooperation on HTA (including criteria/requirements for the coordination hosting function post-2020).

The EUnetHTA collaboration is focused on the technical and scientific assessment. The procedure of appraisal, that is the valuation of the assessment results that supports decision-making, remains the remit of the MS.

¹ http://www.who.int/medical_devices/assessment/en/

² International Journal of Technology Assessment in Health Care (2014) Volume 30 issue 5

EUnetHTA Work Package 7 (WP7) national implementation and impact is one of the work packages in EUnetHTA JA3. The aims of the work package are:

- (1) to provide technical support to EUnetHTA about MS implementation issues, so as to enable EUnetHTA to develop a mechanism of HTA cooperation that successfully takes into account implementation issues at national, regional and local (hospital) levels, and
- (2) to facilitate uptake and use in national, regional and local settings of EUnetHTA products and re-use of HTA reports produced by Member States.

The activities of WP7 start from the foundation that HTA cooperation and use of joint work will be most successful if it fits as far as possible within MS procedural and legal requirements and the HTA documents that are created meet MS information needs. From an understanding of existing working practices, groups of similar working practices can be identified and mechanisms of engagement that complement working practices implemented. Identifying flexibilities and restrictions in procedures supports EUnetHTA to have an understanding of the changes required in MS in order to implement HTA cooperation and the changes EUnetHTA will need to make to implement HTA cooperation. It can also identify areas where MS may need support from EUnetHTA so that implementation challenges can be resolved, so that these are not barriers to cooperation and use.

This study is the first activity of WP7. It aims to describe existing HTA procedures across the different EUnetHTA partners (that is, the 27 EU MS excluding Luxembourg and including Norway and Switzerland), so as to support EUnetHTA to understand how countries could engage in a model of HTA cooperation in Europe and the joint HTA information that would be most valued. The study also supports WP7 to identify ways to support implementation of joint work and sharing of HTA outputs between agencies in different countries. The research builds on the work undertaken in previous EUnetHTA Joint Actions about barriers to implementation³ and the characteristics of national relative effectiveness assessment of pharmaceuticals^{4,5}. It expands the work undertaken in JA1 to include other health technologies and examines each stage of the HTA procedure in more detail.

This report starts by describing the methods of the research (chapter 1) and presenting an overview of the data received (chapter 2). Data provided by agencies for each stage of the procedure is then described and analysed in turn: horizon scanning and topic selection (chapter 3); scoping (chapter 4); assessment and evaluation procedures (chapter 5); quality assurance procedures (chapter 6); timing (chapter 7); use of HTA to inform advice and decision making (chapter 8);

³ [http://www.healthpolicyjrn.com/article/S0168-8510\(15\)00034-2/pdf](http://www.healthpolicyjrn.com/article/S0168-8510(15)00034-2/pdf)

⁴ <http://eunetha.eu/sites/5026.fedimbo.belgium.be/files/Final%20version%20of%20Background%20Review%20on%20Relative%20Effectiveness%20Assessment%2Bappendix.pdf>

⁵ [http://www.valueinhealthjournal.com/article/S1098-3015\(12\)01609-9/fulltext](http://www.valueinhealthjournal.com/article/S1098-3015(12)01609-9/fulltext)

reassessment procedures (chapter 9) and stakeholder involvement (chapter 10). Each chapter summarises key implementation challenges in the HTA processes and makes recommendations for a model of HTA collaboration. The final chapter (chapter 11) describes how within existing HTA and reimbursement procedures, EUnetHTA partner countries can (1) engage in HTA cooperation, (2) use jointly produced EUnetHTA HTA information and (3) re-use national, regional and local HTA information from other jurisdictions. The report is supported by two annex, the first tabulates agency data provided for the analysis and the second includes the case studies used to support the analysis and recommendations.

Chapter 1: Methods of the research

Overall aim

The overall aim of the WP7 study is:

To analyse existing HTA and reimbursement procedures within EUnetHTA partner countries and to identify how these countries within their existing procedures can (1) engage in HTA cooperation, (2) use jointly produced EUnetHTA HTA information and (3) re-use national, regional and local HTA information from other jurisdictions.

Scope of the work

The research included procedures for evaluating pharmaceutical and non-pharmaceutical health technologies used in inpatient and outpatient settings including general practice settings. The research included production of HTA and also use of HTA to inform decision making in national or regional settings. It included national or regional procedures that use HTA-type information (for example reviews of the clinical evidence and economic information) to support decision making.

Public health agencies and academic groups preparing HTA were not included except where WP7 were told that their work directly informed national or regional decision making about the use of health technologies.

Identification of relevant procedures

Relevant procedures were identified using the list of agencies that had been involved in the work undertaken in previous EUnetHTA Joint Actions. This list was cross-checked with published sources including the World Health Organisation Healthcare in Transition reports (WHO HiTs) and the Centre for Innovation in Regulatory Science (CIRS) database. EUnetHTA partners were contacted to ask about other relevant agencies in their country and a protocol including a list of relevant agencies was circulated to partners taking part in the research. A list of agencies contributing information is given in Appendix 1.

Collection of documents

Initially agencies were asked to provide relevant documents such as:

- General documents, articles and presentations describing the health system, how the different agencies in the country interact with each other and their roles within the health system
- Agency procedural documents (for example HTA procedures and policies)
- Legal documents – legislative documents

The initial request was sent via EUnetHTA partners and the request expanded to include other agencies who were not EUnetHTA partners as required.

Documents from centralised sources such as the CIRS database, WHO HiTs, Pharmaceutical Pricing and Reimbursement (PPRI) reports and Gesundheit Österreich GmbH (GOEG) posters and abstracts were also obtained. Documents were requested in English or if not available in English in the local language(s). All documents were centrally stored on the EUnetHTA intranet.

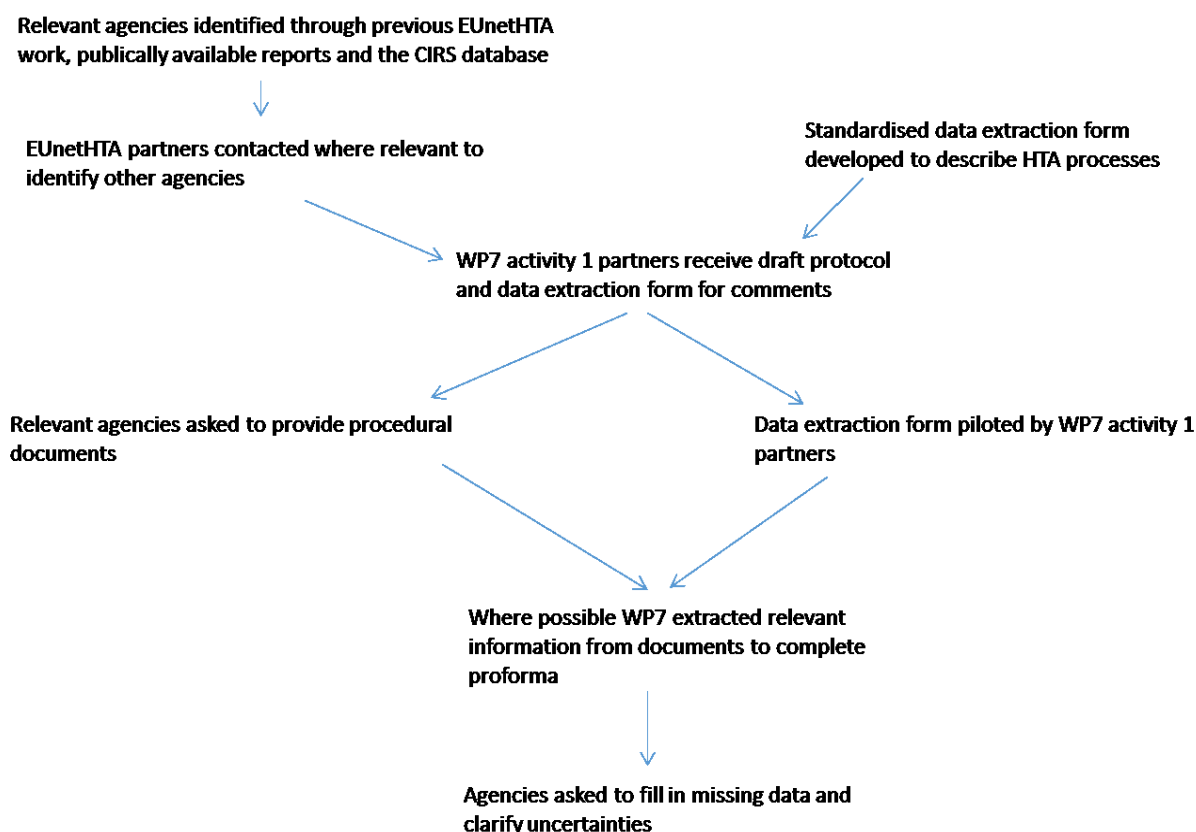
Data extraction

Information about HTA procedures was collated in a standardised Excel data extraction form (appendix 2) including detailed procedural information about the procedure of and responsibility for (1) horizon scanning, topic selection and prioritisation, (2) scoping, production or evaluation and (3) advice and decision making. Information was also gathered about legal and procedural constraints, reassessment procedures, stakeholder involvement, HTA information that agencies hold that could be of relevance to other agencies and HTA information from other jurisdictions that is used to inform work being undertaken by the agency.

The data extraction tool was developed by NICE and used documents developed in EUnetHTA JA2 by ZIN. The tool was piloted by WP7 activity 1 partners (SUKL (Czech Republic), NIPN (Hungary), ISCIII (Spain), SHTG (Scotland), SMC (Scotland), AOTMiT (Poland)) on their own HTA procedures to develop an understanding of the terms and to identify which questions needed to be amended and clarified or if any questions needed to be added.

Following piloting, the data extraction tool was finalised and the other data extractions completed. Initially the project was designed as document analysis, that is the WP7 partners involved in the research would use the documents provided to complete the standardised data extraction forms for each of the EUnetHTA partner countries. However, for many countries sufficiently detailed procedural documents were not available or only partially available in English and these countries completed the data extraction form as a questionnaire. Agencies who were not EUnetHTA partners were contacted either by the EUnetHTA partner for the country or by NICE to try to secure involvement in the project. If an agency could not complete the data extraction form, as much data as possible were obtained from publicly available documents and the agency asked to check.

Figure 1: The data collection and data extraction procedure



Case studies

To support the data analysis, case studies were completed with agencies. The case studies explored agency procedures in detail and also one of two areas (1) how agencies had used EUnetHTA assessments and the adaptations they were making to them, and (2) existing collaborations between agencies to produce HTA.

Six case studies were carried out face to face where NICE met with agency representatives, 3 case studies were carried out virtually, again involving NICE and agency representatives. Participants in the case studies were asked to review the write-up of the case study and also the documents to be made public.

Write up and analysis

The data included in the data extraction forms were written up to describe:

- The similarities and differences in the procedures for producing and using HTA within EUnetHTA partner countries, to include:
 - Procedure and responsibility for topic selection and prioritisation
 - Procedure and responsibility for scoping, production and evaluation
 - Procedure and responsibility for advice and decision making

- Timelines for each stage
- Differences between policies and procedures for the assessment of pharmaceuticals and other technologies
- Legal and procedural restrictions applicable to the procedures
- The re-use of HTA information from other jurisdictions that already occurs

The information was written up by EUnetHTA partners: NICE (England), Agenas (Italy), NIPN (Hungary), SUKL (Czech Republic).

The descriptive write up was used to respond to the following questions:

- Given existing HTA and reimbursement procedures in EUnetHTA partner countries for different types of health technologies.
 - How could (1) collaborative HTA, and (2) HTA products from other jurisdictions be introduced into existing working practices?
 - At what points in the HTA procedure could agencies best engage in HTA cooperation?
 - What products and mechanisms of engagement would be valued by agencies given their ways of working?
- What changes within (1) EUnetHTA procedures and (2) EUnetHTA partner countries could further optimise use and engagement in cooperation

To support this procedure EUnetHTA WP7 activity 1 partners were sent the descriptive write up and a questionnaire (appendix 3) asking them for an agency perspective on the products and engagement they would value given their working practices and also given the data, what recommendations they would make.

The draft report was consulted on with EUnetHTA partners, other HTA agencies who provided data for the analysis and the HTA Network stakeholder groups. Agencies providing data were asked to validate the data used in the report.

Chapter 2: Overview of data received

Key messages

- Data were received from 59 agencies in the 29 countries
- A majority of countries (94%) use some elements of HTA to support decision making about the use of pharmaceuticals.
- HTA activity is generally less established for non-pharmaceutical health technologies with 29% of countries not using HTA to support decision making.
- Of the agencies that assess non-pharmaceutical health technologies few restrict their assessments to medical devices, the majority assess any kind of non-pharmaceutical health technology.
- For pharmaceuticals, all countries consider outpatient pharmaceuticals but 7 (24%) do not consider inpatient pharmaceuticals.
- Countries on average carry out a larger number of assessments of pharmaceuticals than of non-pharmaceutical health technologies.
- For pharmaceuticals:
 - initial assessments with a single intervention are more commonly completed than assessments with multiple interventions
 - the approach used in the assessment is most commonly an assessment of clinical effectiveness and economic information
- For non-pharmaceutical health technologies:
 - initial assessments with multiple interventions are commonly completed as well as assessments of single interventions
 - clinical effectiveness and economic analyses are a common approach, but full HTA is also common and no single approach dominates.

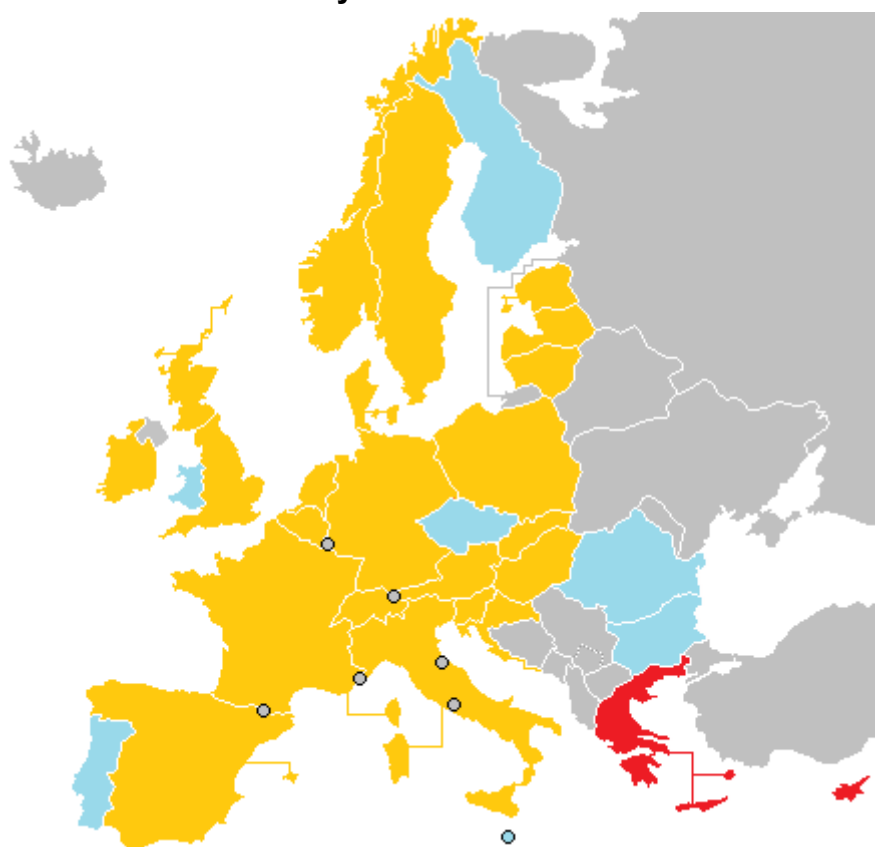
Description of the data received

Countries and agencies providing data

Data were received from 59 agencies in the 29 countries who are part of EUnetHTA (that is, 27 EU Member States excluding Luxembourg and including Norway and Switzerland). Fifty-one of the agencies were EUnetHTA partners. In the majority of cases data received were national. However, for the UK, data were received for England, Scotland and Wales separately, and Spain and Italy provided information about national HTA activities and also regional activities.

Nine case studies were completed involving 21 agencies (including 19 EUnetHTA partners and 2 agencies who are not part of EUnetHTA) in 9 countries. All case studies explored agency procedures, 4 case studies involving 5 countries explored how countries had set up collaborations (Spain, Italy, Netherlands, Belgium and Austria) and 6 explored how agencies had used EUnetHTA products and the adaptations they were making to the products (Finland, Spain, Croatia, Hungary, Scotland and Austria).

Figure 2: Overview of HTA activity



Key: N=31 countries with England, Scotland and Wales counted separately; red = no current HTA procedure; blue = pharmaceuticals only; yellow = both pharmaceuticals and non-pharmaceuticals

All except 2 countries (Greece and Cyprus; figure 2) reported national HTA activity for pharmaceuticals. Both Greece and Cyprus indicated that they are developing HTA procedures to inform reimbursement decisions about pharmaceuticals. Not all countries indicated that they have formal HTA procedures rather they include elements of HTA in their reimbursement procedures. For example:

- Slovenia do not have formally established HTA procedures, but elements of HTA are used for the pricing and reimbursement of medicinal products by their Agency for Medicinal Products and Medical Devices (JAZMP) and in the Health Insurance Institute of Slovenia (HIIS).
- Estonia noted that HTA is formally completed by the University of Tartu to support decision making about technologies to be included in the list of reimbursed health services. However, elements of HTA are also used in the reimbursement procedures of the Estonian Health Insurance Fund (EHIF).
- In Romania the HTA procedure for pharmaceutical reimbursement is in development and is currently based on a scorecard system which takes account of the reimbursement status in other countries, budget impact and availability of local real world data.

In the analysis of pharmaceutical procedures England, Scotland and Wales are counted separately. Therefore the analysis is of 29 countries.

Nine countries indicated that they do not currently have HTA activities for non-pharmaceutical medical technologies. In 2 of these countries procedures are in development to inform reimbursement decisions (Greece and Wales), in a third some HTA activity is carried out but this is not yet routine (Portugal) and in a fourth the HTA procedure is currently subject to reorganisation (Finland). In the analysis of non-pharmaceutical health technologies England and Scotland are counted separately. Therefore the analysis is of 22 countries.

For Italy and Spain information about regional HTA activity was provided in addition to national HTA activity (see case studies 1 and 2). Profiles from 8 regional agencies were received (2 regions in Italy and 6 regions in Spain). All regions carry out HTA activities for non-pharmaceutical health technologies, 6 regional agencies (OSTEBA, SCS, AQuAS, avalia-t and AETSA all in Spain and Veneto in Italy) also carry out activity for pharmaceuticals.

Case study 1: Involvement of the regions in national HTA in Spain

Healthcare in Spain was originally centralised but became decentralised between 1980 and 2000. Each region (17 Autonomous Communities and 2 Autonomous Cities) is responsible for the healthcare budget and provision of healthcare products within their territories. The National Health System is coordinated by the Interterritorial Council of the National Health System (ICNHS), where all the Regional Health Authorities sit under the presidency of the Minister of Health. From this high level governing body, there are multiple technical commissions and working groups that include representatives from the regional Health Services and the national Health Ministry. Although health care is decentralised, there is a common portfolio of services for the National Health System that is comprehensive, both in the extension of coverage and the scope of services included and which must be provided and guaranteed by the regions. The regions can widen this common portfolio of services, depending upon having enough financial resources and informing the ICNHS of the reasons for such measures. The updating of the common portfolio of services legally requires conducting health technology assessment, however, the reports are not binding.

Non-pharmaceutical health technologies

The Spanish Network of HTA Agencies is a collaboration of eight HTA agencies (7 regional and 1 national) working together to produce national HTA of non-pharmaceutical technologies in Spain. HTA is completed by each agency individually and there is mutual recognition of reports between agencies and shared methods and templates. The agencies work collaboratively to develop guidelines and tools to support their procedures. The reports produced by the Spanish Network are

commissioned and funded by the Spanish Ministry of Health to inform decisions about any update of the NHS common portfolio of services. The decision to include a new technology in the common portfolio is proposed by the Committee for Provision, Insurance and Financing (including representatives from each of the regions in Spain) by consensus, signed off by the Interterritorial Council and the Ministry of Health makes the final decision through a legal instrument. These reports can also be useful to help regional decision making.

Pharmaceuticals

The Spanish Medicines Agency (AEMPS) produce assessments of medicinal products called therapeutic positioning reports. The therapeutic positioning reports are developed and adopted by consensus within the Co-ordination Group for Therapeutic Positioning (GCPT). The GCPT includes representation from AEMPS, Directorate-General for NHS Basic Services Portfolio and Pharmacy (DGCBSF) and the 17 regional health authorities, responsible for the healthcare budget and provision of healthcare products within their territories. The GCPT support the topic selection, prioritisation (if required), scoping and work allocation process. The first draft of the report written by AEMPS is then reviewed by usually 2 regional health authorities who will agree with AEMPS on a draft to be reviewed by stakeholders. The conclusions in the reports are adopted by consensus with the 17 regional health authorities and are expected to be followed by those authorities in the exercise of their competences. The recommendations tend to be general rather than specific allowing for some flexibility in their implementation to also ensure that decision makers responsible for procurement are able to negotiate their own purchasing arrangements. The conclusions in the reports are also taken into account as a non-binding initial step in the process of Pricing and Reimbursement of the medicine, led by the DGCBSF in the Ministry of Health. The DGCBSF produce therapeutic/pharmacoeconomic reports as part of the formal Pricing and Reimbursement process to give support to Pricing Committee decision making.

Case study 2: The Italian Network of HTA

Since 2010 there has been a voluntary HTA network in Italy (La Rete Italiana di HTA (RIHTA)) that includes Agenas and representatives of 13 of the 21 regions. The aim of the network is to reduce duplication in assessment and support training and capacity building. Agenas coordinates the RIHTA network and regions take part in the network in different ways depending on their capacity.

The network assesses non-pharmaceutical health technologies. Topics for assessment are sent to the MoH from a public notification system. Referrals are most frequently from clinical and scientific associations, MoH, regions and hospitals. Topics referred are prioritised by a Committee including the MoH, Agenas and representatives of the regions (the regions elect a small number of regional representatives to reflect the regional perspective, rather than the perspective of

their own region). The regional representatives tend to be from those regions who are most active in HTA with an interest in the topic. Once topics are selected and prioritised Agenas coordinate the allocation of work to agencies.

To carry out an assessment, 2-4 agencies will be involved in supporting development of the PICO and carrying out the assessment. The group will decide which agencies are involved in which sections of the assessment. The network has produced a manual that describes the procedures and methods to be used and there is a single report structure for assessments. Reports are completed using an adapted version of the HTA Core Model[®] and use EUnetHTA tools to support assessment. The reports include all areas of HTA including comparison of the cost of comparable alternatives.

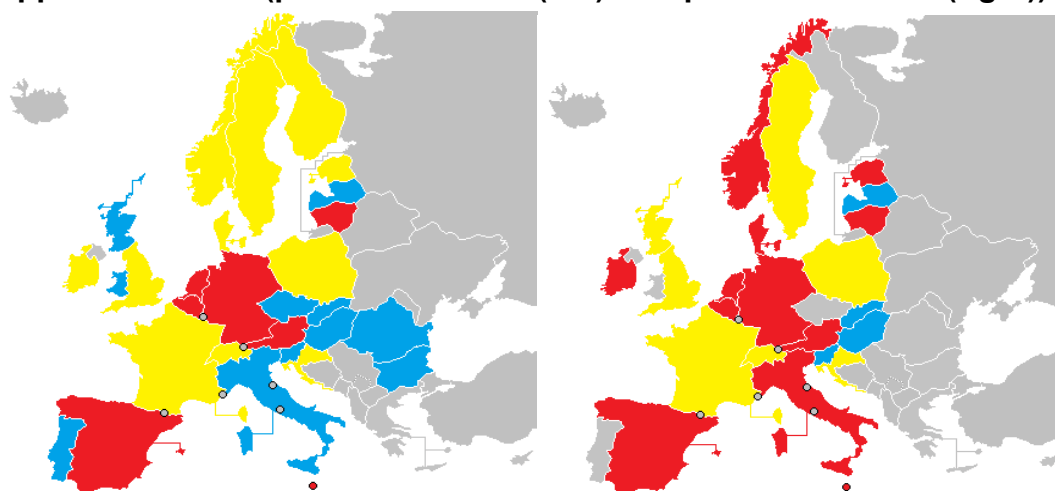
Assessments completed through the RIHTA network contain recommendations to inform decision making. The recommendations may be directed to national decision makers (for example, the Commissione Nazionale LEA (the Committee for the basic level of healthcare)), regional healthcare directorates and procurement agencies and local healthcare trusts and hospitals. The reports have public consultation before being finalised and are published on the Ministry of Health and Agenas websites.

Assessment and evaluation

Some agencies carry out HTA and some evaluate the appropriateness of HTA information that is usually provided by industry (figure 3; see also case study 3). For pharmaceuticals, 7 countries (24%) only carry out their own assessments, 11 countries (38%) only make decisions by receiving a submission of evidence and evaluating its appropriateness and 11 countries (38%) carry out some assessments, but their number may be limited. For example, in Poland, England, Croatia, Finland, Ireland, Switzerland and Estonia the majority of decisions about using a technology are made by evaluating a company submission rather than an agency undertaking their own HTA. In addition, some agencies combine approaches, for example ZIN (the Netherlands) and RIZIV (Belgium) undertake their own REA assessment, but evaluate company submissions of cost effectiveness evidence.

For non-pharmaceutical health technologies 11 countries (50%) carry out their own assessments, only 4 countries (18%) solely evaluate information provided in submissions of evidence and 7 countries (32%) use both approaches.

Figure 3. Countries with agencies carrying out assessment of REA and appraisal of REA (pharmaceuticals (left) non-pharmaceuticals (right))



Key: Red = agencies in country carry out REA assessment, Blue = agencies in country evaluate REA submissions of evidence, Yellow = some agencies or programmes within an agency carry out REA assessment activities while some evaluate assessments provided by industry.

Case Study 3: Assessment and appraisal in Croatia

Production of HTA at AAZ

The Agency for Quality and Accreditation in Health Care and Social Welfare (AAZ) produces HTA on a range of health technologies as STA or MTA to support national decision making by CHIF and the MoH. The reports produced by AAZ include information about the condition, the technology, clinical evidence, cost and a summary of published cost effectiveness evidence. For non-pharmaceutical health technologies relevant information about organisational, legal and ethical issues will also be included. AAZ include recommendations in their report. These include information about the use of a technology and also how a technology should be used. Once AAZ have delivered a report they are not involved in the decision making.

Appraisal of HTA information at CHIF

The Croatian Health Insurance Fund (CHIF) make decisions about the reimbursement of pharmaceuticals and non-pharmaceutical health technologies. CHIF do not produce assessments, instead they appraise evidence that is provided by a company when it submits for reimbursement. Production of HTA in Croatia is not currently mandatory within decision-making procedures, therefore CHIF do not have to request HTA from AAZ to support their decision making. CHIF ask AAZ to produce HTA for them to use in situations where they require further information to

inform their decision, for example where there is significant budget impact or a large number of treatments coming to market in quick succession.

Inpatient and outpatient

In the majority of countries the HTA procedures apply to both inpatient and outpatient interventions and are carried out by the same agency. In 3 countries, different agencies are involved depending on whether the intervention is inpatient or outpatient (Denmark, Finland and Austria).

For pharmaceuticals, 7 countries only carry out HTA assessments of outpatient treatments (Austria, Czech Republic, Germany, Latvia, Lithuania, Slovakia, and Switzerland). For non-pharmaceutical health technologies 2 countries reported using HTA to assess outpatient interventions (Latvia, Slovakia). A third country (Austria) reported that HTA is carried out for inpatient interventions and that some HTA is carried out for outpatient interventions but activity is not routine.

The definition of an inpatient and an outpatient intervention differs between countries. Most commonly an inpatient pharmaceutical was one where the dispensing status was limited to use in hospitals. However, for some countries the definition was more or less stringent. For example health insurance legislation in Switzerland defines an inpatient treatment as a treatment that requires a patient to spend at least one night in hospital. In contrast in Finland an inpatient treatment is 1) a medicine intended to be used mainly in public hospitals; 2) payer of the medicine is the hospital; 3) administration of the treatment requires a hospital environment.

Other restrictions to types of technologies assessed

Twenty-one countries reported no other restrictions to the type of pharmaceuticals they would assess, 8 reported that they do not assess generics or that a generic treatment has a simplified assessment. Some countries indicated that they only do new international non-proprietary names (NCPHA, Bulgaria) while others indicated that they usually only do new medicines or indications (AEMPS, Spain; NCPE Ireland). In addition, 3 countries specified they do not assess vaccines (NICE, England, SMC, Scotland, NIPN, Hungary). One each indicated that they do not assess haemophilia (NICE, England), treatments for HIV (NICE, England), contraceptives (HVB, Austria) and blood products (SMC, Scotland).

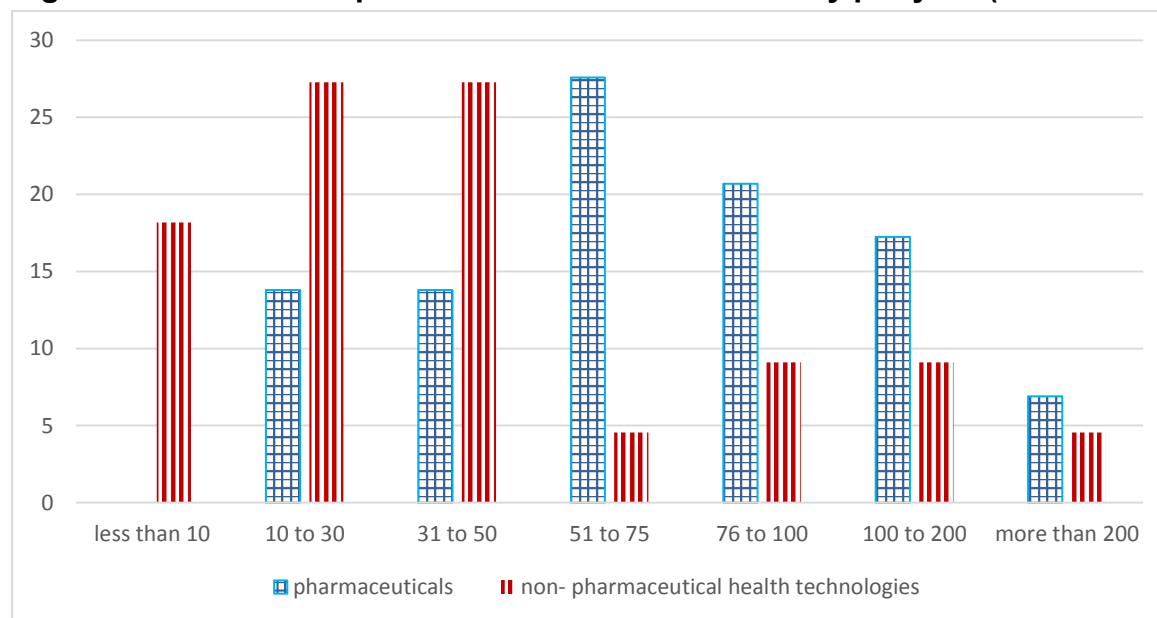
For non-pharmaceutical health technologies 4 countries indicated that the data provided was for the assessment of medical devices (Slovakia, Latvia, Lithuania, Hungary). In other countries data were received from multiple agencies or for multiple programmes within a single agency, where some had a narrower remit while others had a broader remit (for example, Belgium (RIZIV vs KCE), Estonia (EHIF vs UT), Sweden (TLV vs SBU)). Thirteen countries indicated there were no restrictions in the type of non-pharmaceutical technology they would assess, one country indicated that they would only usually assess high risk (IIb and III) medical devices

(LBI-HTA, Austria) and other countries indicated that there were specific restrictions to particular programmes, for example the medical technology needed to offer the same benefits at lower costs or more benefits at equivalent costs (MTEP programme NICE, England) or be a diagnostic, prognostic or monitoring technology (Diagnostics assessment programme, NICE, England), to be a medical device for patient use (NIPN, Hungary), or a medical device for use by physicians in hospitals (NIPN, Hungary), to be innovative (SHTG, Scotland) or to be suitable for potential disinvestment (HTA programme, Switzerland). One of the regional agencies (ASSR-RER, Italy) indicated that they would assess capital equipment (for example CT scanners, MRIs, Linear Accelerators, PET scanners, surgical robots), technologies with a significant economic impact and innovative technologies. Other regional agencies indicated no restrictions to the type of technologies assessed.

Number of topics

The number of topics considered across the countries varies considerably (figure 4). The number of assessments or evaluations of pharmaceuticals ranges from approximately 20 per year to 500. For non-pharmaceutical health technologies the range is less than 10 per year to up to 400. In general, across countries a greater number of pharmaceutical than non-pharmaceutical HTAs are carried out. Among the regional agencies the number of assessments carried out ranges from an average of 3 (UETS Madrid, Spain), to 40 (AQuAS, Spain).

Figure 4: Number of topics considered in each country per year (% countries)



Key: Data for 29 countries (pharmaceuticals) and 22 countries (non-pharmaceutical health technologies)

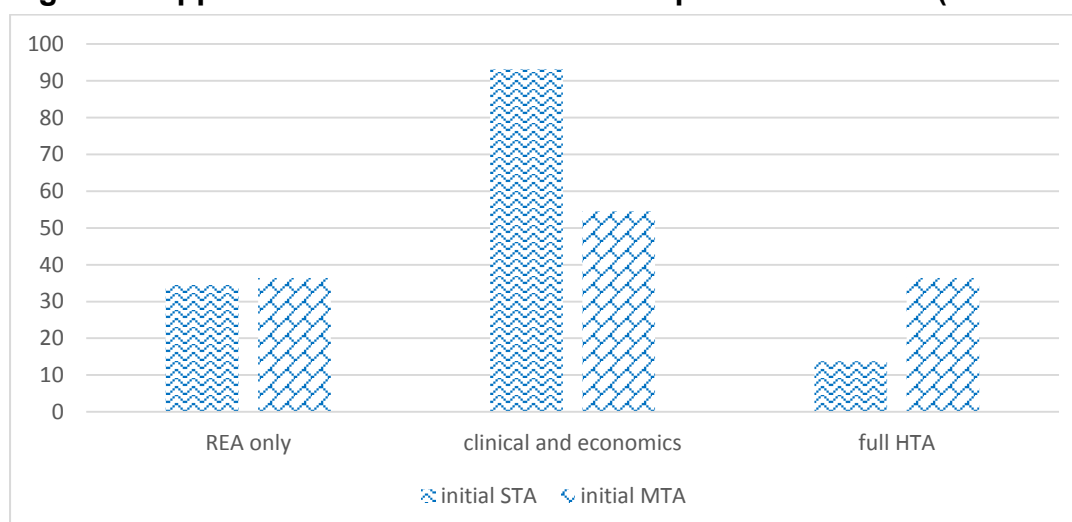
Type of initial assessment carried out for pharmaceutical technologies

For pharmaceuticals, all countries (100%) reported carrying out initial assessments of pharmaceuticals where there is a single intervention compared to one or more comparator products (single technology assessment; STA). Eleven out of 29 countries (38%) also reported carrying out initial assessments of pharmaceuticals where the assessment can include more than one intervention or indication (multiple technology assessment; MTA). MTA is rarely used across all programmes and agencies in a country, for example in Austria, GOEG but not HVB may do MTA, in Sweden, SBU but not TLV, in Norway NIPHNO but not NOMA.

The approach used in initial STA of pharmaceuticals is most frequently assessment of clinical effectiveness with economic analyses (93%; figure 5). Economic analyses can include health economic modelling using cost effectiveness or cost utility analysis, reviews of health economic literature, budget impact analysis or cost comparisons. Less frequently initial STA is carried out either as only relative effectiveness assessment (REA) (34%) or as a full HTA (14%) (that is, including clinical effectiveness and economic analyses but also legal, ethical and social aspects).

In contrast, in countries completing initial MTAs there is less difference between the proportions completing REA, REA and economic analyses and full HTA (36%, 55%, 36% respectively). In the majority of countries a single approach to the assessment is adopted, but 5 countries (Poland, Sweden, Switzerland, Austria (GOEG), Netherlands) indicated that the approach to completing initial assessments can vary. The reasons given for using different approaches included data availability or the requirements of the decision maker. The Netherlands indicated that the approach depends primarily on the result of the REA.

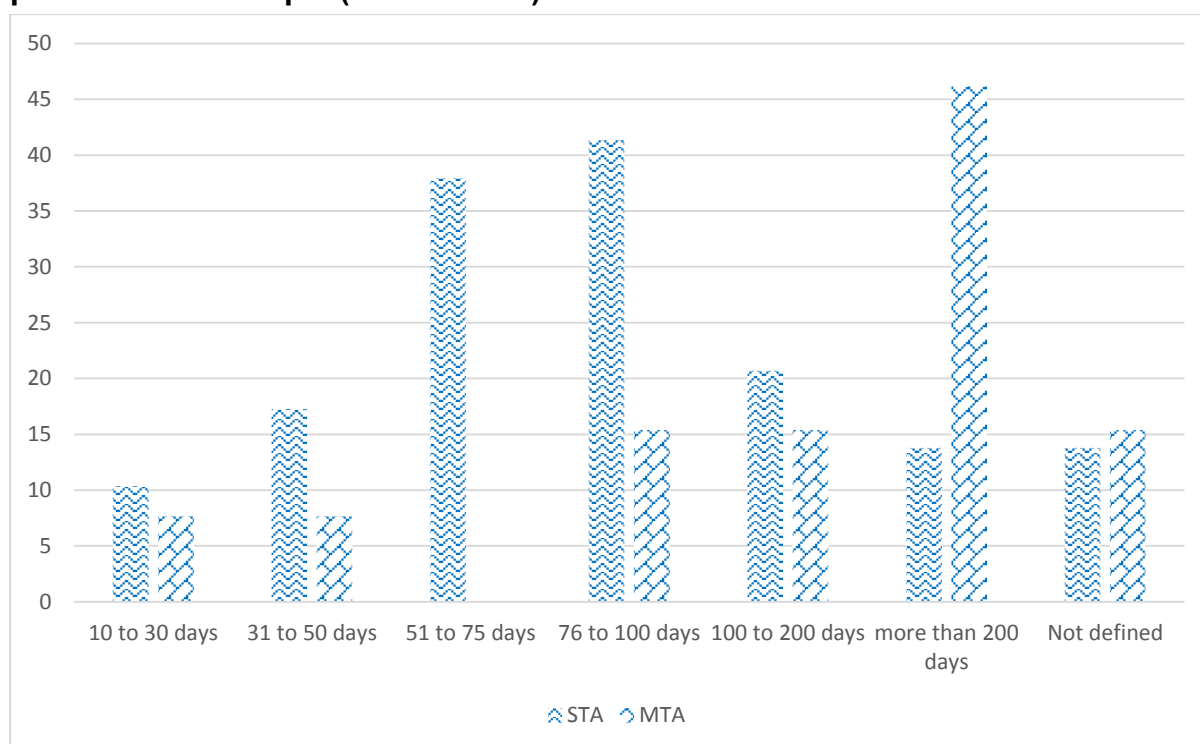
Figure 5: Approach to initial assessment of pharmaceuticals (% countries)



Key: Data for 29 countries. Agencies coded multiple categories so data may add up to more than 100%.

The time taken for an STA (figure 6) varies from a minimum estimate of 1-2 weeks (provided by GOEG (Austria) for a quick assessment within a limited timeframe) to the longest time 14 months (KCE, Belgium). The time taken for an MTA varies from 2 weeks (minimum estimate provided by CHIF for an appraisal in Croatia) and 24 months (maximum estimate provided by SBU for an assessment in Sweden).

Figure 6: Time taken to complete an assessment or evaluation of a pharmaceutical topic (% countries)



Key: Data for 29 countries (pharmaceuticals). Agencies coded multiple categories so data may add up to more than 100%.

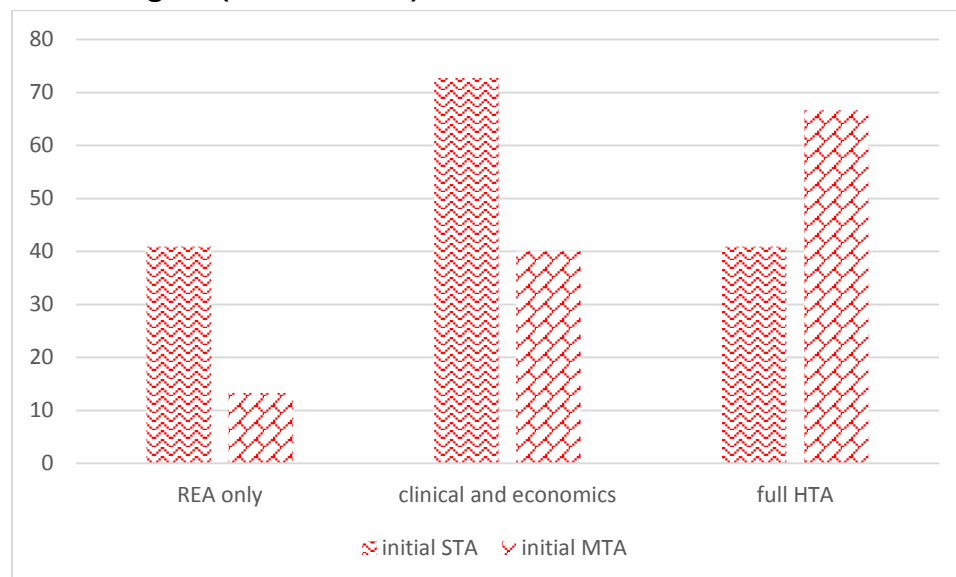
Type of assessment carried out for non-pharmaceutical health technologies

All countries (100%) with procedures for non-pharmaceutical health technologies carry out initial STA. Fifteen countries (68%) also carry out initial MTA. All regional agencies carry out initial MTAs and 5 out of 6 (all except ASSR-RER) carry out initial STAs.

The approach used in STA of non-pharmaceutical health technologies is most frequently assessment of clinical effectiveness and economic analyses (73%). Less frequently initial STA is carried out either as only REA (41%) or as a full HTA (41%). In contrast in countries completing initial MTAs, these are more likely to be completed as full HTAs (67%). The majority of countries used a single approach to the assessment, 7 countries indicated that the approach to completing initial assessments can vary depending on need. The Netherlands indicated that the

approach depends primarily on the result of the REA and that they rarely carry out cost effectiveness analysis for non-pharmaceutical health technologies (figure 7).

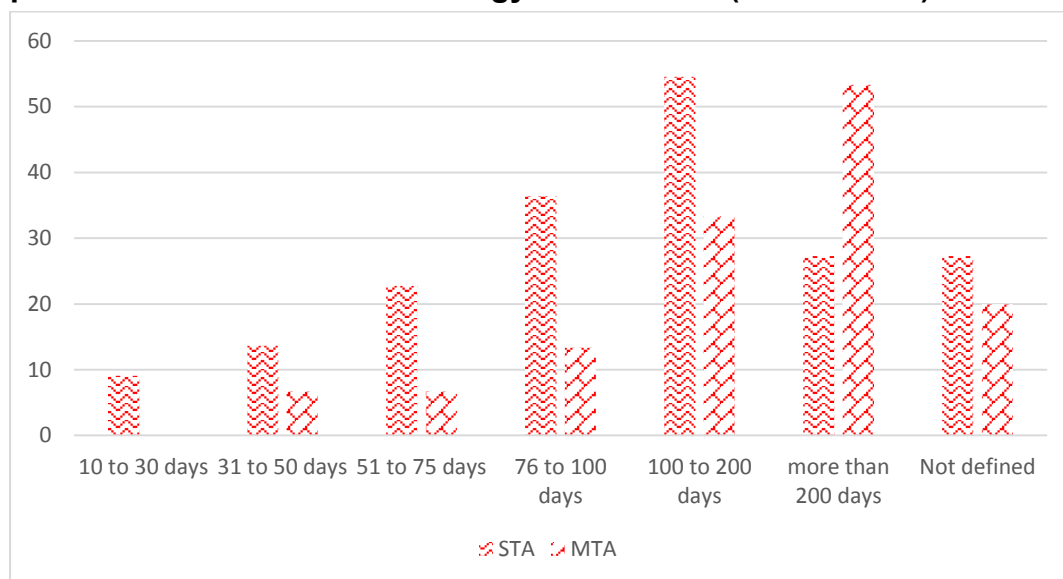
Figure 7: Approach to initial assessment of non-pharmaceutical health technologies (% countries)



Key: data for 22 countries. Categories not mutually exclusive so data may add up to more than 100%.

The time taken for an STA varies (figure 8) from a minimum estimate of 1-2 weeks provided by GOEG for a quick assessment with a limited timeframe in Austria to 24 weeks for an assessment provided for the diagnostics assessment programme in NICE, England (assessments in this programme would normally be MTAs, but where there is a single intervention, the timelines for an STA are the same as for MTA). For MTA the lowest value was provided by the Croatian Health Insurance Fund (CHIF) of 15-60 days for an appraisal and the highest value provided by FOPH in Switzerland with 1.5 to 2 years for an assessment. Among the regional agencies the range of timings for an assessment also vary with a lower estimate of 4 weeks provided by AQuAS and an upper estimate of 76 weeks provided by OSTEBA.

Figure 8: Time taken to complete an assessment or evaluation of a non-pharmaceutical health technology assessment (% countries)



Key: Data for 22 countries. Agencies coded multiple categories so data may add up to more than 100%.

Information from other jurisdictions used to support national procedures

For pharmaceutical assessments 21 out of 29 countries (72%) indicated that they use information from other jurisdictions to support their procedures. Both Wales and Scotland indicated that the other information used comes from the other countries of the UK. Ireland (NCPE) and Germany (G-BA) indicated that information if it is used at all is only used for background purposes or additional information. For non-pharmaceutical health technologies 18 out of 22 countries (82%) indicated that they use information from other jurisdictions to support their assessment procedure.

Some agencies in their responses cited using documents from other agencies in their country rather than from agencies in other countries. For example in Croatia information from AAZ is used by CHIF, in Belgium RIZIV make use of information from KCE and in Sweden TLV make use of information from SBU, the medicines agency, guidelines from National Board of Health and Welfare and County Councils. In addition, in some countries the initiator of the assessment is asked to supply information about assessments and recommendations for a technology in other countries as part of the submission procedure rather than an agency having to identify this information directly.

Chapter 3: Horizon scanning and topic selection procedures

Key messages

- Horizon scanning and topic selection procedures support the timely, identification of appropriate assessment topics.
- A minority of countries (34% and 45% for pharmaceuticals and non-pharmaceutical health technologies, respectively) have horizon scanning procedures to support topic selection.
- For pharmaceuticals, in 90% of countries industry play a key role in topic selection and the timing of an assessment, usually through submission of an application for reimbursement or pricing which then initiates a procedure.
- In approximately half of countries the HTA agency has a role in choosing the topics. Aside from industry, organisations frequently responsible for topic selection are payers and MoHs, and additionally for non-pharmaceutical health technologies regional authorities, medical societies and providers.
- Approximately half of countries (52%) use topic selection and prioritisation criteria for pharmaceuticals. A larger proportion use them for non-pharmaceutical health technologies (68%).
- Where prioritisation criteria are applied the most frequently used criteria are:
 - economic and resource impact;
 - potential health benefits;
 - severity or burden of the disease;
 - population size;
 - importance to healthcare and/or innovativeness.
- Countries rarely have significant advance notice that an assessment is required (76% and 50% with no advance notice for pharmaceuticals and non-pharmaceutical health technologies, respectively).
- HTA collaboration should be forward-looking and build predictability into the system to respond to the unpredictability of HTA requests in many countries

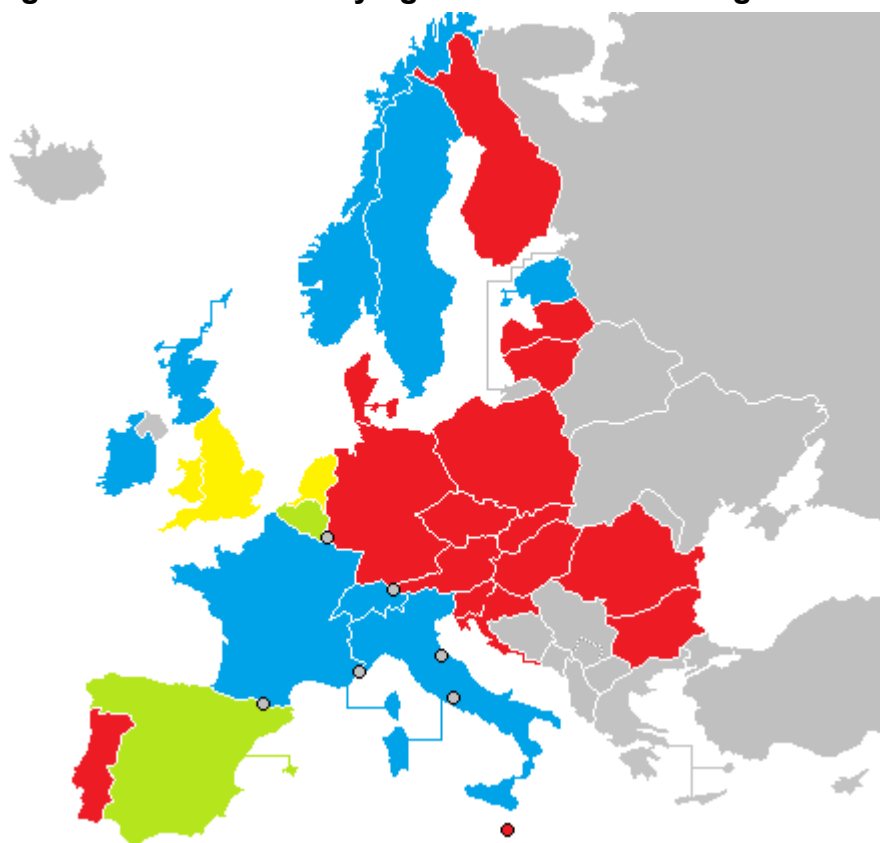
Description of horizon scanning systems to support topic selection and workload planning

For pharmaceuticals, 10 countries out of 29 (34%) use horizon scanning (that is, the systematic identification of health technologies that are new, emerging or becoming obsolete and that have the potential to affect health, health services and/or society) to support topic selection or workload planning. Horizon scanning may not be used formally, for example RIZIV (Belgium) and in some agencies horizon scanning is only used for certain technologies. For example ZIN (Netherlands) and HAS (France) indicated that horizon scanning activities occur for activity that is planned by the agency rather than activity initiated through a company submission. In some countries systems are currently in development, for example TLV (Sweden), DPA/MFH (Malta) and INFARMED (Portugal) (See figure 9).

For non-pharmaceutical health technologies, 10 out of the 22 countries (45%) use horizon scanning. For one agency (RIZIV, Belgium), the procedure is used for invasive medical devices only. Three countries (NICE, England; TLV, Sweden and FOPH, Switzerland) indicated that horizon scanning systems are in development.

In countries where horizon scanning is not used, in most cases industry submit an application and the agency assesses all submitted applications. In other cases the topic is requested by a decision maker (e.g. MoH) or payer.

Figure 9. Countries carrying out horizon scanning



Key: **Red** = countries which do not carry out horizon scanning **Blue** = countries which carry out horizon scanning for pharmaceuticals and non-pharmaceutical health technologies **Yellow** = countries which carry out horizon scanning for pharmaceuticals only **Green** = countries which carry out horizon scanning for non-pharmaceutical health technologies only

For pharmaceuticals, of the 10 countries using horizon scanning, 5 use internal procedures, 2 use external procedures and 3 use a combination of both internal and external procedures. External systems include using documents from other HTA agencies (for example produced by KCE in Belgium) or from other academic organisations (for example the UK, National Institute for Health Research Innovation Observatory (NIHRIO)) or active engagement with decision makers and providers (such as MoHs, County Councils, professional organisations). Internal systems include databases that companies use to notify topics (for example UK Pharmscan)

or requiring companies to submit horizon scanning documents in advance of applying for reimbursement (Ireland, NCPE).

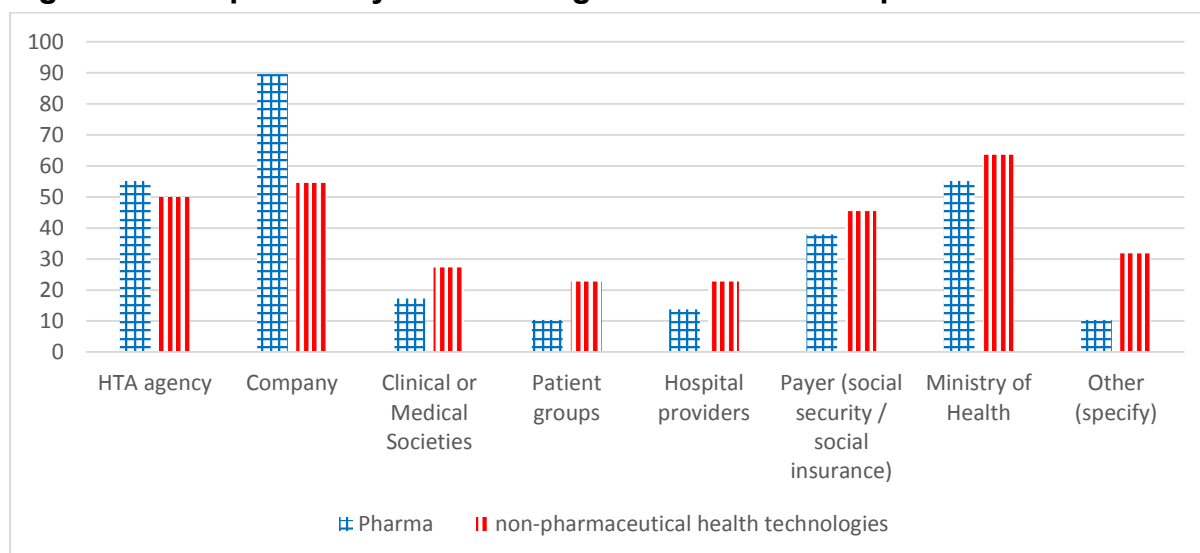
For non-pharmaceutical health technologies, of the 10 countries using horizon scanning 3 report external procedures (the same external procedures as used for pharmaceutical horizon scanning) and 7 report internal horizon scanning procedures. For non-pharmaceutical health technologies internal horizon scanning includes literature searching, database analysis, as well as other sources such as companies, clinical and patient experts and notification systems.

Among the regional agencies, horizon scanning is undertaken by 4 regional agencies. The three Spanish regional agencies (AETSA, avalia-t, OSTEBA) described a coordinated approach between the agencies (also including a Spanish national agency ISCIII) where each agency is responsible for scanning one or more information sources and the compiled results are provided to the MoH. The procedure undertaken includes literature searches, liaison with experts, media scanning and searching other databases such as Euroscan, the ECRI Institute and The International Network of Agencies for Health Technology Assessment (INAHTA). Formal compilation occurs annually, but the horizon scanning procedure is in place continuously through the year. ASSR-RER (Italy) indicated that some horizon scanning may occur for medical device short reports and reassessments. This is undertaken internally through literature searching.

Description of topic selection procedures

Topic selection: Responsibility for choosing assessment topics

Figure 10. Responsibility for choosing the assessment topics



Key: pharmaceuticals N=29, non-pharmaceutical health technologies N=22. Agencies coded multiple categories so data may add up to more than 100%.

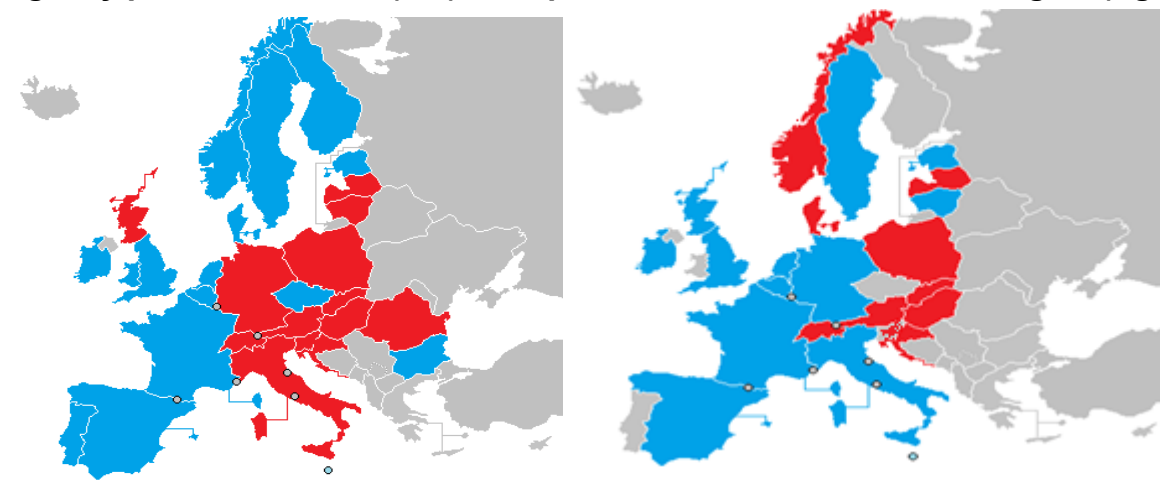
For pharmaceuticals, the group most frequently cited as having a responsibility for topic selection were industry (26 out of 29 countries (90%)), followed by the HTA agency (16 out of 29 countries (55%)) and MoHs (16 out of 29 countries (55%)). 'Other' groups with a responsibility for topic selection include policy experts, regional health authorities and other government Ministries. The involvement of the agency varies between agencies within a country for example, in Finland FIMEA has involvement in topic selection but not HILA, in Estonia UT but not EHIF and in Sweden SBU but not TLV (case study 4; figures 10 and 11).

Case study 4: Responsibility for selecting assessment topics at ZIN in the Netherlands

The largest number of assessments produced by Zorginstituut Nederland (ZIN) are for non-hospital pharmaceutical technologies. ZIN does not have to carry out assessments of all pharmaceutical technologies (e.g. not all pharmaceuticals used in hospital) and will not assess generics. For non-hospital pharmaceuticals the company initiates the assessment by applying for reimbursement. For inpatient pharmaceuticals ZIN selects technologies for assessment and plans assessment activity. For non-pharmaceutical health technologies requests for assessment can be received from a range of stakeholders (including patients, payers and industry) and ZIN will assess whether the request for assessment is appropriate before undertaking activity. However, ZIN are obliged to carry out assessment following a request from the Ministry of Health.

For non-pharmaceutical health technologies, there is less involvement of industry, and MoHs are the most frequent group involved (14 out of 22 countries (64%)) followed by industry (12 out of 22 countries (55%)), payers (10 out of 22 countries (45%)) and the HTA agency (11 out of 22 countries (50%)). The 'other' groups coded for non-pharmaceutical health technologies are similar to pharmaceuticals but there is also greater involvement of regional groups (e.g. Denmark, Italy, Norway and Spain). A small number of countries mentioned they have open referral systems where anybody can submit topics (for example Scotland and Italy). As with pharmaceuticals not all agencies in all countries are necessarily involved in the procedure.

Figure 11. Map showing responsibility for topic selection resting with the HTA agency pharmaceuticals (left); non-pharmaceutical health technologies (right))



Key: **Red** = countries where HTA agency is not responsible for selecting the topics for assessment, **Blue** = countries where at least one HTA agency has some responsibility to select the topics for assessment

All regional agencies in Spain indicated that the regional MoHs have a responsibility for topic selection. In half of the agencies the HTA agency also has responsibility for choosing the assessment topic and the procedure is often also supported by clinical experts and hospital managers from the regions. In Italy ASSR-RER indicated that they select the topics that they assess with requests coming from regional health trusts or departments or Committees of the health directorate.

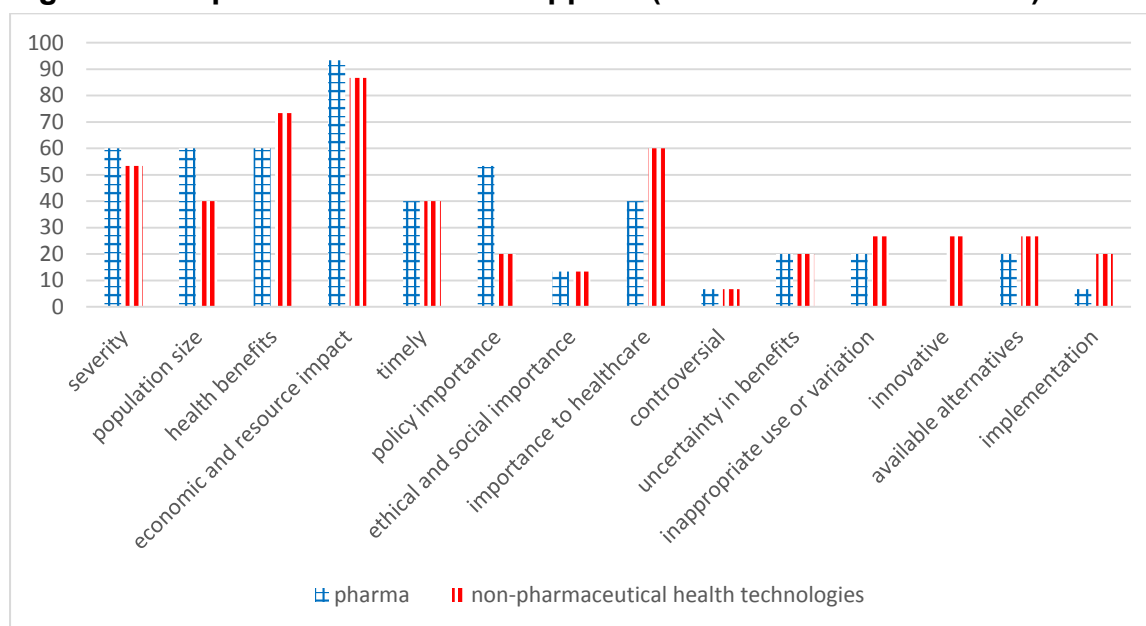
Topic selection criteria

Not all countries use topic selection criteria and prioritisation criteria because they complete assessments for all technologies for which an application is submitted or requested, or which meet certain general product criteria. However, in some countries, agencies may choose from the eligible pool of topics or prioritise the topics once an assessment is requested. This is more common for non-pharmaceutical health technologies than for pharmaceuticals.

For pharmaceuticals, 15 out of 29 countries (52%) indicated that there are some kind of topic selection or prioritisation criteria. In two countries these are mainly practical or pragmatic criteria, for example in Bulgaria (NCPHA) the procedure is terminated if there is negative guidance produced by the UK, France or Germany. In Austria (HVB) a product must be available and deliverable by the company and for chronic diseases appropriate pack sizes must be available for treatment initiation and longer term treatment. In addition in Scotland (SMC) selection criteria are only applied to minor licence extensions where, if the population size is very low, a submission might not be requested. In Wales (AWTTC) criteria based on expected health

benefits and likely economic impact are applied to decide whether a full or limited submission is required (figure 12).

Figure 12: Topic selection criteria applied (% countries with criteria)



Key: pharmaceuticals N=15, non-pharmaceutical health technologies N=15. Agencies coded multiple categories so data may add up to more than 100%.

For pharmaceuticals, the most commonly used criteria are:

- economic and resource impact
- severity or burden of the disease
- potential health benefits
- population size

For non-pharmaceutical health technologies, 15 out of 22 countries (68%) have topic selection or prioritisation criteria.

- economic and resource impact
- potential health benefits
- importance to healthcare and/or innovativeness
- severity or burden of the disease

In Spain the prioritisation criteria for assessment are coordinated between the regional HTA agencies and all use the PriTec tool. The criteria for prioritising assessments include:

- characteristics of the population and the disease (frequency of use, disease burden, health impact, vulnerable populations),

- the characteristics of the health technology (effectiveness, safety, innovative technology, invasive technology, with other potential uses)
- the available evidence on comparative results
- issues related to implementation (organizational and budget impact, ethical, social, cultural and legal implications) and use of the technology (benefits for the health care practice, benefits for clinicians, interest/demand and rate of adoption)

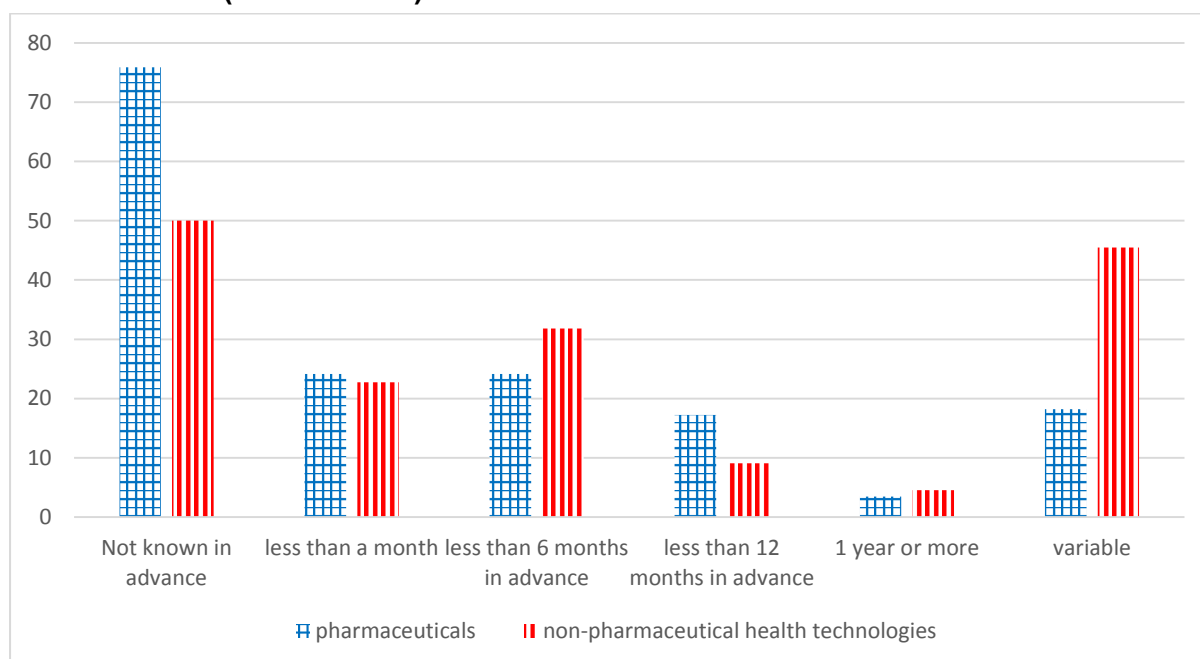
In Italy Veneto indicated topic selection and prioritisation takes account of topics carried out by EUnetHTA and the Italian HTA agency Network (RIHTA) and also economic and/or organisational impact and risk of inappropriate use.

Predictability of timing of assessment initiation

For pharmaceuticals, in 22 out of 29 countries (76%) at least one agency in the country does not know in advance that they will need to carry out an assessment. In addition Portugal, and Malta indicated that the period of advanced notice is variable, but that there can be no notice and Croatia indicated that they may only receive a couple of days notice and up to 2 weeks notice (case study 5). In some of these instances even though there may be no notice the agency expects that all products meeting eligibility criteria will be considered (for example, HVB, Austria; AEMPS, Spain; SMC, Scotland; AWTTC, Wales) and in the case of Scotland and Wales they use horizon scanning and actively engage companies so that it is known in advance when the procedure may be initiated. Of the countries who usually have advanced notice the longest notice is for NICE, England where it can be longer than 12 months. Ireland (NCPE) may have up to 12 months notice as may France (HAS) and the Netherlands (ZIN) for some technologies only (figure 13).

For non-pharmaceutical health technologies there are fewer countries where agencies do not know in advance that they will need to carry out an assessment (11 out of 22 countries (50%)) and compared to pharmaceuticals the period of notice that an assessment is required is more likely to be variable. However, for agencies who do receive advanced notice of an assessment being required, the period of notice is still relatively short and normally less than 6 months.

Among the Spanish regional agencies the assessments that are coordinated as part of the Spanish Network are part of an annual work plan. For assessments conducted for regional authorities the agencies tend to know 1 month in advance that they have to carry out an assessment.

Figure 13. How far in advance does an agency know it will need to carry out an assessment? (% countries)

Key: pharmaceuticals data for 29 countries, non-pharmaceutical health technologies N 22. Agencies coded multiple categories so data may add up to more than 100%.

Case study 5: Predictability of assessment in Croatia

Topic requests for assessment to AAZ come from the decision makers: Ministry of Health, The Croatian Health Insurance Fund (CHIF) or hospital managers. AAZ does not select the topics that it assesses and decision makers do not have to ask AAZ for HTA because the use of HTA is not mandatory for decision making in Croatia. This means there is little predictability about the topics that will be requested for HTA. Once an assessment is requested it is often needed at short notice. For pharmaceuticals there is a written requirement in the law to provide an HTA within one month of the request. This timeframe can be met where there is an existing HTA (from another country or EUnetHTA) that can be adapted, but is difficult to meet in other situations. These factors mean that there are challenges when coordinating requests from national decision makers with topic selection for EUnetHTA assessments and that AAZ may not be able to do a national adaptation of EUnetHTA assessments immediately after the publication.

AAZ manage this challenge by alerting decision makers to the topics that are undergoing EUnetHTA assessment and producing a translated summary of the EUnetHTA assessment. AAZ prepares a summary of the EUnetHTA assessment in Croatian with information about the technology, comparators and regulatory status. These summaries are published on the AAZ website, with links to the full EUnetHTA assessment. These documents are not used for decision making, but if a decision maker subsequently requests the topic as an assessment from AAZ, the report is updated with additional information required for the Croatian decision making context.

and including recommendations about the health technology. Because of the risk of appeals from stakeholders AAZ do not create HTAs with recommendations that are not requested by decision makers.

Information from other jurisdictions used to support horizon scanning and topic selection

Eight out of 29 countries (28%) report using information from other jurisdictions to support horizon scanning for pharmaceuticals and 9 out of 22 countries (41%) for non-pharmaceutical health technologies. The corresponding figures for topic selection are 10 (34%) and 10 (45%), respectively. The relatively low figures for horizon scanning and topic selection are likely explained by the fact that for a number of countries, assessment particularly of pharmaceuticals are primarily initiated by industry or other organisations rather than the HTA agency.

Of the countries offering further information, in Bulgaria (NCPHA) pharmaceutical HTAs from other countries are reviewed, if a pharmaceutical has a negative assessment from the United Kingdom, France and Germany the topic will not be selected for assessment. In the Netherlands (ZIN) and in Finland (FIMEA) agencies will look at what other agencies are completing and use English language documents available to support their procedure.

For non-pharmaceutical health technologies, in Scotland (SHTG) a variety of databases are used to support horizon scanning including the EUnetHTA databases (POP and EVIDENT) and the INAHTA database. In Italy, Agenas use published HTA and systematic reviews in English, French and Italian to support the horizon scanning and topic selection procedure.

Analysis of horizon scanning and topic selection procedures

Horizon scanning procedures

Horizon scanning helps identify topics that are likely to be priorities for HTA. Less than half of countries currently engage in horizon scanning. However, a number of other countries report that they are setting up or considering using horizon scanning systems. Horizon scanning tends to include both local (e.g. national industry affiliates, local clinical experts) and also international sources (e.g. database and media searches). Therefore, although currently duplication is not extensive, as more countries explore the use of horizon scanning duplication will increase. Supporting collaborative horizon scanning now can help prevent duplication arising in the future.

Collaborative horizon scanning could be either decentralised or centralised:

- Agencies currently carrying out horizon scanning collaborate with each other to develop a shared horizon scanning procedure. Other agencies then fit into the procedure where there is interest.

- Horizon scanning becomes a part of sustainable HTA cooperation.

In both instances results of horizon scanning activities should be formally compiled and disseminated through permanent HTA structures. As HTA agencies are not usually solely responsible for topic selection and prioritisation, dissemination at an HTA Network level as well as at the level of the HTA agencies is appropriate.

Pharmaceuticals

The availability of existing centralised procedures (e.g. regulatory procedures and procedures for each dialogue) means that it would be most efficient to build pharmaceutical horizon scanning into existing structures rather than developing a new EU procedure of horizon scanning for collaborative HTA. For example, it could be carried out with cooperation from the European Medicines Agency (EMA) and following up pharmaceuticals that have been part of early dialogues.

Non-pharmaceutical health technologies

For non-pharmaceutical health technologies, procedures would have to be developed building on the national procedures already in place. If an agreed horizon scanning procedure and set of sources were identified, work could then be shared between agencies with experience in horizon scanning or centrally housed.

Topic selection procedures

Topic selection procedures support the identification of appropriate assessment topics that reflect national priorities. Implementation of collaborative HTA will only occur when it is a topic that is relevant to a MS. The nature of the issues associated with topic selection are different for the different types of technologies. A relatively small number of pharmaceuticals are launched each year and many receive marketing authorisation for all countries at the same time. For non-pharmaceutical health technologies there is a wider range of possible topics and the timescales in which a technology becomes a national priority for assessment are more variable. In addition, agencies on average consider more pharmaceutical topics and fewer non-pharmaceutical health technologies each year. This means that different approaches to topic selection are required for pharmaceuticals and non-pharmaceutical health technologies.

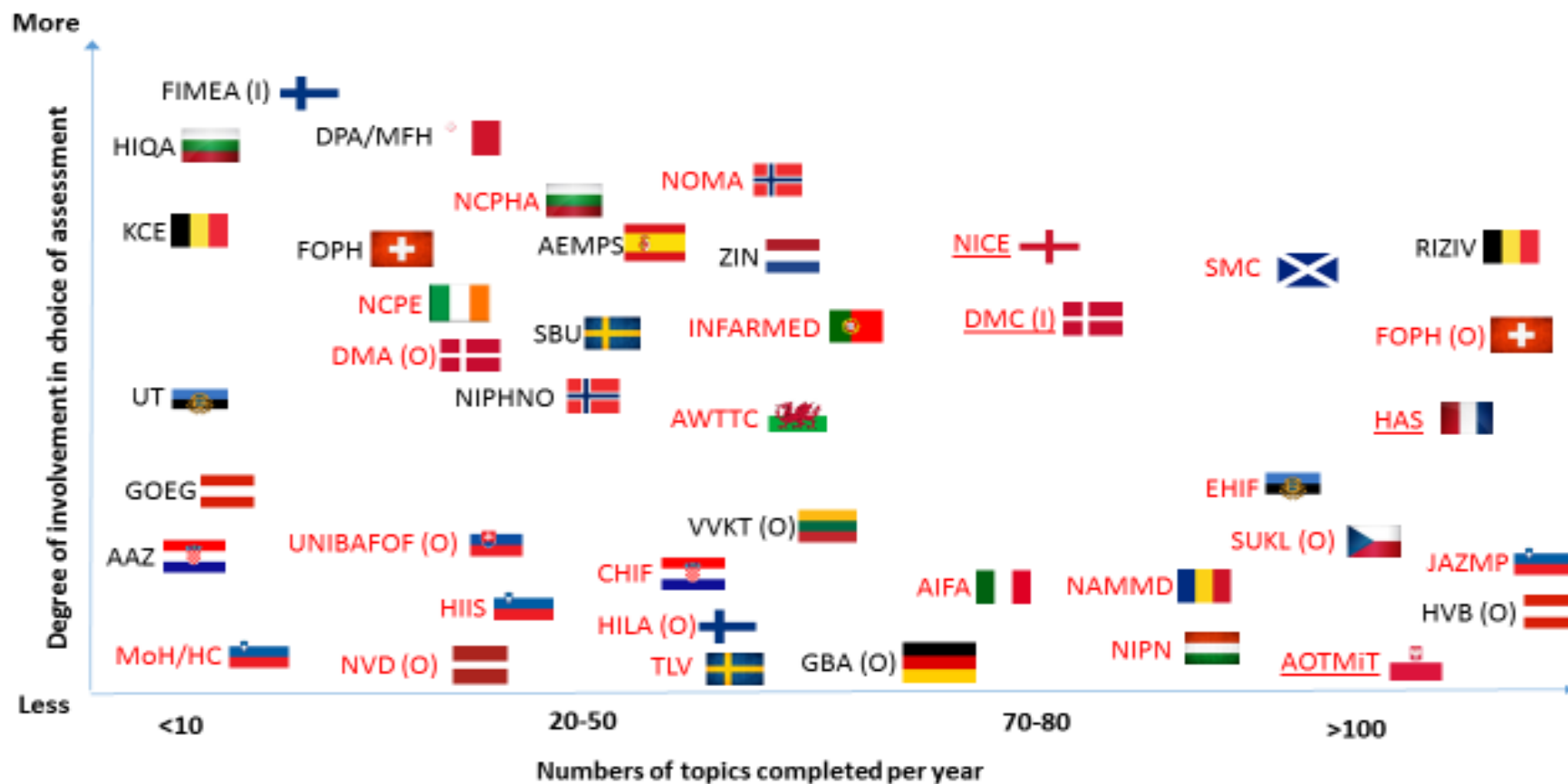
In addition, collaborative HTA has to address the challenge that agencies may not know in advance which topics they will need to assess and therefore priority topics for collaborative HTA will have to be identified before national priorities are known. This arises because for all technologies agencies can have a limited responsibility for choosing topics for consideration and little advanced notice of when a topic will be notified to them (figures 14 and 15). This has three implications:

- (1) Collaborative HTA should support countries to identify in advance technologies that are likely to become national priorities and to have HTA

prepared in advance so countries can respond quickly when national requests are made

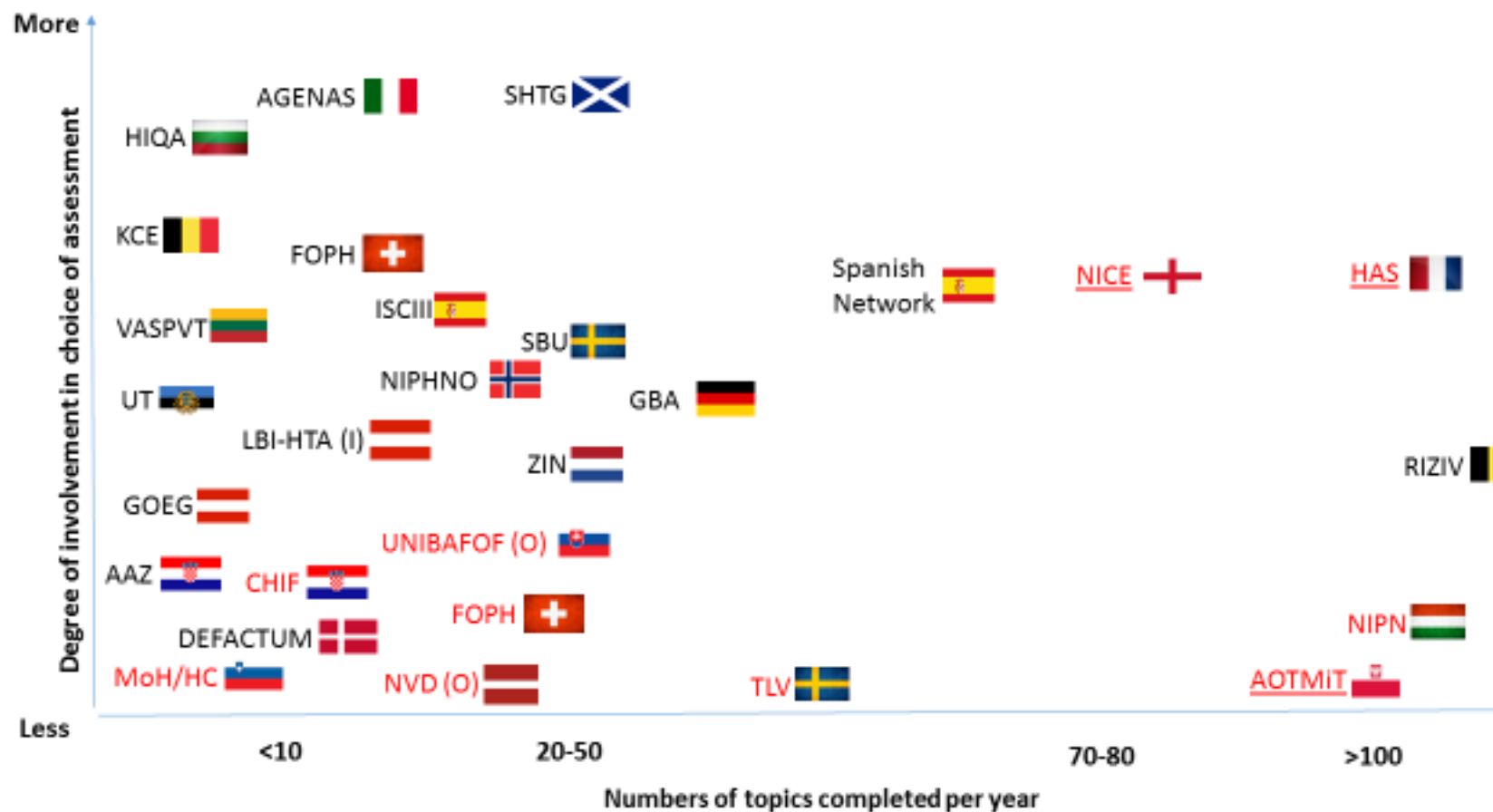
- (2) Collaborative HTA should be predictable so as to respond to rather than add to the unpredictability in some countries
- (3) Countries may not be able to commit in advance that a topic will be assessed in a national procedure (and therefore a collaborative HTA can be used) because they may not know if they will have to assess a topic.

Figure 14: Number of topics completed by agency involvement in procedure – pharmaceuticals



Key: Black = agencies creating own REA assessment; Red = agencies appraising submissions and evaluating this rather than creating own REA assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only. Degree of involvement in choice of assessment = agencies at the bottom of the figure are not involved, agencies in the middle are involved alongside other agencies, agencies at the top choose their own topics

Figure 15: Number of topics completed by agency involvement in procedure – non-pharmaceutical health technologies



Key: Black = agencies creating own REA assessment; Red = agencies appraising submissions and evaluating this rather than creating own REA assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only. Degree of involvement in choice of assessment = agencies at the bottom of the figure are not involved, agencies in the middle are involved alongside other agencies, agencies at the top choose their own topics

Pharmaceuticals

Possible topics for collaborative HTA can be identified from horizon scanning. Topic selection and prioritisation criteria could then be completed either by:

- Central application of a set of prioritisation criteria agreed by all MS to all topics identified, with selection of topics based on their meeting the criteria and then ratification of the list of selected topics by MS; or
- For each possible topic identified, MS prioritise topics according to a set of agreed criteria. The prioritisation procedure would then feed into the selection of topics at a meeting of MS to agree the final selection of topics.

The requirement to apply topic selection and prioritisation criteria and the way in which it is done will depend on the capacity of any collaborative HTA programme (e.g. if all new pharmaceuticals and extensions were to be assessed then a much simpler system can be put in place than if only a selection are completed).

It may not be necessary to include all MS in this prioritisation procedure, some MS assess almost all pharmaceuticals and therefore are likely to always assess a topic that is assessed as part of HTA collaboration, as long as it is marketed in their country. However, prioritisation that included all MS would help identify the topics where collaborative HTA would be most valued. In addition, these procedures would be of particular value for those MS assessing less than 30 products a year so as to maximise likelihood of identification of relevant topics. The selected topics could then be published as a work plan, this would act to support early awareness of collaborative HTA.

The opinion of MS decision makers as well as HTA agencies should inform prioritisation because this group also frequently decides on topics to be considered. Industry also has involvement in topic selection at a national level by making the decision to apply for reimbursement and thereby initiating the national procedure. To maximise national implementation, procedures will require coordination with industry to identify topics that will be launched across multiple countries in such a way that having a centralised collaborative HTA will be timely and provide value (e.g. if launch will only be in a small number of countries or launch will be significantly delayed or staggered in many countries, carrying out a collaborative HTA will add less value).

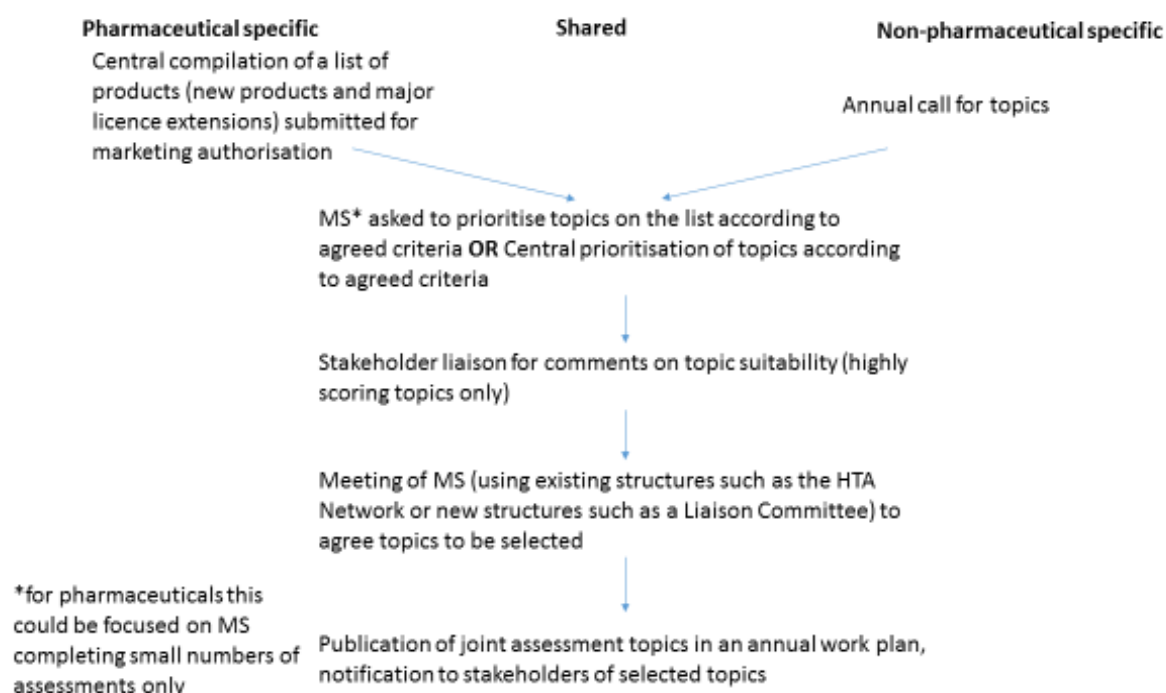
Non pharmaceutical health technologies

For non-pharmaceutical health technologies, because of the smaller number of topics that are assessed, incorporating a call for priority topics based on collaborative horizon scanning outputs and other national sources will increase the identification of appropriate topics. The organisations within an MS that may need to be involved in this include HTA agencies, but also payers, clinical and medical societies and Ministries of Health. HTA agencies may also need to seek feedback from providers and regional organisations.

The submitted topic proposals would need to be prioritised using a set of agreed criteria that should be transparent and publically available. This could be done using the same procedures as for pharmaceuticals and would act to bring together a group of MS who are interested in an assessment of the topic within a similar timeframe. The selected topics would then be completed as collaborative HTA as part of an annual work programme. As with the approach adopted by the Spanish Network (case study 6) a number of assessment slots could be kept free each year for assessments of topics that arise at short notice. The topic selection procedure for these assessments could be similar to that which is currently used by EUnetHTA for collaborative assessments e.g. a country identifies a priority and alerts EUnetHTA, a call for collaboration is issued and an authoring team is put together.

Figure 16 describes possible topic selection approaches for pharmaceuticals and non-pharmaceutical health technologies.

Figure 16: Topic selection procedures



Collaborative HTA does not currently cover all pharmaceuticals that receive a marketing authorisation and given the volume of possible non-pharmaceutical topics, there are likely to be national priorities that are not reflected in the collaborative HTA work programme. Topics where there are no centralised collaborative HTA but there are multiple countries where an assessment will be completed would be appropriate topics for formal information sharing or collaboration between jurisdictions. Such information sharing will be more feasible in countries who plan activity in advance

and produce work plans as they are more able to share topics and timelines in a timely manner. Existing databases such as the EUnetHTA POP database provide a means of recording and sharing these data.

Case study 6: Topic selection and prioritisation procedures for the Spanish Network

Proposals for topics to be assessed by the Spanish Network are submitted to the Ministry of Health on an annual basis. These proposals are presented to the Committee for Provision, Insurance and Financing by regional governments, the Ministry of Health and three special health insurance providers (that are available only for public officials), on their own initiative, or following a reasoned request from other third interested parties (professional societies, patient associations, etc).

The proposed topics are then prioritised for HTA assessment by the above-mentioned Committee, which contains representatives from all the regional health services, and an agreement on topics that will be assessed is reached.

The Spanish Network has developed a process for topic prioritisation so as to create a common prioritisation process that will be used to identify relevant topics from 2016 onwards. The prioritisation scoring tool (PriTec tool) was initially developed by one of the regional agencies (avalia- t) and has been adapted for use at a national level. The tool is applied by the Committee for Provision, Insurance and Financing, which includes policy representatives from all regions. The scoring is revealed and discussed at a meeting of this Committee and consensus reached on the topics to be chosen for assessment. The use of the PriTec tool means that the prioritisation process is transparent and systematic. However, certain flexibility is allowed and a topic which may not score highly, can still be chosen for assessment.

Approximately 70 topics are proposed each year and of these approximately 40 chosen for assessment and distributed equitably among the agencies depending on their work burden. Each year a series of work slots are held free for topics that require assessment at short notice (for example from ministerial departments and patient associations). This is important in case new evaluation needs come up during the year that have to be included in the annual work plan.

Topic types

Pharmaceuticals

From an implementation perspective for pharmaceuticals fewer agencies carry out assessments of inpatient technologies and therefore currently these will have lower rates of implementation given existing procedures.

Pharmaceutical topics that are most likely to be assessed by MS are new products and major licence extensions. In the short term while collaborative HTA is unable to address all new products and major licence extensions, the following criteria are

likely to identify pharmaceutical topics that are national priorities with greatest likelihood of implementation of collaborative HTA:

- economic and resource impact
- severity or burden of the disease
- potential health benefits
- population size

Non-pharmaceutical health technologies

Based on agencies existing procedures, it would appear unnecessary to restrict non-pharmaceutical assessments to specific product types or only those topics with an industry sponsor as in many cases this is not a restriction placed on agency work. The use of a call for proposed topics and an agreed set of prioritisation criteria would allow MS preferences for assessments of different types of health technologies to be reflected in HTA collaboration without placing any topic restrictions. The following criteria are likely to identify non-pharmaceutical topics that are priorities:

- economic and resource impact
- potential health benefits
- importance to healthcare and/or innovativeness
- severity or burden of the disease

In addition to the above criteria, for both pharmaceuticals and non-pharmaceutical health technologies, assessments where agencies may find it more challenging to carry out work are more likely to produce highly-valued collaborative HTA with higher rates of implementation. Situations identified include:

- Where it is known that there is a need to go beyond the direct head-to-head clinical trial data (e.g. there is a need for indirect comparisons or extrapolation techniques) or evidence is more uncertain (for example pharmaceuticals with conditional approval or outcomes based on surrogate endpoints).

These topics may be more valued as part of collaborative HTAs as they require statistical capacity which fewer agencies have access to and may be subject to greater uncertainty in estimates of relative effectiveness.

- Products for rare diseases or small populations

Although fewer countries assess products for rare diseases and small populations, among those that do, carrying out assessments is often more methodologically

challenging because the available evidence may be from a small number of individuals using non-randomised or uncontrolled evidence with disease and product expertise held by a few individuals. Collaborative HTAs provide added value because they can gather data, experience and expertise across countries.

- Advanced therapy medicinal products (ATMP)

As with products for rare diseases collaborative HTA may add particular value because of the ability to share expertise from across countries rather than relying on national expertise that may be held within a few individuals.

Recommendations for Horizon Scanning and Topic selection procedures

Key implementation challenge	Recommendations for centralised cooperation	Recommendations for agencies
<ul style="list-style-type: none"> HTA is not established for all types of technologies in all countries. Low predictability of topics requiring assessment: <ul style="list-style-type: none"> HTA agencies not always involved in topic selection Small number of agencies currently using horizon scanning HTA agencies can have little advance notice of topics requiring an assessment. Some agencies consider only a small number of topics each year Topics being considered may be confidential Data for the topic being considered may be confidential 	<ul style="list-style-type: none"> A set of agreed topic selection and prioritisation criteria to identify topics Centralised topic selection and prioritisation procedure involving all MS resulting in agreement of the topics to be assessed jointly. Opportunity for agencies to propose short notice national priorities for collaborative HTA. Build greater predictability into procedures, including: <ul style="list-style-type: none"> Collaborative horizon scanning to foster shared awareness of new and emerging topics among MS Advanced notification of topics for joint assessment and Publication of an annual work plan with timelines for completion Include users of the HTA in topic selection procedures to identify the topics of most value Coordinate horizon scanning with industry to establish launch patterns across the EU and identify the optimum time for completion 	<ul style="list-style-type: none"> Incorporate into standard operating procedures searching the EUnetHTA website and POP database to identify ongoing and published assessments Identify the characteristics of the topics where collaborative HTA would be most valued Develop national procedures that allow relevant MS agencies, national stakeholders and experts to input into collaborative HTA topic selection and prioritisation procedures

Chapter 4: Scoping

Key messages:

- A relevant scope for collaborative HTA is fundamental to being able use the report. If collaborative HTA is not relevant then it will either not be used or may require significant adaptation.
- The majority of countries (55% and 68% for pharmaceuticals and non-pharmaceutical health technologies, respectively) define the scope of an assessment in advance of work starting. However, this is usually just before work starts.
- The responsibility for defining the scope of the work rarely lies only with the HTA agency.
- In the majority of countries (19 for pharmaceuticals (66%) and 15 for non-pharmaceuticals (68%)) the population considered does not have to include the full authorised population.
- Unpublished data can be included in the assessment in approximately 64% of countries for pharmaceuticals and 73% for non-pharmaceutical health technologies.
- HTA collaboration should support agencies to be involved in early scoping so as to maximise the relevance of the assessment scope

Description of scoping procedures

Timing of scoping procedures

For pharmaceuticals, 16 out of 29 countries (55%) define the scope or decision problem before the procedure formally starts. In 8 of these countries (50%) there is variation between the agencies or HTA programmes in the country with some agencies or programmes defining the scope in advance while others do not. Half of the 16 countries who have a scoping procedure before work starts indicated that the scope is created immediately before or just before work starts. A small number of agencies indicated that scopes are available in advance: RIZIV (Belgium) stated 90 days, NICE (England) stated that the scope is created between 1-4 months before the appraisal starts but updated just before the appraisal starts and NCPE (Ireland) stated scoping can occur up to 6 months before work starts.

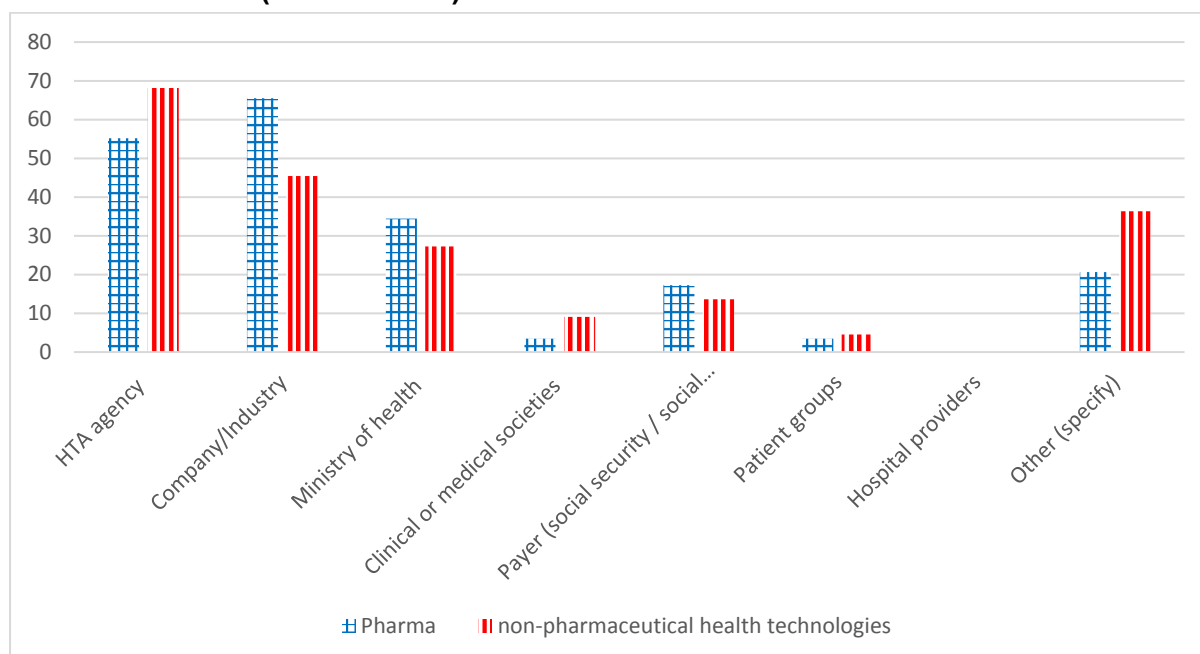
For non-pharmaceutical health technologies, 16 out of 22 countries (73%) define the scope or decision problem before the procedure formally starts. In 5 of these countries (31%) there is variation between the agencies or HTA programmes in the country with some agencies or programmes defining the scope in advance while others do not. Of the 16 countries who indicated that they have a scoping procedure before work starts, 13 of these (81%) indicated that the scope is prepared immediately before or just before work starts. Of the other countries, the longest amount of time a scope would be available before an assessment starts is 3 months.

In countries where the scope is not defined in advance of the procedure starting, guidelines for the contents of the scope tend to be in a guideline or legislative document, companies submitting for assessment are expected to follow these, and the scope of the company submission is then evaluated for appropriateness when the assessment starts.

All regional agencies have a procedure for defining the scope of the assessment before it starts. However ASSR-RER noted that they define a scope in advance only for their high cost technologies programme. In regard to timing of scoping compared to assessment the Spanish agencies all indicated that the scope is available just before the assessment starts (between 1 to 3 weeks).

Responsibility for defining scope contents

Figure 17: Parties responsible for defining the scope or decision problem of the assessment (% countries).



Key: pharmaceuticals N=29, non-pharmaceutical health technologies N=22. Agencies coded multiple categories so data may add up to more than 100%.

The responsibility for defining the scope is with the HTA agency for 16 out of 29 countries (55%) for pharmaceuticals and 15 out of 22 countries (68%) for non-pharmaceutical health technologies. However, in 13 (81%) and 7 (47%) of these countries, respectively, other parties are also responsible for deciding the contents of the scope including policy makers, Ministry of Health, external committees, stakeholders and experts. The pattern of results is associated with whether the agency produces their own assessment or evaluates an industry submission. Agencies are more likely to prepare their own scope if they carry out their own assessment (figure 17).

In Italy the regional agency ASSR-RER defines the scope of the assessment. In Spain all 6 regional agencies consult with other organisations to define the scope of the assessment. The most commonly involved organisations are hospital providers and the Ministry of Health. Two agencies also take into account input from clinical or medical societies and one agency consults with payers.

Contents of the scope

For all health technologies, of the countries that include a scoping phase the majority (>90%) of countries include PICO in their scope. In general other information is also included such as study design, economic analysis/indicators, cost impact, ethical aspects, subgroups and therapeutic value. The Spanish regional agencies reported including additional information in the scope such as context analysis, stakeholders input and patient's preference.

Acceptable scope for the assessment

Intervention

For pharmaceuticals, 16 out of 28⁶ countries (57%) consider each indication (as opposed to only the main indication) for which a product is authorised. However a number indicated that the assessment will be for only those indications specified by the party requesting the assessment. In the other 12 countries (43%) the scope of the intervention to be considered varies with some agencies or programmes assessing each indication, some assessing only those requested or defined in the scope and a small number (3 agencies in 3 countries) only assessing the main indication. The scope of the indication to be considered is incorporated in a legal act/guideline for at least one agency in 23 out of 28 countries (82%).

Population

For pharmaceuticals, in 19 out of 28⁷ countries (68%) the party requesting the assessment can request that only a subgroup of the indication is considered. In a further 3 countries (10%) it varies with some agencies or programmes within the country assessing the full indication while others may not. The requirement about the scope of the population to include in the assessment is incorporated in a legal act or guideline in at least one agency in 20 out of 28 countries (71%).

For non-pharmaceutical health technologies, in 15 out of 22 countries (68%) the party requesting the assessment can request that only a subgroup of the indication is considered. In a further 2 countries (9%) it varies with some agencies or programmes within the country assessing the full indication while others may not. For non-pharmaceutical health technologies, the requirement to include the whole

⁶ Romania responded NA

⁷ Romania responded NA

population is incorporated in a legal act or guideline in at least one agency in 8 out of 22 countries (36%).

While in most cases the assessment does not need to include the whole population, defined subgroup analyses to be included in the assessment or submission of evidence are specified in only a minority of countries. Specific sub-group analyses are required in 9 out of 28 countries⁸ (32%) and 6 out of 22 countries (27%) for pharmaceuticals and non-pharmaceutical health technologies, respectively.

Among the regional HTA agencies all indicated that the assessment does not have to include the whole population. Subgroup analyses are not required except for pharmaceutical technology appraisals by AETSA, where predefined subgroup analyses must be performed, as specified in a guideline.

Comparator

Restrictions about acceptable comparators were reported in 23 out of 29 countries (79%) for pharmaceuticals and in 10 out of 22 countries (45%) for non-pharmaceutical health technologies. Restrictions included gold standard treatment, standard of care, reimbursed treatments, routinely used intervention in clinical practice, active substances in the same 4th ATC level group. These restrictions are reported in a legal act or guideline in 20 out of 22⁹ countries (91%) for pharmaceuticals and 9 out of 10 countries (90%) for non-pharmaceutical health technologies.

No restrictions for comparators were reported among the regional HTA agencies in Italy and Spain, except for AETSA pharmaceutical technology appraisals, which specifies in a guideline that gold standard is the relevant comparator.

Study type

For pharmaceuticals, no restrictions to the type of study design accepted as evidence were reported in 17 out of 28¹⁰ countries (61%) and in a further 7 countries (25%) the presence of restrictions to the type of study design varies between agencies or programmes with some applying restrictions and others not. AEMPS (Spain) indicated that they have no restrictions to the type of study designs accepted. However, the information contained in the Marketing Authorisation Dossier is the evidence primarily used for assessment.

For non-pharmaceutical health technologies, no restrictions were reported in 15 out of 22 countries (68%) and in a further 2 countries (9%) the presence of restrictions to the type of study design varies between agencies or programmes (figure 18).

⁸ Romania answered not applicable

⁹ Romania missing data

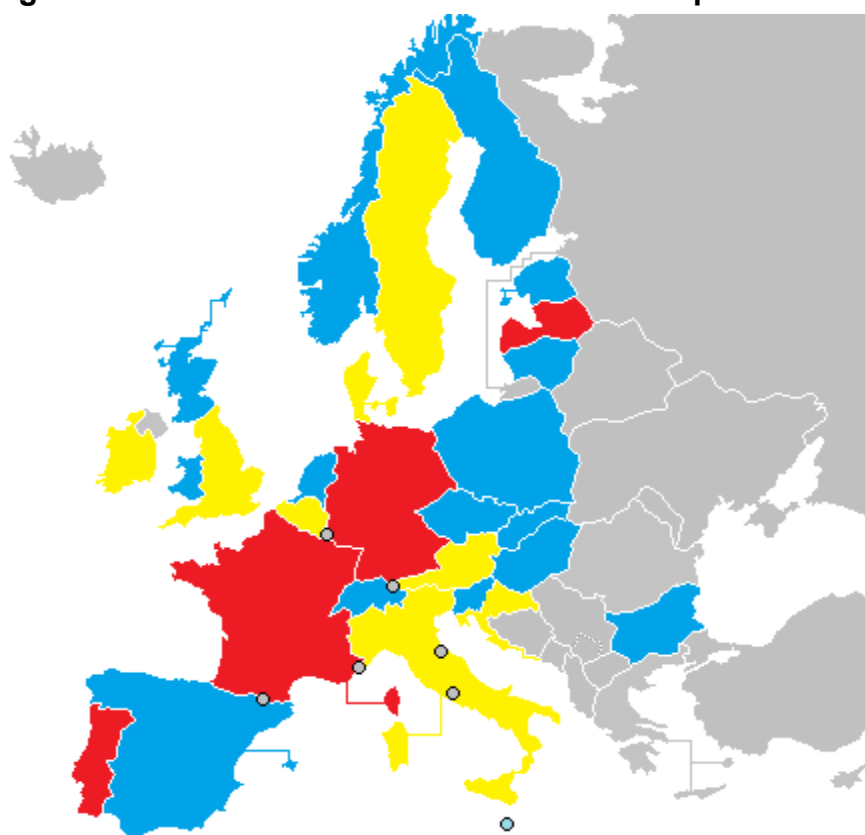
¹⁰ Romania answered not applicable

The type of restrictions placed on studies accepted include:

1. submission of a specified number of studies (HVB (Austria)), Evidence Summaries programme (NICE; England),
2. RCT data (CHIF (Croatia), FIMEA (Finland), G-BA (Germany), NVD (Latvia), MoH (Slovenia), KCE (Belgium) and DMC (Denmark)).

Among the regional agencies there are no restrictions to the type of study designs and evidence accepted in Spain. In Italy, Veneto reported no restrictions, whereas ASSR-RER noted a procedural document with restrictions regarding acceptable data.

Figure 18: Presence of restrictions about acceptable studies



Key: Red restrictions to acceptable data, Blue no restrictions to acceptable data, Yellow some agencies or programmes/departments have restrictions others do not (Romania NA)

Table 1: Countries where either some agencies or some programmes/departments have restrictions to study types and others do not

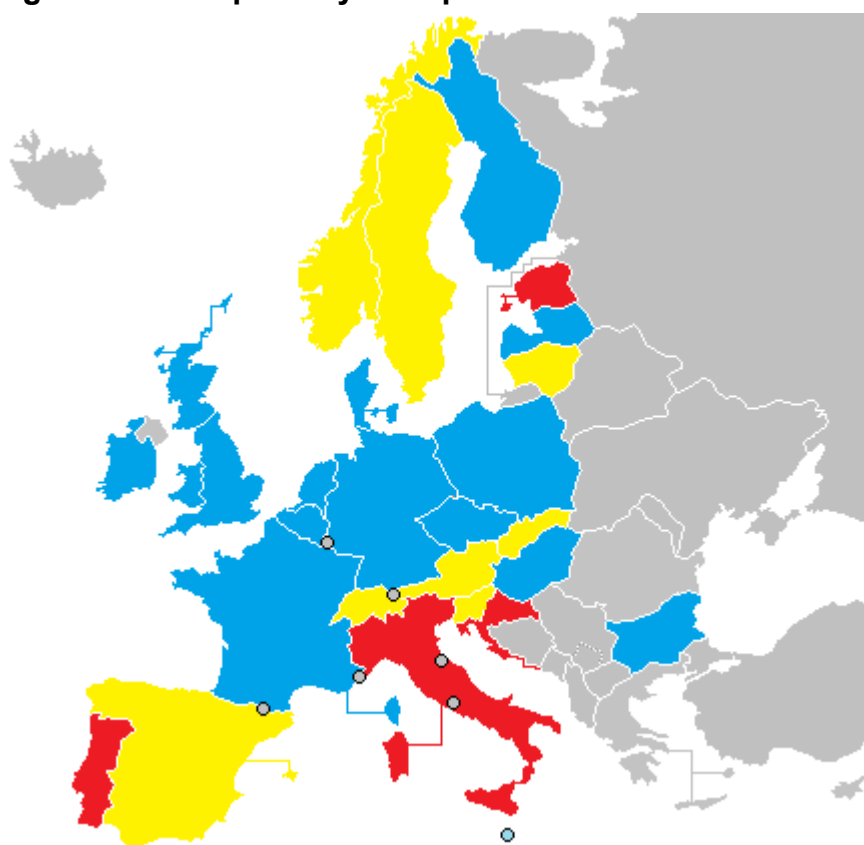
	YES	NO
Austria	HVB	GOEG, LBI-HTA
Belgium	KCE	RIZIV
Croatia	CHIF	AAZ
Denmark	DMC	DMA, DEFACTUM
England	Evidence Summaries	Other programmes

Ireland	HIQA	NCPE
Italy	Agenas	AIFA
Sweden	SBU	TLV

For pharmaceuticals, unpublished data are acceptable in 18 out of 28¹¹ countries (64%) and in a further 3 countries (11%) at least one agency or programme in a country accept unpublished data. For non-pharmaceutical health technologies, unpublished data are acceptable in 16 out of 22 countries (73%) and in a further it 2 countries (9%) it varies between agencies. The Netherlands indicated that unpublished data may be used for cost effectiveness analysis only and not for the assessment of therapeutic effect (figure 19).

Among the regional agencies unpublished clinical data are not accepted in Italy and in some regions of Spain (AETSA, UETS Madrid, AQuAS,) and are accepted in other regions (avalia-t, OSTEBA, SCS).

Figure 19: Acceptability of unpublished data in the assessment



Key: Red unpublished data unacceptable, Blue unpublished data acceptable, Yellow for some agencies it is acceptable while for others it is not (Romania NA)

¹¹ Romania answered not applicable

Table 2: Countries where either some agencies or some programmes/departments accept unpublished data and others do not

	YES	NO
Austria	HVB, GOEG	LBI-HTA
Lithuania	VVKT	VASPV
Norway	NOMA	NIPHNO ¹²
Slovakia	UNIBAFOF MedTech	UNIBAFOF Pharma
Slovenia	JAZMP, MoH	HIIS
Spain	Spanish Network, ISCIII	AEMPS
Sweden	TLV	SBU
Switzerland	FOPH (MedTech)	FOPH (Pharmaceuticals outpatient)

Analysis of scoping procedures

Collaborative HTAs must reflect a scope that is relevant to a MS. If an assessment is not relevant then it will either not be used or may require significant adaptation. Collaborative HTA should aim to establish a procedure that develops a scope which reflects the requirements of all MS who will consider the topic.

Agency procedures for scoping are comparable regardless of whether the technology is a pharmaceutical or a non-pharmaceutical health technology. In most countries either the scope of an assessment is not defined in advance of the procedure starting or scoping is undertaken at the start of or just before the start of the procedure (figures 21 and 22). There is an association with an agency not producing a scope in advance and the agency evaluating an industry submission. Even among agencies who carry out their own assessments scoping is often only done close to the start of the assessment, reflecting that agencies can be responding to relatively short notice requests from decision makers.

Within existing practices even if an agency identifies that a topic selected for a collaborative HTA is likely to come to them for a national assessment, they are unlikely to have available topic specific documents to support a review of the collaborative HTA scope and project plan. This presents with some implementation challenges. First to provide input agencies may need to rely on past assessments in a similar area. Reliance on past experience can be challenging particularly for non-pharmaceutical HTA where the range of topics is broad and capacity smaller than for pharmaceutical HTA. Second, to provide comments on scopes when such documentation isn't available to the agency will require more resources, meaning that some agencies within their current capacity may be unable to take part. These issues represent a weakness because they may lead to greater uncertainty associated with the most relevant scope of the collaborative HTA. MS may require

¹² Not applicable rather than not accepted, there are no specific rules but normally only published data are included

support from HTA cooperation to specifically develop procedures and capacities for informing the scopes of collaborative HTA.

A procedure for scoping a collaborative HTA needs to be built in to the system and for most countries an early contribution to this procedure will be an additional step to national agency procedures. There are two places in the procedure where scoping could be inserted into collaborative HTA (figure 20):

- Either, at topic selection, whereby a proposed topic has a preliminary scope of assessment worked up centrally to inform MS prioritisation
- Or, following topic selection before assessment starts with the development of a scope by the assessment authors and review by others.

In either procedure all interested MS should be given the opportunity to input into the appropriateness of the scope so as to maximise the likelihood of relevancy of the assessment across the EU. However, not all MS may be able to contribute because of resourcing or unfamiliarity with the topic area.

Incorporating the scoping phase into topic selection procedures may be easier to implement because MS would get the opportunity to comment on the scope at the same time as the request for their input into topic prioritisation. In addition, providing scope information along with topic selection information will help to support better decision making about topic prioritisation and appropriateness. When the assessment starts the scope could then be updated if needed, but the topic selection scoping document could provide the basis for industry to start developing any submission of evidence and also the collaborative HTA project plan.

Figure 20: Addition of scoping to possible topic selection procedures

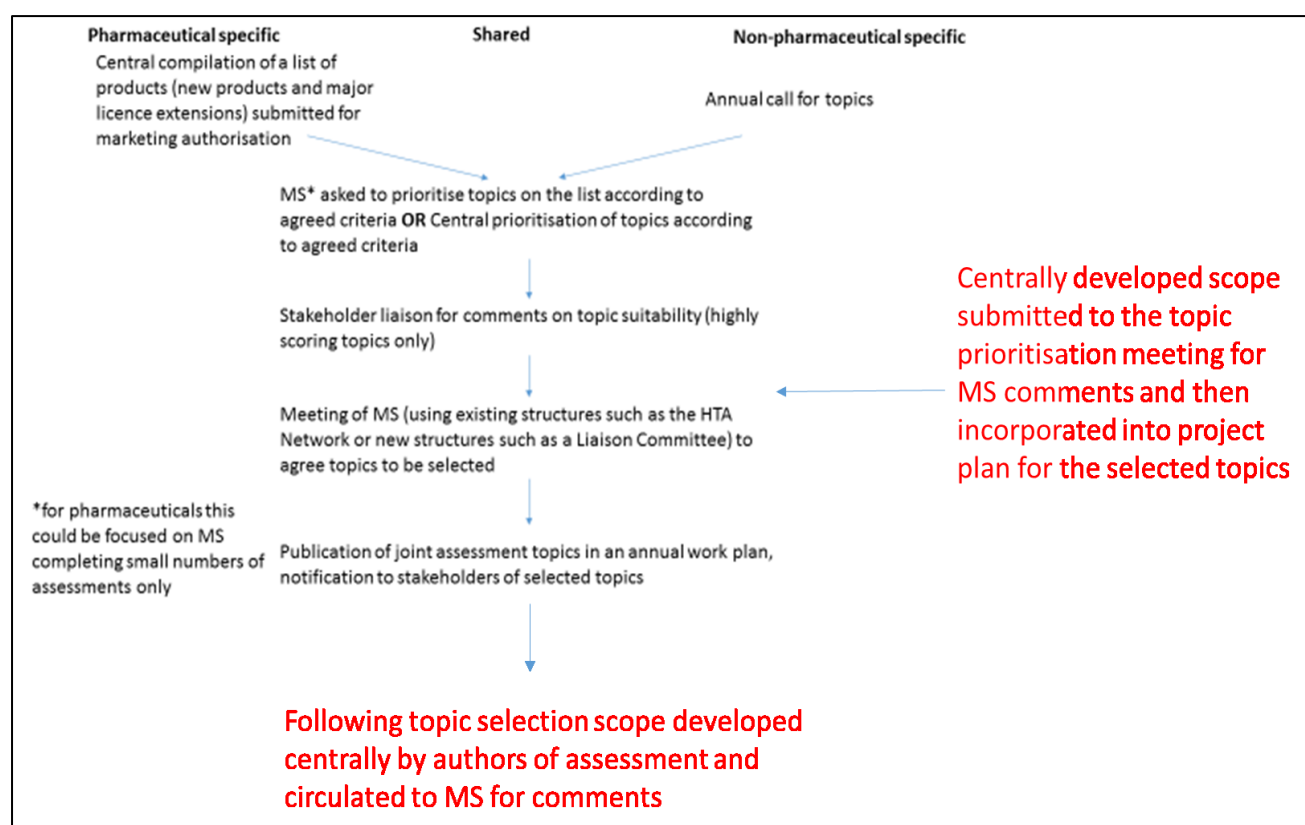
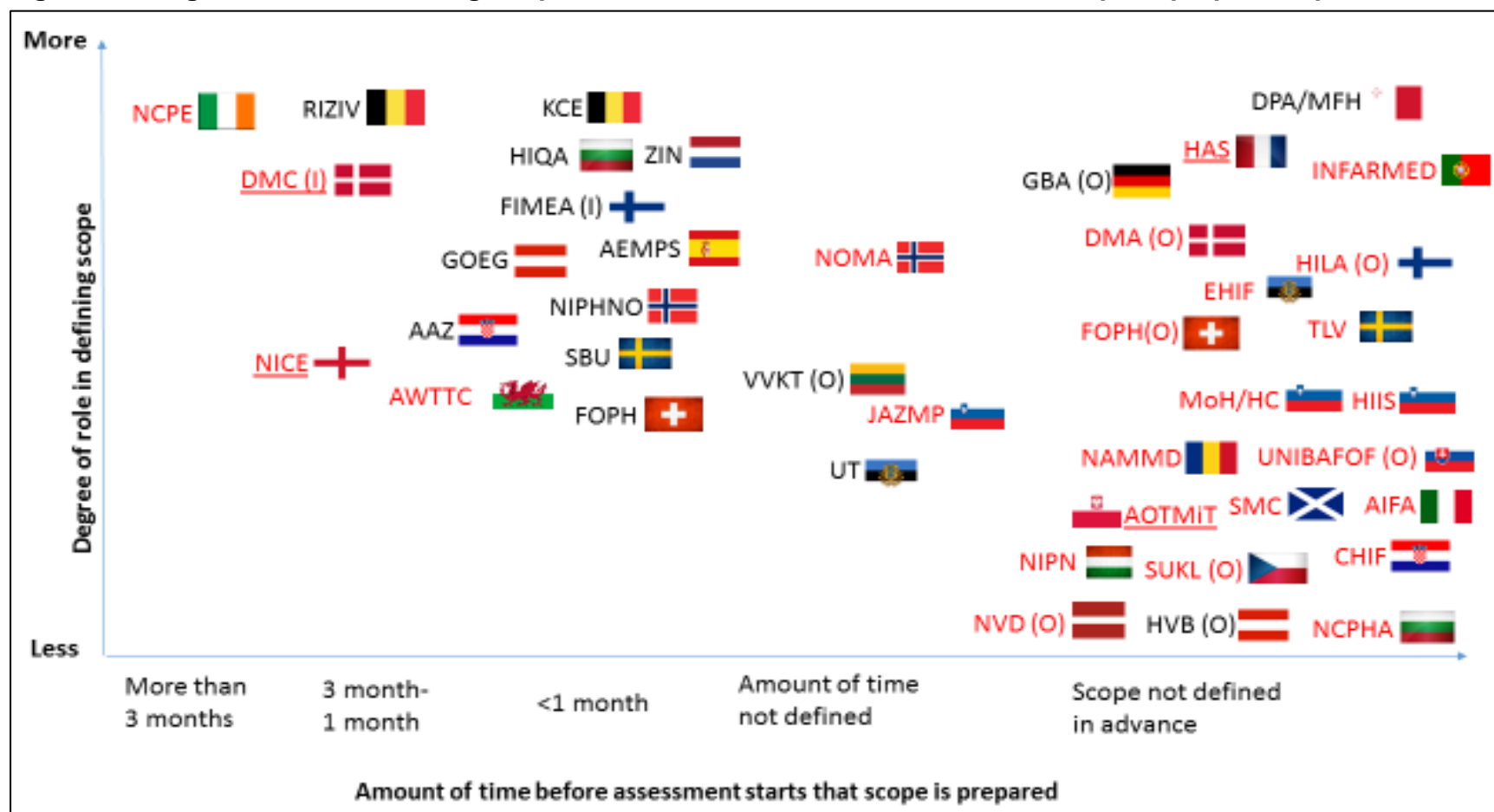
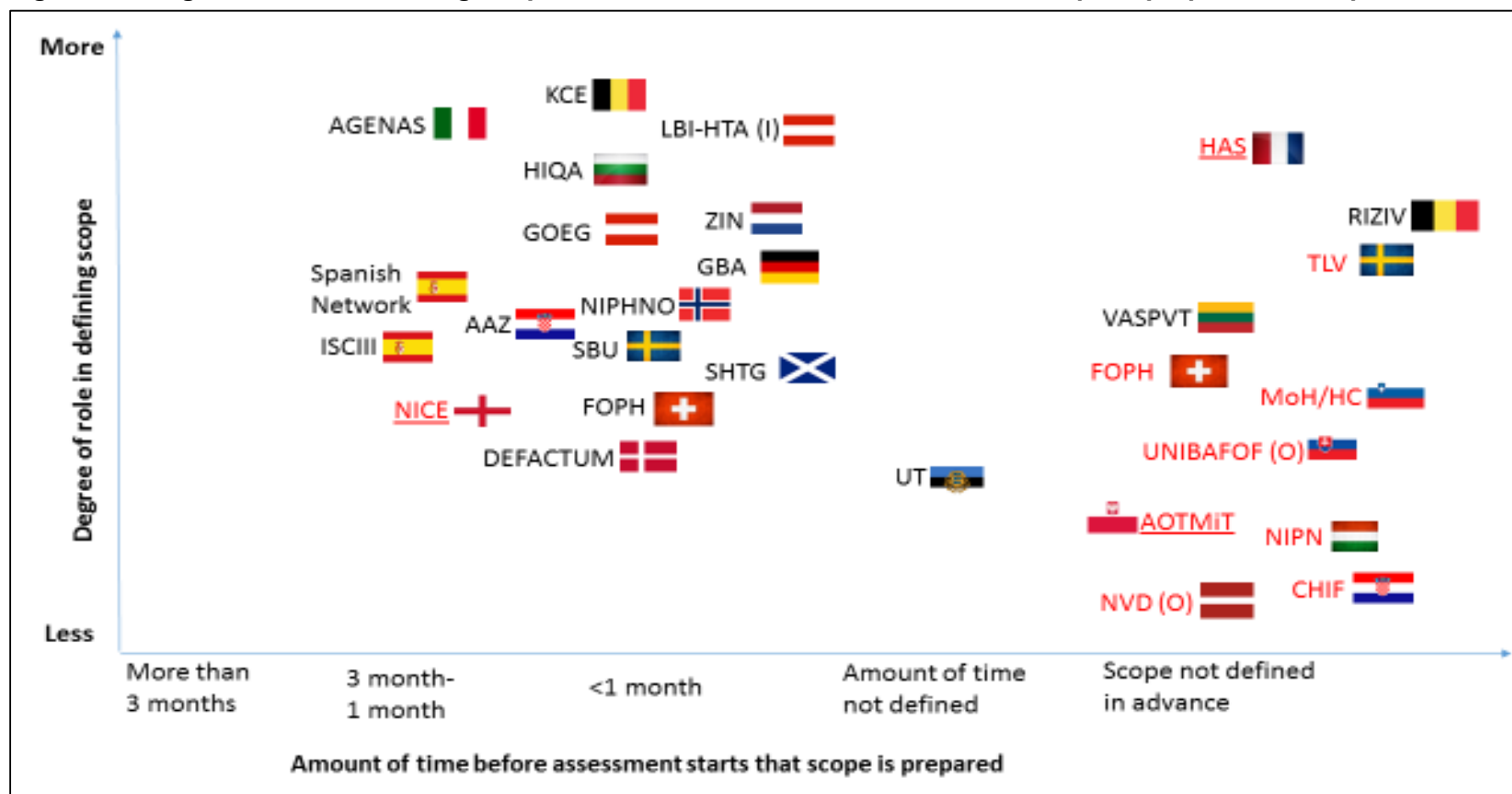


Figure 21: Degree of role in defining scope and amount of time in advance that scope is prepared - pharmaceuticals



Key: Black = agencies creating own assessment; Red = agencies appraising submissions and evaluating this rather than creating own assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only. Degree of involvement in defining the scope = agencies at the bottom of the figure are not involved, agencies in the middle are involved alongside other agencies, agencies at the top define their own scope

Figure 22: Degree of role in defining scope and amount of time in advance that scope is prepared – non pharmaceuticals



Key: Black = agencies creating own assessment; Red = agencies appraising submissions and evaluating this rather than creating own assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only. Degree of involvement in defining the scope = agencies at the bottom of the figure are not involved, agencies in the middle are involved alongside other agencies, agencies at the top define their own scope

Scope of the assessment

Agencies usually assess each indication for which a product is authorised, although this may only be indications requested. Collaborative HTA of licence extensions may be subject to slightly lower levels of implementation as a small number of agencies only assess the initial or main indication to be authorised.

In the majority of agencies, the scope of the assessment does not need to reflect the whole population for which a technology may be used. If the collaborative HTA reflects the whole population and the national assessment requested reflects only a subgroup, then this could affect implementation because a subgroup may have different comparators and different clinical data underpinning it. In addition agencies may seek to identify subgroups for whom an intervention may be more clinically effective or cost effective. There is a need to involve agencies across MS in a scoping phase and coordination with industry to reduce the risk that the collaborative HTA is not relevant because it does not target the correct population.

Among agencies there is variation in the acceptable data for assessments. The majority of countries include no restrictions to study type but for other countries restrictions are placed on the number of studies submitted and the type of studies submitted. Likewise, some countries accept or request unpublished data while some do not. From an implementation perspective these differences create a tension. If collaborative HTA includes only data from particular study types or only published data, then agencies who want all available data will have to obtain all other data, on the other hand if an assessment contains all data then those agencies who do not want to have all data for decision making will have to extract the data that are relevant requiring more extensive adaptation.

For non-pharmaceutical assessments it may be possible to incorporate inclusion of appropriate study types and publication status as questions for MS in the topic selection and scoping phase. However, this is less likely to be implementable for pharmaceuticals as procedures are less flexible. Therefore, for pharmaceuticals it may be necessary to include all available data and provide a clear structure in the report so that the evidence by study type and publication status are separated and agencies who need to extract data from the assessment can do so easily. Unpublished data also creates a challenge as this is also more often confidential and data in a collaborative HTA must at a minimum be made available to all agencies who are going to use the collaborative HTA and not only those producing or reviewing the collaborative HTA.

Recommendations for scoping and project planning procedures

Key implementation challenge	Recommendations for centralised cooperation	Recommendations for agencies
<ul style="list-style-type: none"> • PICO may not be available in advance of the national procedure starting • Agencies may not have resources available to support advance scoping or project planning before the national procedure starts • Agencies may have to rely on (outdated) past experiences to inform the PICO of assessments that have not yet started • Agencies may not define PICO • Variation in acceptability of different data types and publication status • Acceptable parameters of the PICO may be defined in legal and procedural documents • Requests for assessment may only be for a subgroup rather than the full licensed population • Agencies may actively identify subgroups, but these are not always specified before work starts 	<ul style="list-style-type: none"> • Include advance project planning and scoping as part of topic selection • Support and resource agencies to be involved in early project planning and scoping, to create an opportunity for all agencies interested in a topic to provide input • Include all available evidence in collaborative HTAs and provide a clear reporting structure to ensure that where needed agencies are able to extract information if only certain study types are required • Involve people responsible for making adaptations of collaborative HTA in work to refine the report structure so that information is easily extracted for use • Develop a procedure whereby unpublished and confidential data may be submitted centrally to EUnetHTA and shared with agencies working on the topic 	<ul style="list-style-type: none"> • Record in the POP database details of agency projects (either HTA or evaluations of industry submissions) including links to documents • Work towards making project plans and the scope of the assessment available for agencies in other countries to help them assess the relevance of national assessments being carried out in other countries for their own use

Chapter 5: Assessment and evaluation procedures

Key messages:

- Agency procedures define how they can engage in collaborative HTA both in terms of using collaborative HTA and taking part in joint work.
- For pharmaceuticals, in 76% of countries the assessment used in decision making is produced by industry and its appropriateness evaluated by the HTA agency. In contrast in 82% of countries assessing non-pharmaceutical health technologies the assessment is completed by the agency.
- When relative effectiveness and economic information are included in an assessment, the work is usually carried out in parallel or as a combined assessment in 24 out of 29 countries (83%) for pharmaceuticals and 20 out of 22 countries for non-pharmaceutical health technologies (91%).
- For the majority of countries there are restrictions to the language used to produce document. For pharmaceuticals 79% of countries report language restrictions compared with 59% for non-pharmaceutical health technologies.
- Given the high levels of evaluation of company submissions of evidence. A model of HTA collaboration needs to define how collaborative HTA should be used in national procedures:
 - as an alternative to a national submission
 - in addition to a national submission
 - incorporated into the national submission
- HTA collaboration will need to include flexible implementation of joint HTA while systems establish and change

Description of Assessment and Evaluation Procedures

Responsibility for producing the assessment

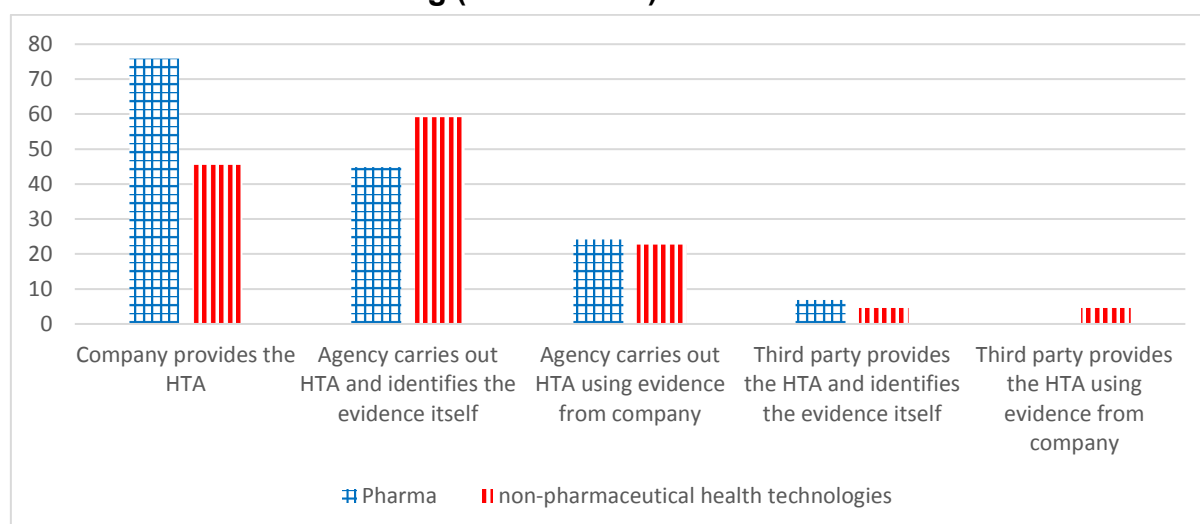
For pharmaceuticals in 22 out of 29 countries the assessment is provided by industry and evaluated by the agency (76%). In contrast for the assessment of non-pharmaceutical health technologies, in 18 countries (82%) the assessment is completed by the HTA agency which produces its own assessment either using evidence from the company or by identifying the evidence itself (case study 7).

In countries with more than one agency the most common pattern of production was for a national HTA agency or academic organisation with responsibility for HTA to carry out their own assessment, while another organisation such as an insurance body or social security institution evaluates company submissions. For example, in Croatia AAZ prepares syntheses of evidence while CHIF evaluates company submissions. Similarly, in Estonia UT produces HTA and EHIF evaluates company

submissions. Likewise, in Sweden SBU produces HTA whilst TLV evaluates company submissions (see also Finland and Austria).

Two countries indicated that for some programmes the assessment may not be carried out by the agency or industry. Slovenia indicated their Health Council evaluated submissions that can come from: the MoH, HIIS, health care providers, professional associations and societies, Medical Chamber of Slovenia, Pharmaceutical Chamber of Slovenia, Chamber of Nursing and Midwifery Services of Slovenia and other legal entities. NICE (England) indicated that HTA can be provided by academic groups either commissioned by NICE directly or commissioned by the National Institute for Health Research (NIHR) (figure 23).

Figure 23: Summary of the overall procedure for producing the assessment that informs decision making (% countries)



Key: pharmaceuticals N=29, non-pharmaceutical health technologies N=22. Agencies coded multiple categories so data may add up to more than 100%.

Case study 7: Description of production and evaluation procedures among case study countries

Evaluation of a company submission in Hungary:

The company submits an application and submission of evidence to the National Health insurance Fund (NHIF). NHIF sends the submission to the National Institute of Pharmacy and Nutrition (NIPN). NIPN reviews the evidence submission from the company and then provides a report to NHIF. In their review NIPN will check the appropriateness and robustness of the company's submission and consistency of clinical data with cost effectiveness modelling.

Production of an assessment using company evidence in Belgium:

The company submits an application and submission of evidence to Rijksinstituut Voor Ziekte- en Invaliditeitsverzekering (RIZIV). Agency staff prepares a health technology assessment using evidence from the application and other sources. This

assessment forms the basis of a proposal for reimbursement that is developed by the Commission for the Reimbursement of Medicines.

Production of an assessment with identification of the evidence by the agency in Spain:

The Spanish Medicines Agency (AEMPS) mainly use staff responsible for the regulatory clinical assessment to complete their assessment (therapeutic positioning reports). AEMPS have access to the regulatory documents that underpin the marketing authorisation procedure and mainly use these documents to complete the assessment of therapeutic effectiveness. Economic aspects can also be considered in a second phase of the procedure. In this case, the economic assessment is voluntarily carried out by the regional health authorities and shared internally among GCPT participants. Additional clinical evidence may be used if significant evidence exists outside the regulatory submission identified by the organisation itself or provided by the marketing authorisation holder.

Within a single agency different approaches can be used depending on the technology. For example, in England the procedure for producing assessments for pharmaceuticals depends on the programme to which the product is allocated. For highly specialised technologies and for single technology appraisals, it is the company that provides the HTA. However for multiple technology assessments it is an academic organisation that produces the HTA which may or may not take into account a submission by the company. Other countries also vary their approach, for example Poland (AOTMIT), Denmark (DMA and DMC), Scotland (SHTG), France (HAS) and Switzerland (FOPH) review company submissions and also carry out their own HTA. Production of HTA rather than evaluation of a submission occurs in situations where it is a (re)assessment of a technology group (DMA, DMC, HAS), the topic is identified as a national priority (SHTG), the MoH requests an assessment (AOTMiT), there is no sponsor of the technology (HAS, FOPH) or it is a possible topic for disinvestment (FOPH).

For both pharmaceuticals and non-pharmaceutical health technologies when REA and economic analyses are included in an assessment, the work is usually carried out as a combined assessment: for pharmaceuticals 22 out of 28 countries¹³ (79%) assessments are always combined and in 20 out of 21¹⁴ countries for non-pharmaceutical health technologies (95%). Countries producing separate assessments include VVKT (Lithuania) HAS (France), INFARMED (Portugal), DMA (Denmark), CHIF (Estonia) and AEMPS (Spain). For pharmaceuticals, in France and Lithuania assessments are carried out separately, but to meet timelines activity occurs in parallel.

¹³ Germany not applicable REA only

¹⁴ Germany not applicable REA only

Among the regional agencies ASSR-RER in Italy carries out its own HTA, however in the high cost technology programme the agency identifies the evidence to use itself whilst for the medical devices programme the agency uses evidence provided by the company. In Spain, the majority of regional agencies produce HTA and identify the evidence to use themselves, SCS reported that it can use evidence provided by the company to support assessment production.

Responsibility for evaluating submission of evidence

In situations where an HTA or submission of evidence is received by the agencies to be used in the decision making, an evaluation of the evidence is completed.

For pharmaceuticals, in 19 out of 22 countries (86%) it is the HTA agency who is responsible for evaluating the submission. In 3 countries (14%) it is a committee who does the evaluation, in 2 countries (9%) it is a decision maker and in 1 country (5%) it is an external group (academic group)¹⁵.

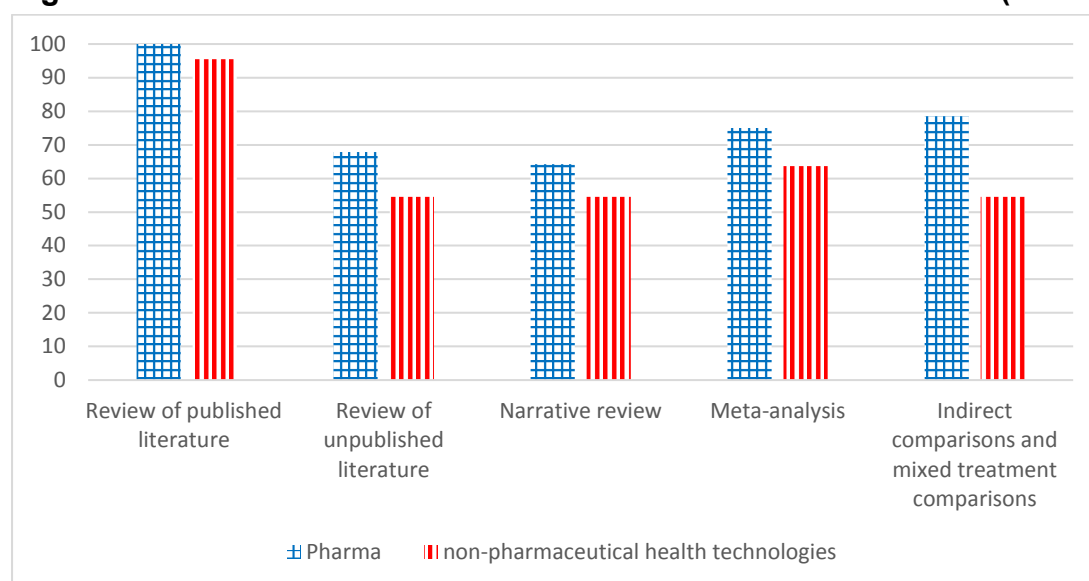
For non-pharmaceutical health technologies, in 7 out of 11 countries (64%) it is the HTA agency that carries out the evaluation, in 2 countries it is an external group (18%) and in 2 countries committees (18%).

Content of the REA assessment

For pharmaceuticals all countries indicated that the REA includes a review of published literature. For non-pharmaceutical health technologies, one agency (NIPN Hungary)) reported that the REA did not include a review of published literature but stated that the assessment of non-pharmaceutical health technologies includes evidence of the efficacy and effectiveness of the technology. In terms of the other components of the assessment, areas are similar, but pharmaceutical assessments are more likely to include indirect comparisons and mixed treatment comparisons (figure 24).

¹⁵ Figures can add up to more than 100% because agencies could indicate that more than 1 group were responsible for evaluation the submission

Figure 24: Contents of REA or clinical effectiveness assessment (% countries)

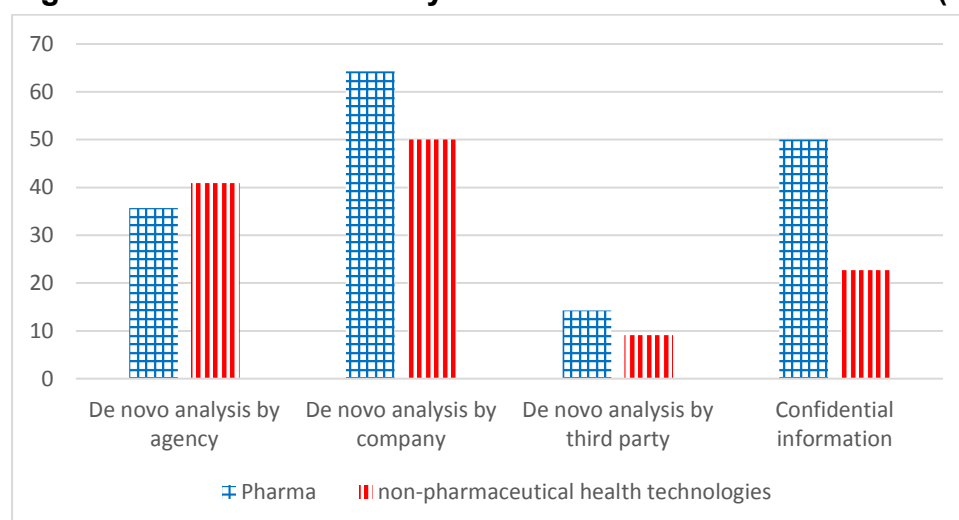


Key: pharmaceuticals N=28 (Romania N/A), non-pharmaceutical health technologies N=22. Agencies coded multiple categories so data may add up to more than 100%.

Assessments of pharmaceuticals are more likely to include de novo analysis completed by the company and confidential information, whereas non-pharmaceutical health technology assessments are more likely to include de novo analysis completed by the agency. A small number of countries indicated that analyses may be provided by 'third parties' for example academic groups (e.g. England and Switzerland) (figure 25).

In Spain, all the regional agencies include a review of published literature and narrative review in the assessment. Additionally, all technology appraisal programmes may include meta-analysis whilst the other programmes include a review of the unpublished literature. Only AETSA includes indirect comparisons and mixed treatments comparisons. All agencies reported that they may carry out de novo analysis.

Figure 25: Inclusion of analysis and confidential information (% countries)

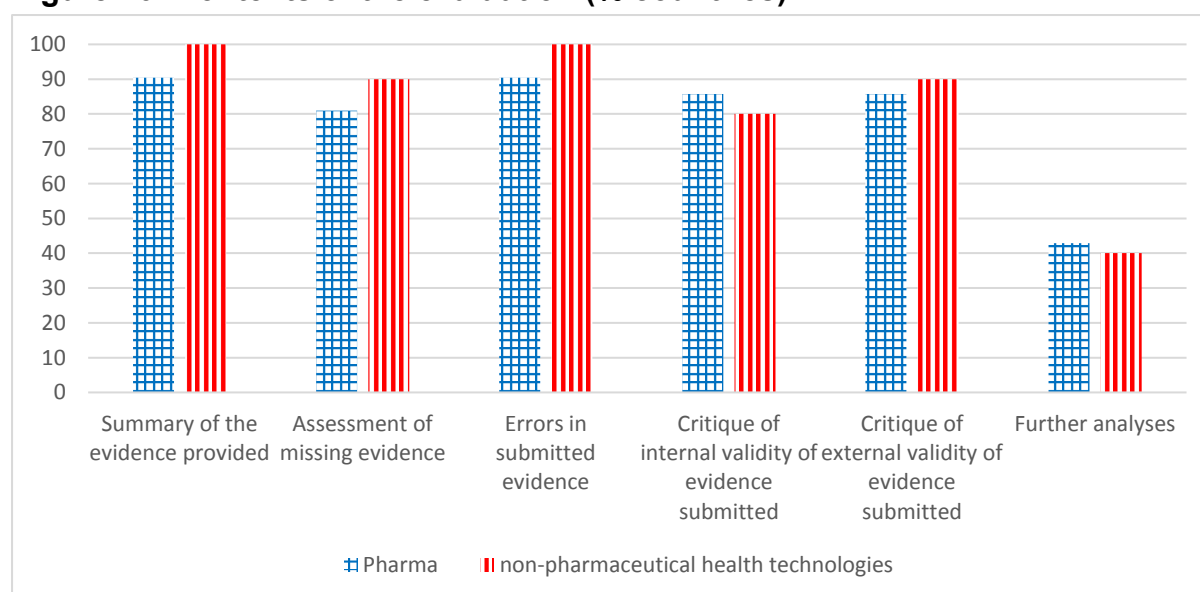


Key: pharmaceuticals data for 28 countries (Romania N/A), non-pharmaceutical health technologies data for 21 countries. Agencies coded multiple categories so data may add up to more than 100%.

Contents of the evaluation

In general the contents of the evaluation for pharmaceuticals and non-pharmaceutical health technologies is similar (figure 26). In the majority of countries the evaluation contains a summary of the evidence provided, an assessment of missing evidence, errors in submitted evidence and critique of internal and external validity. A minority of evaluation also contain further analysis. Other components of the evaluation may include information on comparative treatment, therapeutic value and information on the epidemiology of the disease.

Figure 26: Contents of the evaluation (% countries)



Key: pharmaceuticals N=21 countries (Romania N/A), non-pharmaceutical health technologies N=10 (CHIF (Croatia) N/A) with procedure whereby submissions of evidence are evaluated. Agencies coded multiple categories so data may add up to more than 100%.

Language restrictions

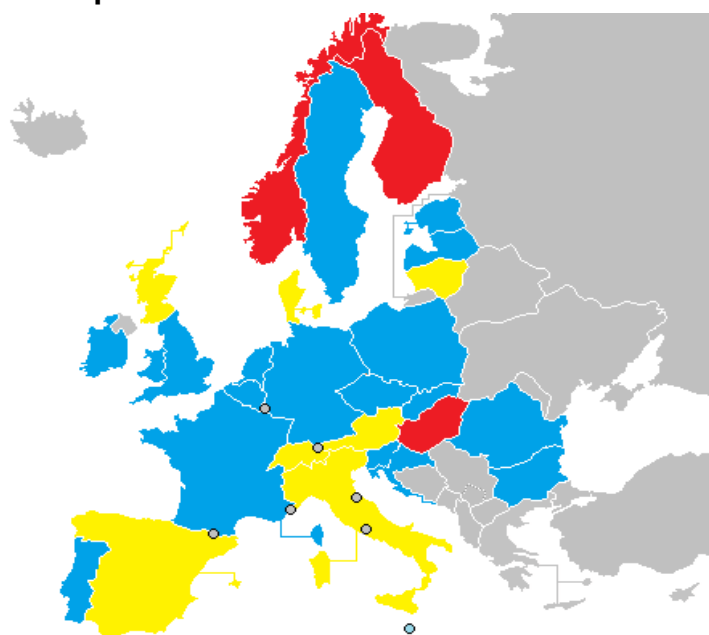
For pharmaceuticals, 23 out of 29 countries (79%) report that their work needs to be in the national language and in a further 3 countries (10%) it varies between agencies or programmes within the country. Of the 26 countries with language restrictions, half indicated this is a legal restriction and half a procedural reason.

For non-pharmaceutical health technologies 13 out of 22 countries (59%) report that their work needs to be in the national language. Of the 13 countries for whom the assessment needs to be written in the national language, in 9 (69%) it is a legal restriction and in 4 countries it is a procedural restriction (31%).

Some countries indicated that because the assessment is used for local decision making there is a need for it to be written in the national language, some agencies noted official language laws (e.g. France, Latvia, Poland) and other countries mentioned the requirement as part of specific legal ordinances for HTA or the procedures of the health insurance fund (e.g. Croatia).

Some countries indicated that only certain documents need to be in the national language. Slovenia noted that the technical documents in the application can be submitted in English, but that the decision must legally be written in the national language. TLV (Sweden) also noted that the company submission can be in English but documents TLV produce have to be in Swedish, while the Netherlands indicated that a summary and the advice must be in Dutch but the rest of the report can be in English.

Figure 27: Presence of requirements on the use of local or national language in the procedure



Key: Red no requirement on use of national language, Blue requirement for use of national language
Yellow some agencies are required to use national language others are not

Table 3: Countries where the national language isn't English and where either some agencies or some programmes/departments must write in the local language and others do not need to

	YES	NO
Austria	HVB	LBI-HTA, GOEG
Denmark	DMC	DMA, DEFACTUM
Italy	AIFA	AGENAS
Lithuania	VVKT	VASPV
Spain	AEMPS	Spanish Network, ISCIII
Switzerland	Pharmaceuticals submissions	HTA programme and medtech submissions

Among the regional agencies, there are no language requirements in Italy, whereas in Spain the assessments must be written in national or local language. This is specified in a legal document.

Publication status of the assessment or evaluation

For pharmaceuticals in 4 out of 29 countries (14%) the assessment or evaluation is kept confidential, in 7 countries (24%) it is made public, in 6 countries (21%) public but with confidential information removed and in 11 countries (38%) it varies between agencies or programmes within the country.

For non-pharmaceutical health technologies in 2 out of 22 countries (9%) the assessment or evaluation is kept confidential, in 9 countries (41%) it is made public, in 6 countries (27%) public but with confidential information removed and in 5 countries (23%) it varies between agencies or programmes within the country.

Table 4: Publication status of assessments or evaluations in countries where it varies between agencies considering the same technology type

Country	Status		
	Public	Public but with confidential information removed	Confidential
Austria	GOEG, LBI		HVB
Belgium	KCE		RIZIV
Croatia	AAZ		CHIF
England	Evidence summaries	Other programmes	
Estonia	UT	EHIF	
Finland		FIMEA	HILA
Ireland		HIQA	NCPE
Norway	NIPHNO	NOMA	
Slovenia	HIIS		JAZMP, MoH HC

Spain	HTA reports	Early awareness and alert system	
Sweden	SBU	TLV	
Switzerland	HTA programme	Pharmaceutical submissions	MedTech submissions

Case study 8: Confidentiality of the procedure at Hauptverband der Österreichischen Sozialversicherungsträger

Hauptverband der Österreichischen Sozialversicherungsträger (HVB) has legal responsibility for the management of the Austrian social security system which includes decision making about reimbursement and pricing of pharmaceuticals. Their procedure keeps documents relating to the reimbursement and pricing process confidential. In the instance of a legal challenge, the court decision is published.

Collaborative working would require agreement with the company involved in the procedure that information can be shared with the other relevant organisations and groups involved in the collaboration. For the BENELUXA collaboration this would mean the other BENELUXA HTA agencies (in Belgium, Luxembourg and the Netherlands), national industry affiliates and other national stakeholder groups (e.g. in the Netherlands draft assessment reports are consulted on with patient and professional groups and payers, and in Belgium some of these groups are represented in their Commission who formulate the reimbursement proposal). For aspects such as price negotiations, this may be a particular challenge as information is sensitive.

Information produced by other agencies used to support assessment

Twenty-two countries out of 29 (76%) used information from other jurisdictions to support the assessment or evaluation of pharmaceuticals and 18 out of 22 countries (82%) used information from other jurisdictions to support the assessment or evaluation of non-pharmaceutical health technologies.

Countries tended to use HTA reports and published recommendations and guidelines to support the assessment procedure. Reports from the following countries were specifically mentioned as being sources used from other countries: England, NICE (4 instances); Canada, CADTH (3 instances); Scotland, SMC (2 instances); Germany, IQWiG and G-BA (2 instances); France, HAS (2 instances); Australia, PBS (1 instance). EUnetHTA reports were also identified as being used to support assessment. In most cases agencies were only able to make use of reports written in English, in some cases reports written in French and German could also be used in addition to reports in shared languages. Comments indicated that the information tended to be used as supporting information, for example to support a more detailed insight, or as background information.

Three agencies, all assessing non-pharmaceutical health technologies, indicated that searching of websites and databases was embedded in routine working procedures. In Austria, LBI-HTA indicated that they would search for existing evidence reviews before carrying out an assessment and both Scotland (SHTG) and Italy (Agenas) indicated they routinely searched agency websites to identify existing assessments to support their national assessment.

Analysis of assessment and evaluation procedures

The agency approach to assessment defines how it can engage in collaborative HTA both in terms of using collaborative HTA and taking part in joint work.

EUnetHTA currently produces an HTA using a company submission, the assessment is designed to stand alone from the company submission e.g. it is published without the company submission and it must therefore be written so that the industry submission is not required to be read alongside.

Current working practices in national and regional agencies broadly reflect:

- Create an HTA using evidence the agency has identified itself
- Create an HTA using evidence provided by industry as one source
- Evaluate a submission of evidence (that includes an HTA or HTA type information) usually provided by industry

An evaluation of an evidence submission is not the same as producing an HTA, and the two are not interchangeable. Agencies who create HTA will be able to adopt or adapt collaborative HTA (where it is timely, relevant and robust). Agencies who evaluate company submissions will within their current procedures use collaborative HTA to inform their evaluation. From an implementation perspective it is important to differentiate between agencies who create HTA and those that evaluate company submissions because this influences the type of use. Case studies 9 and 10 contrast the approaches to using EUnetHTA assessments in instances of HTA production and evaluation of a company submission.

Pharmaceuticals

For pharmaceuticals the routine practice for the majority of agencies is to evaluate the appropriateness of a company submission of evidence rather than creating an HTA. Given the high levels of evaluation of company submissions of evidence it is important to consider how collaborative HTA could be used:

- as an alternative to a national submission (that is instead of asking for a company REA submission the EUnetHTA assessment is used)

- in addition to a national submission (the scenario mainly used currently by EUnetHTA partners),
- incorporated into the national submission (that is the collaborative HTA or company submission for collaborative HTA is used in the national submission)

Agencies need to identify which of these within their legal requirements and requirements for accountability are feasible either currently or in the future and which is perceived to be more desirable.

Non-pharmaceutical health technologies

A greater proportion of agencies create their own HTA and a smaller number evaluate a submission of evidence. Therefore for non-pharmaceutical health technologies implementation will have high rates of adoption and adaptation. While in total there are a smaller number of countries carrying out non-pharmaceutical HTA among these the amount of adoption and adaptation are likely to be higher than for pharmaceuticals because of the differences in current ways of working.

Case study 9: Use of EUnetHTA assessments by FIMEA to support national production of HTA in Finland

Assessments are completed by FIMEA staff normally with involvement of internal or external clinical experts. The reports include an assessment of clinical effectiveness and also costs and budget impact analysis. FIMEA used the EUnetHTA assessment of ramucirumab for advanced gastric or gastro-oesophageal junction adenocarcinoma as the main source document for their national assessment. The adaptation process included:

- Reducing the length of the EUnetHTA assessment
- Adding subgroup information
- Adding national context information
- Adding economic evidence
- Additional clinical searches
- Writing the report in Finnish with summaries in Swedish and English

A FIMEA product is typically approximately 25-35 pages long, of this approximately 60% of the report will be clinical evidence. FIMEA summarised the EUnetHTA assessment. The content of the EUnetHTA report was relevant to the FIMEA assessment, but was in greater detail than FIMEA would usually use. A larger selection of subgroup analyses were included and needed in FIMEA's report considering treatment duration, previous treatments and next line treatments.

Additional clinical searches were run to identify any other evidence including PubMed, Medline and clinical trials.gov.

Case study 10: Use of EUnetHTA assessments by NIPN to support evaluation of industry submissions in Hungary

NIPN review company submissions rather than produce HTAs, therefore NIPN use EUnetHTA assessments and specifically the relative effectiveness data as a source of information in the clinical effectiveness section of their report to support their review process. NIPN used the EUnetHTA assessment of canagliflozin for the treatment of type 2 diabetes mellitus in their national evaluation. The EUnetHTA assessment was used to question the case made by the company about the non-inferiority of the product and check the comparability of the data submitted with that in the EUnetHTA assessment. They were unable to use the data in the EUnetHTA assessment to undertake sensitivity analyses in the economic section of the report because of differences in reporting of outcomes in the report and model.

The availability of EUnetHTA assessments and their use to support the review process is an additional step in the NIPN procedure and so there are currently no time or resource savings from having a EUnetHTA assessment. Instead the EUnetHTA assessment is seen to improve the quality of the NIPN review. The production of more EUnetHTA assessments that have a consistent scope with the NIPN national assessment may make the NIPN review process easier.

Contents of assessment

The contents of an assessment are fundamental to implementation, if collaborative HTA is not relevant to the HTA agency and does not meet the needs of the decision maker, then the collaborative HTA is less likely to be used in a national procedure.

EUnetHTA assessments include:

- REA (including health condition and current use of the health technology, description of the health technology, clinical effectiveness and safety)
- Full HTA (to include REA and also economic, organisational, ethical, legal and patient and social aspects)

Pharmaceuticals

Among existing working practices the contents of an assessment for the majority of national agencies include relative effectiveness information and economic information (figure 28). Economic information may include cost and resource use information, cost comparisons, budget impact, reviews of health economic literature as well as primary cost effectiveness and cost utility modelling. These two components are usually carried out as a combined assessment in parallel.

From an implementation perspective although all agencies include relative effectiveness information in their assessments, for the group of agencies who use primary cost effectiveness and cost utility modelling and complete this in parallel with REA, the ability to use a relative effectiveness assessment from one source (that is, the collaborative HTA) and a cost effectiveness analysis (that by definition also includes relative effectiveness information) from another source (usually from a company) could be challenging as there is an increased risk of data inconsistency between sources that could delay national decision making. Even among agencies reviewing cost-effectiveness studies rather than using primary economic modelling there could still be consistency issues if for some reason the studies included in the collaborative HTA are different to those that have been included in the published economic studies (case study 16).

This implementation barrier will affect few agencies all the time as cost effectiveness analysis is rarely used for all technologies. Nevertheless, this interacts with topic selection criteria because new products and major licence extensions are most likely to be subject to assessment but are also more likely to be subject to cost effectiveness and cost utility analysis. Although these topics are assessed by more agencies they are also associated with more significant implementation barriers.

For agencies to resolve this implementation barrier this would mean either adopting a step-wise approach whereby assessment of relative effectiveness is first completed before economic analyses are carried out or industry must undertake to use the outcomes of the collaborative HTA in their national cost effectiveness submissions. This may be challenging for industry as the agreement to do this may have to occur before the outcomes of the collaborative HTA is known or it may involve waiting for the outcomes of the collaborative HTA to be known. Therefore, within the current timelines of EUnetHTA assessments both of these could act to delay decision making and therefore may not be feasible (for example, if the agency work is governed by the Transparency directive (89/105/EEC)¹⁶ nor desirable (for example, if the agency is charged with producing guidance close to launch of a product to support prescribing and use).

Given the frequency of inclusion of economic information in assessments, collaborative HTAs may be able to add further value to agencies by including aspects of economic information that are not local e.g. published health economic evidence or where the information is local but the collaborative HTA could support

¹⁶ The Transparency Directive (Council Directive 89/105/EEC of 21 December 1988 relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of national health insurance systems) aims to ensure the transparency of measures established by EU countries to control the pricing and reimbursement of medicinal products. The Transparency directive (89/105/EEC) lays down three major requirements with respect to individual pricing and reimbursement decisions:

- decisions must be made within a specific timeframe (90/180 days);
- decisions must be communicated to the applicant and contain a statement of reasons based on objective and verifiable criteria;
- decisions must be open to judicial appeal at national level.

national agencies (e.g. identifying potentially important areas where there may be resource use). In addition including clinical effectiveness data in a format that supports its use in economic evaluations e.g. as QALYs and using the same measurement scales as used in economic evaluations, so that data from the collaborative HTA can be used in sensitivity analyses in the economic submission, will allow more meaningful use of the collaborative HTA in national procedures.

Non-pharmaceutical health technologies

For non-pharmaceutical health technologies there is a wider variation in the contents of a national assessment, and a single set of assessment contents does not dominate (figure 29). Rather than restricting the contents of collaborative HTA to REA or to a full HTA it may be appropriate to build consideration of the important contents of an assessment into the topic selection and prioritisation procedure e.g. MS are asked as part of topic prioritisation and selection about valued areas. This would then allow a more flexible selection of information from the HTA Core model reflecting the varied nature of the HTA being carried out across MS.

Case study 11: Scottish Health Technologies Group (SHTG) adding health economic evidence to relative effectiveness assessments

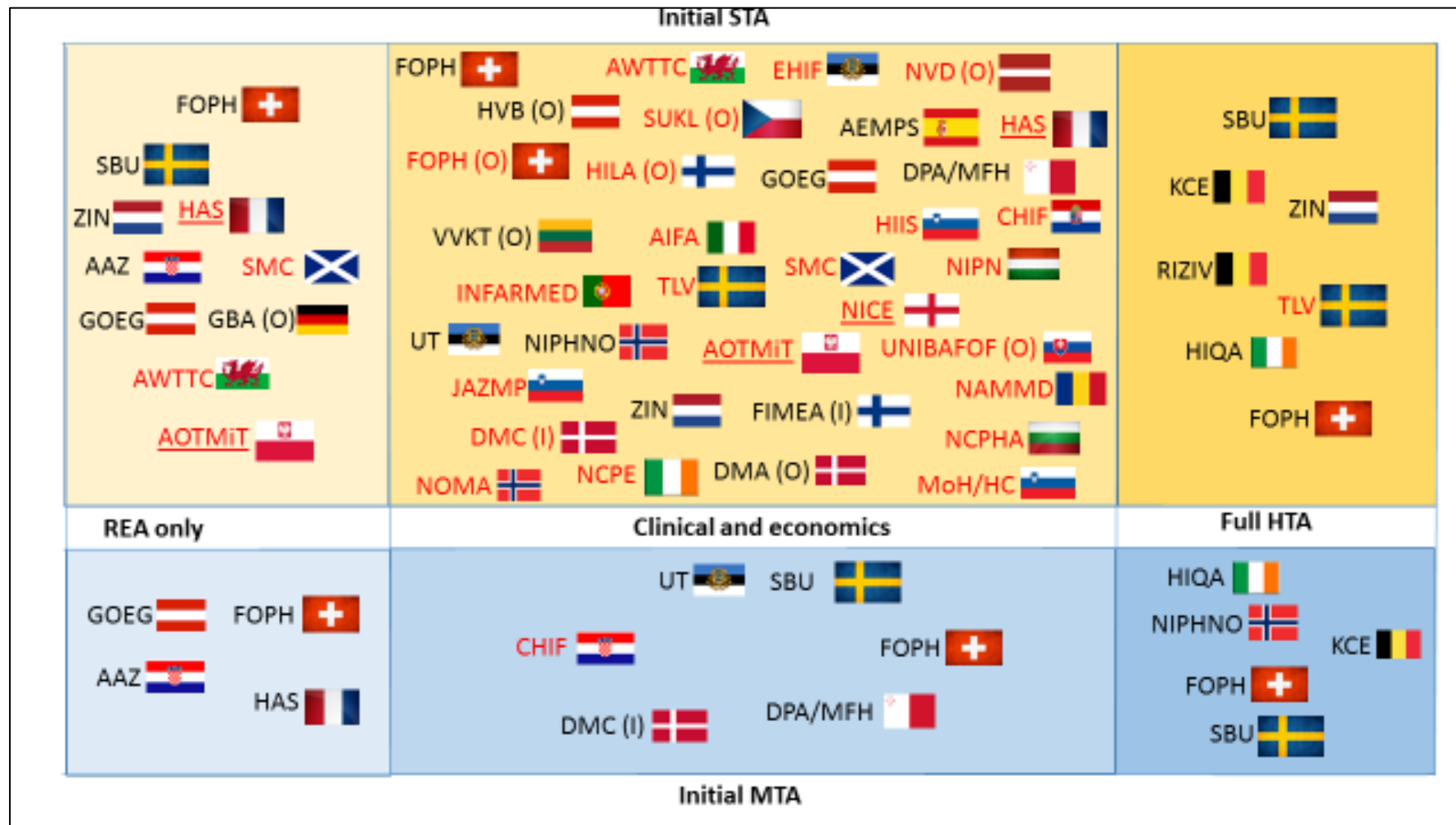
The Scottish Health Technologies Group (SHTG) produce assessments called evidence notes. All evidence notes include a review of cost effectiveness evidence. To adapt the EUnetHTA REA for the Scottish context SHTG had to develop searches to identify economic evidence and then perform a review of that evidence. For one SHTG adaptation (mitral valve repair) the EUnetHTA assessment identified no comparative studies that met its inclusion criteria and the assessment was based on non-comparative data only. The searches by SHTG identified that the economic evidence was largely based on data from a clinical study, one arm of which, given the comparator used, had been correctly excluded from the EUnetHTA assessment. SHTG had to add this study to their evidence note and describe it in the adaptation so that the economic evidence could be fully discussed. The addition of this study to the evidence note was discussed by evidence review committee, and described for the scientific committee who formulate the advice. In this instance where economic analyses were based on a study tangential to the main body of clinical evidence an additional step was required to check and ensure transparency around any potential discrepancies in the inclusion and exclusion of clinical and economic evidence.

Information sharing between jurisdictions

Among agencies who publish assessments or submissions of evidence in a language shared by other countries, information sharing could be facilitated if a core set of relevant information could be agreed among MS (including decision makers to define the relevant set of information). The core set of information could be based on the HTA CORE model assessment elements and the agreement would be that it will regularly be used in national assessments or submission templates. The core set of information could be included with references in national assessments or submission

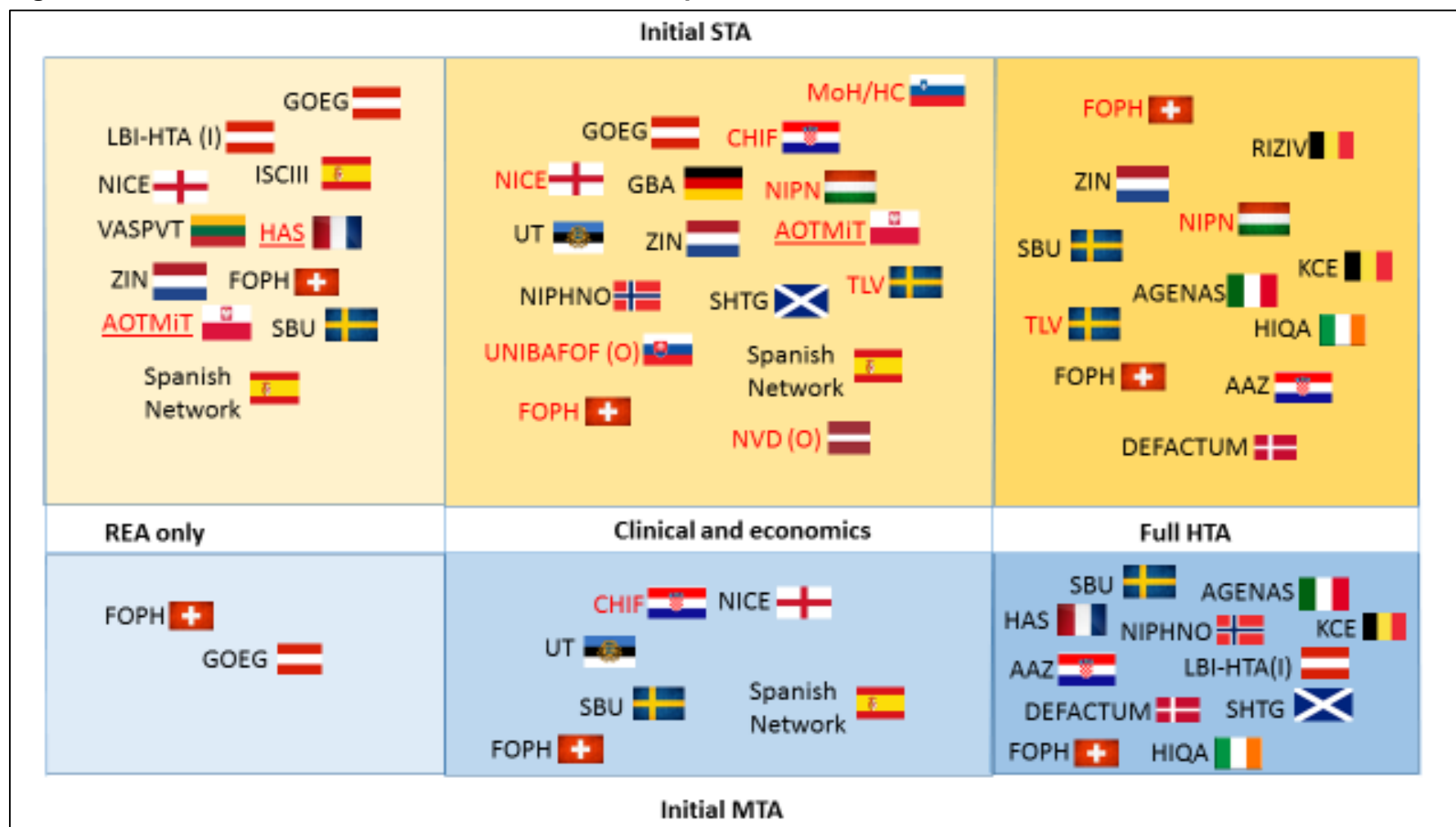
templates with references using the HTA Core model assessment element unique identifier. This would allow the information to be easily searchable for agencies in other countries and facilitate re-use of the contents of the collaborative HTA in national submissions. Existing EUnetHTA tools (e.g. the POP database) or other existing databases (e.g. the HTA database) could be used to develop a register of published assessments and evaluations carried out with links to documentation that includes the unique identifiers.

Figure 28: Content of initial STA and initial MTA - pharmaceuticals



Key: Black = agencies creating own REA assessment; Red = agencies appraising submissions and evaluating this rather than creating own REA assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only

Figure 29: Content of initial STA and initial MTA – non pharmaceuticals



Key: Black = agencies creating own REA assessment; Red = agencies appraising submissions and evaluating this rather than creating own REA assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only

Language of assessment

For the majority of agencies their work is carried out in their national language. This can be for legal reasons (either general language laws for public and governmental affairs, or specific language requirements underpinning HTA legislation), or it may be a procedural requirement (case study 12). There are also practical reasons why HTA is carried out in the national language; working in the national language facilitates quicker and easier and more precise communication between people involved in the national assessment, supports involvement of stakeholders in the procedure, in particular patients and supports implementation of the national report in local contexts.

From an implementation perspective the requirement whether practical, procedural or legal to use national languages means that within some countries the collaborative HTA will require translation for use in a national assessment. In some instances countries who have procedural restrictions or legal restrictions specific to the HTA procedure, may be able to work towards developing or partly developing reports in English. Doing this will facilitate sharing of HTA between jurisdictions and will mean that collaborative HTAs will require less adaptation to be used in national assessments. However, countries will need to clearly identify the audience for the report, their audience's document requirements (e.g. the full HTA or only a summary) and the audience's language requirements. Collaborative HTA provides little additional value if used in a national report that is then not implemented or not fully used in the formal decision making procedure because it is developed in English.

Case study 12: Language requirements in BENELUXA collaboration

The Belgian procedure legally requires that assessments are written in a Belgian national language (French, Dutch, German), therefore joint assessments with the Dutch agency ZIN are produced in Dutch. Companies submitting for a joint procedure between Belgium and the Netherlands must also submit in Dutch as the Belgian procedure requires that the assessment is written in the language in which the submission is received (roughly 60% of submissions will be received in Dutch, 40% in French and none are normally submitted in German).

As with Belgium, the assessments produced by HVB are part of a formal pricing and reimbursement process that can be legally challenged. HVB is bound by law to produce assessments and for companies to submit in the national language German. However, documents supporting the assessment such as published primary studies, systematic reviews or expert statements can also be submitted in English. HVB can ask for a translation into German and if HVB is sued the court may require that any documents initially submitted in English must be translated into German.

In the long term it is hoped that it will be possible for BENELUXA to move to producing reports in English so there is greater transferability between countries.

However, moving to writing assessments in English will initially consume more resources and time as staff will need to become experienced in expressing issues precisely and in detail in English. For HVB, assessments written in English may still need to be translated to German which within the timelines available for assessment would be challenging. However, it may also be possible to use parts of collaborative assessments in English if these are referenced to or cited as an expert statement.

Recommendations for assessment and evaluation procedures

Key implementation challenge	Recommendations for centralised cooperation	Recommendations for agencies
<ul style="list-style-type: none"> • Variation in the end product produced; HTA or an evaluation of a company submission of evidence • Variation in the range of domains needed in the assessment • Risk of inconsistency caused by the relative effectiveness assessment and economic information coming from different sources • Requirements to use national language in assessments or documents the agency creates 	<ul style="list-style-type: none"> • Identify if any tools are needed to support critique and review of industry submissions • Work with users and decision makers to get feedback about: <ul style="list-style-type: none"> ○ readability, depth and degree of critical analysis ○ most valued content of joint assessments ○ suitability of the end product for assessment or evaluation • Early consideration as part of topic selection of the relevant information to include from REA to full HTA • Work with industry to ensure consistency of relative effectiveness information with that used in national submissions • Work with agencies evaluating submissions to identify whether collaborative HTA will be used as an alternative to national REA submissions, in addition to national REA submissions or incorporated into national REA submissions 	<ul style="list-style-type: none"> • Incorporate into standard operating procedures the use of secondary sources of evidence such as collaborative HTA to inform HTA and support evaluation of submissions • Work towards establishing procedures where HTA information that is produced in a shared language is made public so that it can be used by other agencies • Identify whether there are reports or parts of reports that could be produced in English to make the procedure of using collaborative HTA less resource intensive • For agencies producing publically available HTA, work towards including the essential REA assessment elements in the report and identifying this information in the report so the information is searchable and easily identifiable by others

Chapter 6: Quality assurance procedures

Key messages:

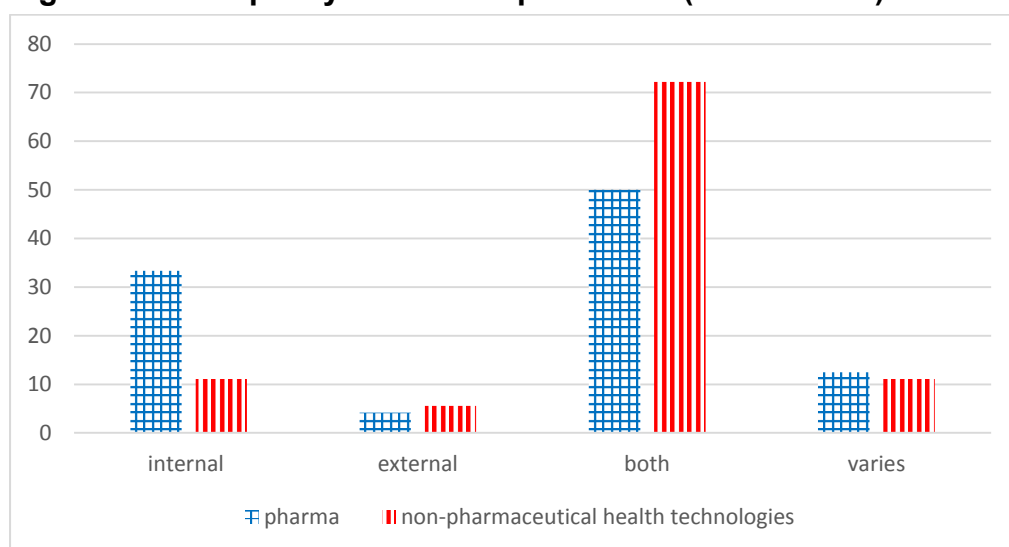
- Appropriate quality assurance supports the rigour of collaborative HTA and creates trust that it is a robust alternative to national HTA
- The majority of countries (83% and 82% for pharmaceuticals and non-pharmaceutical health technologies, respectively) have quality assurance procedures in place for least some agencies and programmes.
- Countries frequently (63% and 72% for pharmaceuticals and non-pharmaceutical health technologies, respectively) include both internal (e.g. review from staff members) and external (e.g. review by clinical or scientific experts, stakeholder review or public review) aspects. For pharmaceuticals quality assurance procedures vary more.
- People carrying out quality assurance are most likely to include other agency staff members, clinical experts, scientific experts and stakeholders.
- Quality assurance procedures are most likely to be used during the assessment production phase (77% and 72% for pharmaceuticals and non-pharmaceutical health technologies, respectively), but also widely occur once the assessment is completed (59% and 66%, respectively).
- Appropriate quality assurance mechanisms should be embedded into the collaborative HTA procedure. If quality assurance in any displaced parts of national procedures are not part of the collaborative HTA procedure then it may not be perceived as a robust alternative.

Description of quality assurance procedures

Quality assurance mechanisms

The majority of countries; 24 out of 29 (83%) for pharmaceuticals and 18 out of 22 (82%) for non-pharmaceutical health technologies have a quality assurance procedure to review the work the agency carries out. In 5 of these countries for pharmaceuticals and 3 for non-pharmaceutical health technologies only some agencies within the country report having quality assurance procedures. For example Finland reports a procedure for FIMEA but not for HILA, Denmark for DMC but not for DMA and Switzerland for the HTA they produce outside of the submission context and for the reviews of company submissions of non-pharmaceutical health technologies, but not for their reviews of company submissions of pharmaceuticals.

Figure 30: The quality assurance procedure (% countries)



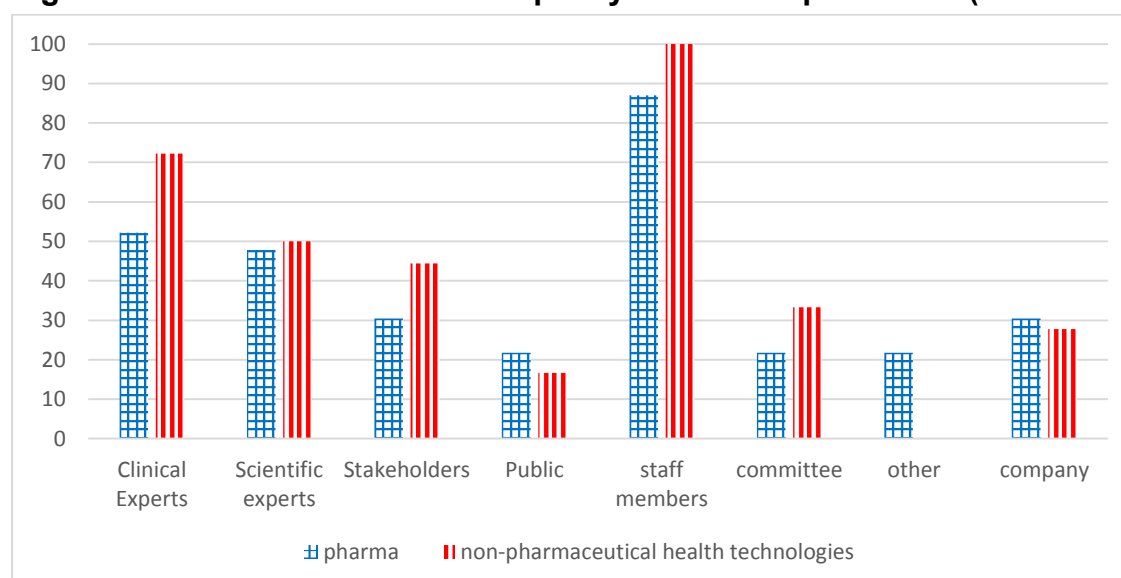
Key: pharmaceuticals N=24 countries reporting a quality assurance procedure, non-pharmaceutical health technologies N=18. Varies = the approach to quality assurance (internal, external or both) varies between agencies or HTA programmes within the country.

For pharmaceuticals, the quality assurance procedure is both internal (e.g. review from staff members) and external (e.g. review by clinical or scientific experts, stakeholder review or public review) in 12 countries (50%), internal in 8 out of 24 countries (33%), external in 1 country (4%) and it varies between agencies or programmes in 3 countries (13%) (figure 30). In 2 of these countries (Austria, England) one agency or programme uses internal quality assurance and the other both internal and external and in the other case (Estonia) one agency uses external and the other both internal and external.

For non-pharmaceutical health technologies the quality assurance procedures are most commonly internal and external (13 out of 18 countries; 72%). In 2 countries (11%) it is internal only, 1 country (6%) external only and in 2 countries (11%) it varies. In one case (Switzerland) one programme uses both internal and external quality assurance and the other internal only. In the other case (Belgium) one agency uses both internal and external quality assurance and the other external only.

As expected given the high use of internal quality assurance procedures, in the majority of countries quality assurance is by staff members (100% non-pharmaceutical health technologies; 87% pharmaceuticals). In general the involvement of external parties was similar between the types of technologies, but there was a greater use of clinical experts and stakeholders among countries assessing non-pharmaceutical health technologies. Other parties involved in quality assurance included international audits, lawyers and government (figure 31).

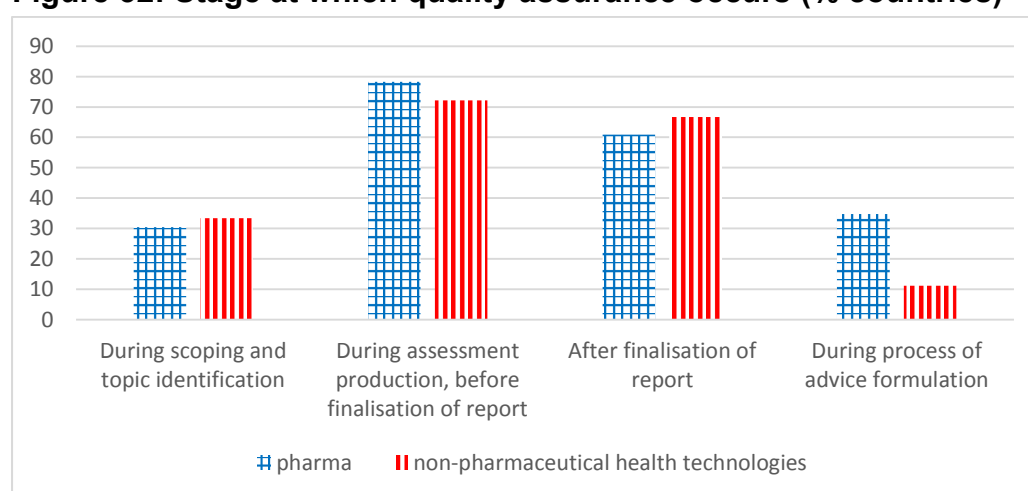
Figure 31: Parties involved in the quality assurance procedure (% countries)



Key: pharmaceuticals N=23 countries (missing data for Romania) reporting a quality assurance procedure, non-pharmaceutical health technologies N=18. Agencies coded multiple categories so data may add up to more than 100%.

For pharmaceuticals quality assurance procedures are most likely to occur during assessment production (18 out of 23¹⁷ countries (78%)) and after finalisation of the report (14 out of 23 countries (61%)). There is a similar pattern for non-pharmaceutical health technologies; quality assurance most frequently happens during assessment production (13 out of 18 countries (72%)) and after finalisation of the report (12 out of 18 countries (67%)) (figure 32).

Figure 32: Stage at which quality assurance occurs (% countries)



Key: pharmaceuticals data for 23 countries reporting a quality assurance procedure (Romania missing data) non-pharmaceutical health technologies N=18. Agencies coded multiple categories so data may add up to more than 100%.

¹⁷ Missing data Romania

Analysis of quality assurance procedures

Quality assurance and stakeholder involvement

Appropriate quality assurance mechanisms should be embedded into collaborative HTA as it is undertaken. In addition, if collaborative HTA seeks to reduce duplication in national assessment and so displace some aspects of national assessment procedures, then quality assurance needs to have a specific focus on those aspects likely to be displaced. If quality assurance in any displaced parts of the national procedure is not part of the collaborative procedure then collaborative HTA may not be perceived as a robust alternative.

The collaborative HTA does not need to incorporate all aspects of quality assurance currently in place in national procedures. The procedure of adaptation and use of the collaborative HTA in decision making will allow agencies to incorporate aspects of quality assurance into their national adaptations or evaluations of submissions (case study 13) and some countries will have to do this as part of ensuring accountability and transparency of the larger procedure that HTA is part of.

However, quality assurance procedures that take place as part of collaborative HTA provide an opportunity to pool clinical and methodological expertise from across countries that may not be available within individual countries, foster trust in the use of the collaborative HTA as the main source document for the national HTA and may reduce the need for some internal national quality assurance procedures. Quality assurance procedures must be balanced with the requirement for timeliness, if quality assurance procedures lengthen the time required to complete an assessment, then this could adversely affect use.

Given the nature of the quality assurance currently undertaken in many countries there is a need to include review from other EUnetHTA partners as part of assessment production and also external review by clinical and methodological experts. Working with MS to identify the aspects of quality assurance that they find most challenging and are most likely to be displaced in the national procedures will help target the quality assurance procedures required by collaborative HTA to the areas of greatest need with minimum lengthening of collaborative HTA procedures.

Case study 13: Scottish Health Technologies Group (SHTG) incorporating quality assurance procedures into adaptations of EUnetHTA assessments

SHTG adapted 2 products from the EUnetHTA JA2 into SHTG evidence notes. The 2 EUnetHTA assessments adapted were transcatheter implantable devices for mitral valve repair in adults with chronic mitral valve regurgitation and endovascular therapy using mechanical thrombectomy devices for acute ischaemic stroke.

The evidence notes developed from the EUnetHTA assessments were able to fit into routine SHTG quality assurance procedures including:

1. consideration of the appropriateness of the topic and scope for assessment by an independent evidence review committee before the adaptation was carried out,
2. internal review of the adapted report once SHTG had carried out their adaptation, and
3. external peer review following internal review with Industry and other stakeholders prior to being discussed by the SHTG scientific committee for formulation of advice.

The EUnetHTA quality assurance procedures and joint production procedures were additional to those that would have been carried out by SHTG in their routine work. The additional quality assurance procedures carried out as part of the creation of the EUnetHTA assessment provided additional value as it meant that the assessment had been seen and reviewed by a wider range of independent people and stakeholders. This is a benefit for small countries where products being assessed are relatively new with limited experience of use and expert knowledge of specialised products might be held only by one or two individuals. The involvement of multiple agencies and stakeholders also reduces the likelihood of information being missed.

Recommendations for quality assurance procedures

Key implementation challenge	Recommendations for centralised cooperation	Recommendations for agencies
<ul style="list-style-type: none"> If quality assurance in any displaced parts of the national procedure is not part of the collaborative HTA procedure then collaborative HTA may not be perceived as a robust alternative to national procedures 	<ul style="list-style-type: none"> Embed internal (that is, among EUnetHTA partners) and external (that is using external experts and stakeholder groups) into collaborative HTA as it is undertaken Quantify and share with MS any impact of adding quality assurance procedures against a lengthening of the assessment procedure as reduced timeliness could adversely affect implementation. 	<ul style="list-style-type: none"> Identify valued quality assurance practices that are most challenging to implement in current national procedures and are most likely to be displaced from national procedures by collaborative HTA.

Chapter 7: Timing

Key messages

- Collaborative HTAs must be timely to reflect national decision making priorities and to fit into any other steps of the procedures that the HTA or evaluation of the company submission is informing.
- The amount of time an agency has to carry out an assessment or evaluate a company submission ranges from a couple of weeks to more than a year.
- The time provided tends to be shorter for pharmaceutical than non-pharmaceutical health technologies.
- For pharmaceuticals, the timing of agency work is most frequently associated with requirements for decision making defined by the Transparency directive (89/105/EEC) rather than the regulatory timetable.
- For pharmaceuticals, the procedure can start before marketing authorisation is granted in 9 countries (31%) and in a further 6 countries (21%) the procedure may start before marketing authorisation for some topics.
- For non-pharmaceutical health technologies, consideration of best possible timing for collaborative HTA should be built into topic selection and prioritisation procedures because of variation in when topics become a national priority in the different MS.
- For pharmaceuticals to maximise implementation collaborative HTA must be available at CHMP opinion. However, collaborative assessments that were available at the time of marketing authorisation at the latest would support implementation in the majority of countries.

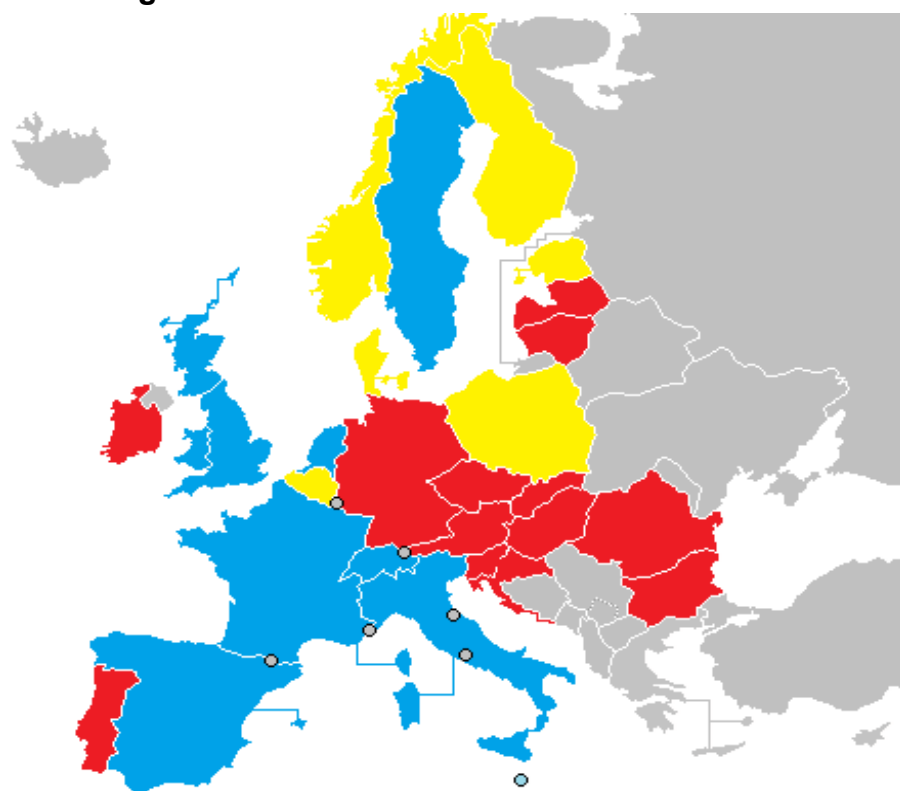
Description of the timing of the procedure

Timing of the initiation of the procedure

In 14 out of 29 countries (48%) the procedure cannot start before marketing authorisation is granted, in 9 countries (31%) the procedure can start before the marketing authorisation decision and in 6 countries (21%) the timing of the start of the procedure varies depending on the agency or topic. For example, in Norway NOMA indicated that procedures can start before marketing authorisation, whereas NIPHNO stated that they do not (figure 33).

Where an assessment can start before the marketing authorisation decision, the earliest it normally starts is at the time of CHMP opinion (for example, Denmark, DMA and DMC, Finland, FIMEA (case study 7), Netherlands, ZIN (some pharmaceuticals only), Scotland, SMC, Spain AEMPS and Switzerland FOPH. In one instance the assessment starts prior to CHMP opinion (England, NICE).

Regional agencies carrying out assessments of pharmaceuticals reported that these usually start after the pharmaceutical has received marketing authorisation.

Figure 33: Countries where the pharmaceutical assessment can start before marketing authorisation

Key: Red must start after marketing authorisation, Blue can start before marketing authorisation, Yellow some agencies in country must start after marketing authorisation but some may start before.

Table 5: Countries where either some agencies or some programmes/departments can start before marketing authorisation and others do not

	YES	NO
Belgium	RIZIV	KCE
Denmark	DMA, DMC(STA)	DMC (MTA)
Estonia	UT	EHIF
Finland	FIMEA	HILA
Norway	NOMA	NIPHNO
Poland	Procedure triggered by MoH	Procedure triggered by Industry

Case study 14: Timing of initiation of assessment at FIMEA in Finland

The HTA unit of the Finnish Medicines Agency (FIMEA) aim to start their assessments after CHMP positive opinion, so a report can be published as soon after marketing authorisation as possible. This is necessary so that the reports are timely to support decision making in hospitals about the introduction of a pharmaceutical close to the time of launch in Finland.

FIMEA adapted the EUnetHTA assessment of ramucirumab for advanced gastric or gastro-oesophageal junction adenocarcinoma. Ramucirumab was technology that had been prioritised by FIMEA for completion of an assessment as part of their normal work. FIMEA acted as a reviewer for the EUnetHTA assessment of ramucirumab and therefore had access to a draft of the EUnetHTA report that they used to complete their national assessment. The final EUnetHTA assessment was not available within the timescales required for FIMEA to complete a national assessment and the 2 reports were published at about the same time.

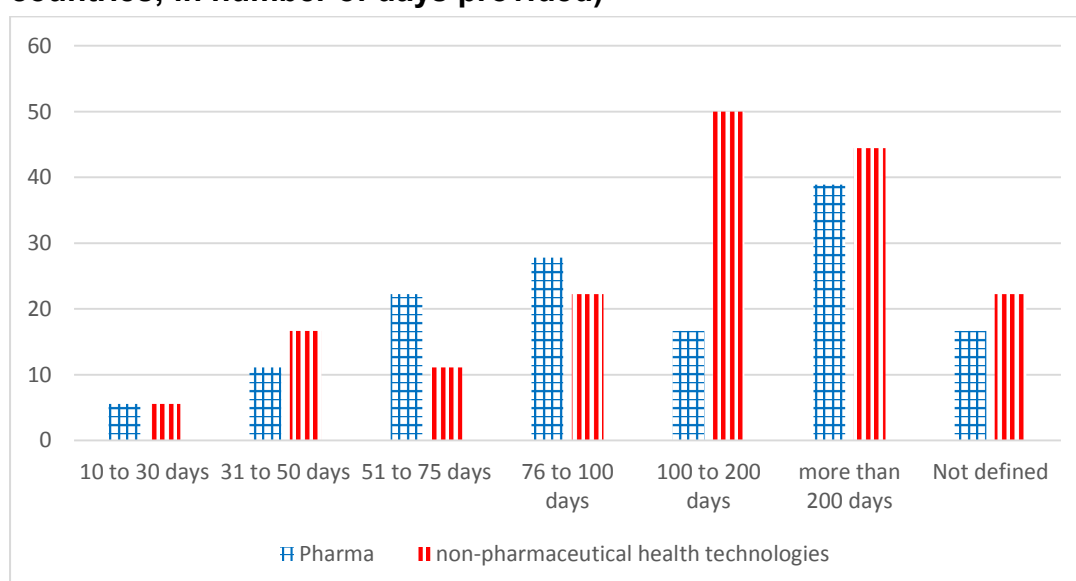
Time provided to carry out an assessment

Eighteen countries do at least some assessments of pharmaceuticals and 18 countries do assessments of non-pharmaceutical health technologies.

For pharmaceuticals there are 2 broad groups of assessments being undertaken. The first group is typically carried out as STA in 2-3 months within the timeframes governed by the Transparency directive (89/105/EEC). The second group is typically carried out over a longer timeframe (approximately a year) outside of the Transparency directive (89/105/EEC). The second group and is more likely to be multiple technology assessments and reassessments (figure 34).

For non-pharmaceutical health technologies the timeframes for completion tend to be longer than for pharmaceuticals most commonly 6 months to 1 year. The timelines for how long the agency has to complete the assessment are less likely to be defined, meaning the agency negotiates with the initiator of the assessment over how long they receive to complete the assessment based on the topic.

Figure 34: Time taken by the HTA agency to complete the assessment (% countries; in number of days provided)



Key: pharmaceuticals data for 18 countries doing assessments, non-pharmaceutical health technologies N=18 countries doing assessments. Agencies coded multiple categories so data may add up to more than 100%.

The Transparency directive (89/105/EEC) determines the timeframe for assessment in at least one agency in 23 countries (79%). Countries in which the Transparency directive (89/105/EEC) did not apply were England, Germany, Scotland, Spain, Switzerland (Not applicable) and Wales. The Transparency directive (89/105/EEC) did not always apply to all agencies within a country (table 6).

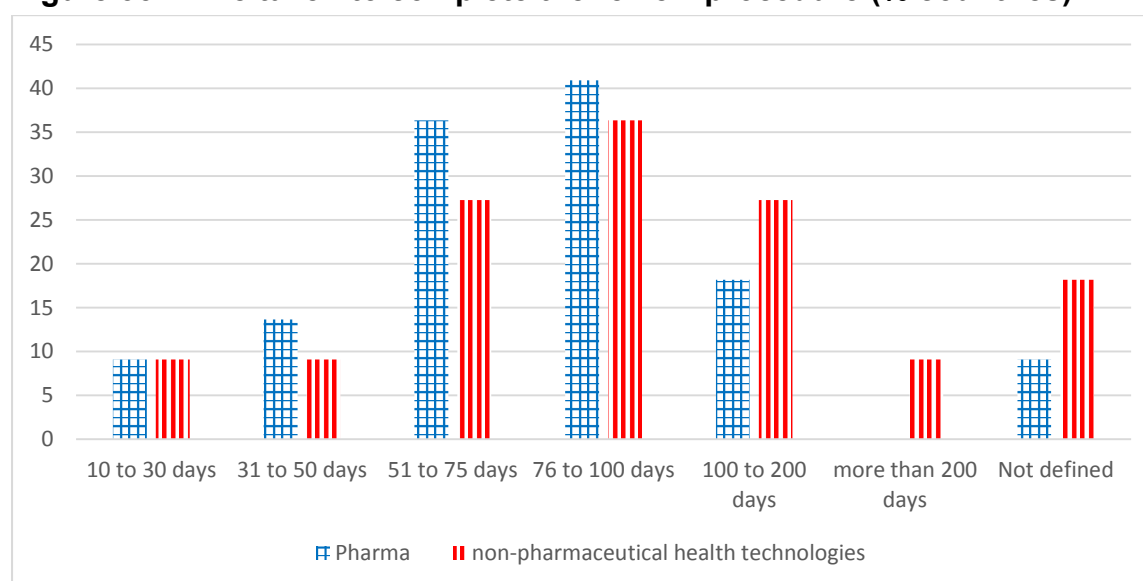
Table 6: Countries where some agencies are bound by the Transparency directive (89/105/EEC) and some are not

	YES	NO
Austria	HVB	LBI-HTA, GOEG
Belgium	RIZIV	KCE
Denmark	DMA, DMC (STA)	DMC (MTA)
Estonia	EHIF	UT
Finland	HILA	FIMEA
Ireland	NCPE	HIQA
Norway	NOMA (outpatient)	NOMA (inpatient), NIPHNO
Poland	Procedure triggered by Industry	Procedure triggered by MoH
Slovenia	HIIS, JAZMP	MoH HC
Sweden	TLV	SBU

None of the regional agencies reported having timeframes bound by the Transparency directive (89/105/EEC) or other restrictions regarding the timeframe of assessments.

Timeframes for evaluating a company submission of evidence

Figure 35: Time taken to complete the review procedure (% countries)



Key: pharmaceuticals N=22 countries, non-pharmaceutical health technologies N=11 with procedure whereby submissions of evidence are reviewed (Croatia (CHIF) marked N/A evaluation as part of an appraisal only). Agencies coded multiple categories so data may add up to more than 100%.

Twenty-two countries evaluate submission of evidence of pharmaceuticals and 12 countries evaluate submission of evidence of non-pharmaceutical health technologies.

For pharmaceuticals the majority of countries have 2 to 3 months to complete their evaluation (figure 35). However, some countries have less, for example Switzerland (FOPH) have 20 days, Bulgaria (NCPHA) have 40 days to produce a draft evaluation of the submission and Hungary (NIPN) has 43 days (case study 15). Longer timeframes for evaluation tend to be for agencies where the HTA and decision making procedures is contained within a single agency.

For non-pharmaceutical health technologies although 2-3 months is also a frequent timeframe for an evaluation, there are more countries who have longer most frequently 4-6 months. The review of company submissions is shortest in Hungary (NIPN; 30 days or less (case study 15)).

Case study 15: Timings of initiation and evaluation in Hungary

All topics for assessment come to the National Institute of Pharmacy and Nutrition (NIPN) through the National Health Insurance Fund (NHIF). It is not known in advance whether or when an assessment will be required. NHIF obtains the topics from companies submitting an application for reimbursement. NHIF forwards submissions to NIPN within approximately 2 days of receipt of the application from the company.

Following receipt, NIPN have 43 days to prepare the review of the evidence submission of a pharmaceutical, 30 days for a healthcare technology and 15 days for a medical aid (a medical device to be used by a patient). These reports are then sent back to NHIF who formulates an initial decision. Ninety days is allowed from submission to initial decision by NHIF. Following the initial decision there is a procedure for making the final decision of NHIF. The final decision is made by a Committee that includes representatives of NHIF, representatives of the Ministry of Human Capacities and representatives of NIPN. Ninety days is allowed from initial decision to final decision. Timings are set by the requirements of the Transparency directive (89/105/EEC).

For pharmaceuticals, companies can submit for reimbursement following receipt of marketing authorisation once a product is reimbursed in 3 other European countries. This requirement is indication specific. The amount of time between a product receiving marketing authorisation and a company submitting for reimbursement is variable, but it can be very short. For non-pharmaceutical health technologies there is no predictability as to when a company may submit for reimbursement and once a

topic is sent to NIPN a report is required in 15 days - 30 days depending on technology type. Therefore although NIPN complete a large number of medical device reports, coordinating the use of EUnetHTA outputs with national assessment activities is challenging.

Analysis of timing of assessment procedures

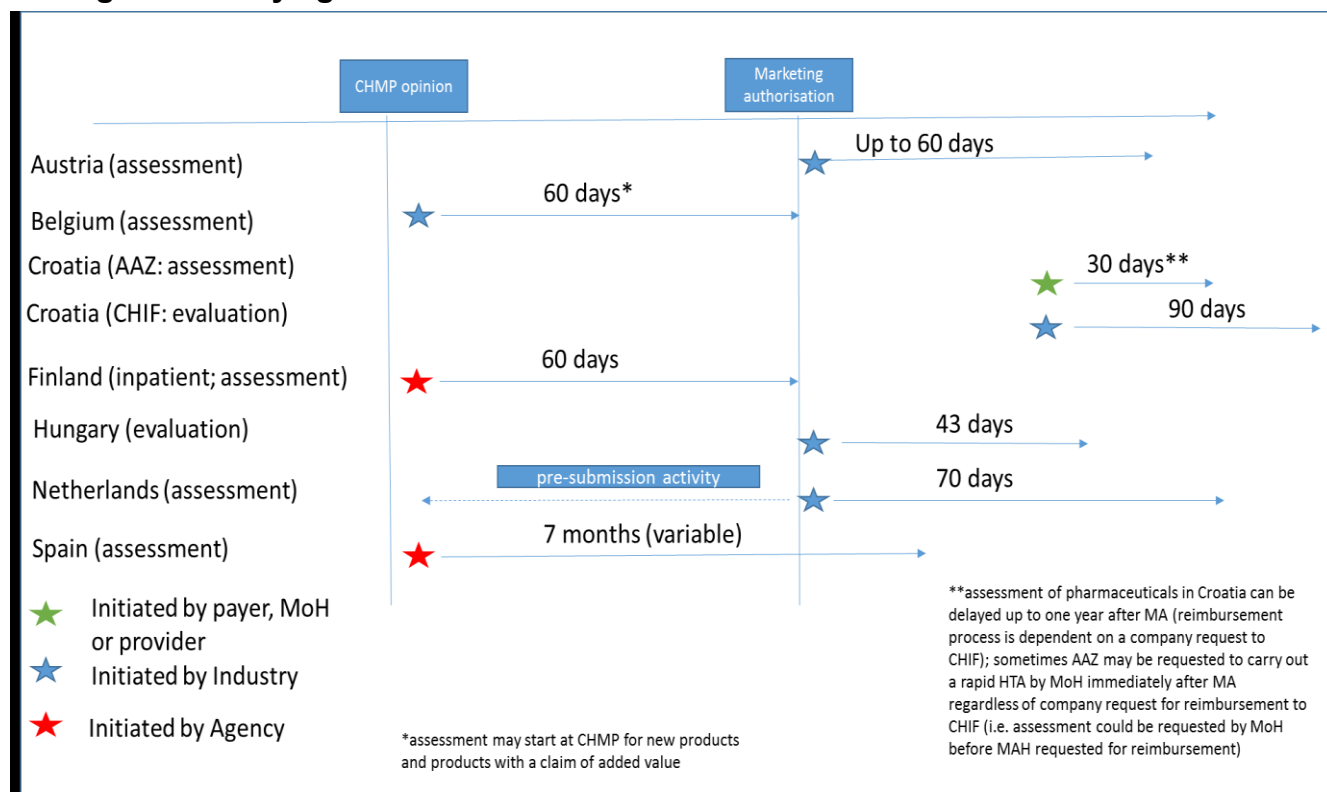
To support national implementation, collaborative HTAs must be timely to reflect national decision making priorities and they must also be able to fit into any other steps of the procedure that the HTA or evaluation of the company submission is informing. While HTA is often part of a longer reimbursement procedure, the HTA production or evaluation component of the procedure occurs at the start of the procedure soon after initiation. This creates challenging timings as collaborative HTA will need to be available when national procedures start.

Pharmaceuticals - initiation

For the majority of agencies the national assessment is initiated after marketing authorisation (figure 36). Following initiation for most agencies the timeframe for the procedure is then governed by the Transparency directive (89/105/EEC). For some agencies the procedure can start at the stage of CHMP positive opinion (sometimes with pre-submission activity, before the formal start; see case study 16), and for a very small number it will start even before this. If a collaborative HTA starts at the time of CHMP positive opinion or before, there will be some countries who will not be able to use the collaborative HTA because it will be completed after or in parallel with the national assessment.

From an implementation perspective HTA cooperation is likely to have to coordinate timing of assessment initiation with industry as in many countries industry initiates the assessment and are therefore best placed to indicate if an assessment will be relevant (e.g. a product will be launched across a number of countries in short succession) and be timely (e.g. the finalisation of the assessment will be completed before product launch in most countries).

Case study 16: Comparison of assessment initiation and completion timings among case study agencies



Note: This figure reflects the timings for the agency work to prepare an assessment of a pharmaceutical product. This is within the context of the assessment being part of a longer 180 day pricing and reimbursement procedure in some agencies.

Pharmaceuticals - completion

For pharmaceuticals in the majority of countries the HTA or evaluation of the company submission is informing a mandatory reimbursement and/or pricing decision for which the Transparency directive (89/105/EEC) applies. This means that timelines for producing the assessment or evaluation can be very short and inflexible depending on how many organisations are involved in the pricing and reimbursement procedure and the number of steps required to support the procedure (for example, some countries will undertake stakeholder involvement, involve advisory committees and involve other organisations to help formulate advice and recommendations). These national procedural steps tend to support national decision making and are important for accountability and governance; reducing the risk of appeal and court action. These procedural steps relating to decision making will not be displaced by a collaborative HTA, meaning the availability of a collaborative HTA will have to fit into any existing national and EU procedural and governance requirements around pricing and reimbursement.

Once an assessment is initiated, most agencies have up to 2-3 months to complete an assessment (figure 37), but for some agencies this timeframe also includes the time required for it to go to a Committee for review and approval and the time

required to schedule and circulate documents beforehand, therefore the actual time preparing the assessment may be less. Importantly this time is often not flexible, once a company has submitted for reimbursement the dates when an agency will be working on the assessment will be set and the period of time when an agency will have to work on the assessment or evaluation will be at the beginning of the formal reimbursement procedure. The importance of pricing and reimbursement decisions means that an agency is unlikely to be able to delay starting their assessment to wait for the collaborative HTA to arrive. The BENELUXA case study (case study 17) highlights the role of project management in collaborative assessments to ensure that documentation is ready to be used in national procedures.

The implementation challenges associated with timing would be removed for almost all agencies if the collaborative HTA was available at the time of CHMP positive opinion. Where this isn't logistically possible having a draft form of the report available to agencies at the time of CHMP opinion would support greater implementation. Having a final collaborative HTA published at the point of marketing authorisation would enable maximum use of collaborative HTAs across the majority of agencies. However this would still be too late for a small group of agencies.

Case study 17: Timings of initiation and assessment BENELUXA collaboration

The collaborative procedure fits into the national procedures which in turn fit into the timelines required by the Transparency directive (89/105/EEC). The differences in timings and roles between the two agencies, and the stringent timelines imposed by the Transparency directive (89/105/EEC) means there is little flexibility in the timings for each stage of assessment production.

For the collaborative procedure a company initiates the assessment at the same time in both countries, this means that the HTA activity in the two countries overlaps and the collaborative procedure can take place.

In regard to completing the collaborative assessment. The timings must be defined in advance and strictly adhered to so the collaborative assessment does not delay the national procedures. The following steps are implemented to minimise issues that can arise from the lack of flexibility in timings:

- early discussions with companies before they submit so the agencies can minimise the risk of the information not being appropriate or sufficient
- collaborative assessments are given priority
- greater overall coordination of the collaborative procedure compared to the national procedures and expansion of the team involved in the joint procedure to include involvement of project managers

-advanced preparation of timelines that indicate when each stage of the procedure has to occur so that the collaborative procedure does not result in delays to the national procedures and that staff time conflicts (either between national assessments or between national assessments and other roles) are minimised

Non-pharmaceutical health technologies - initiation

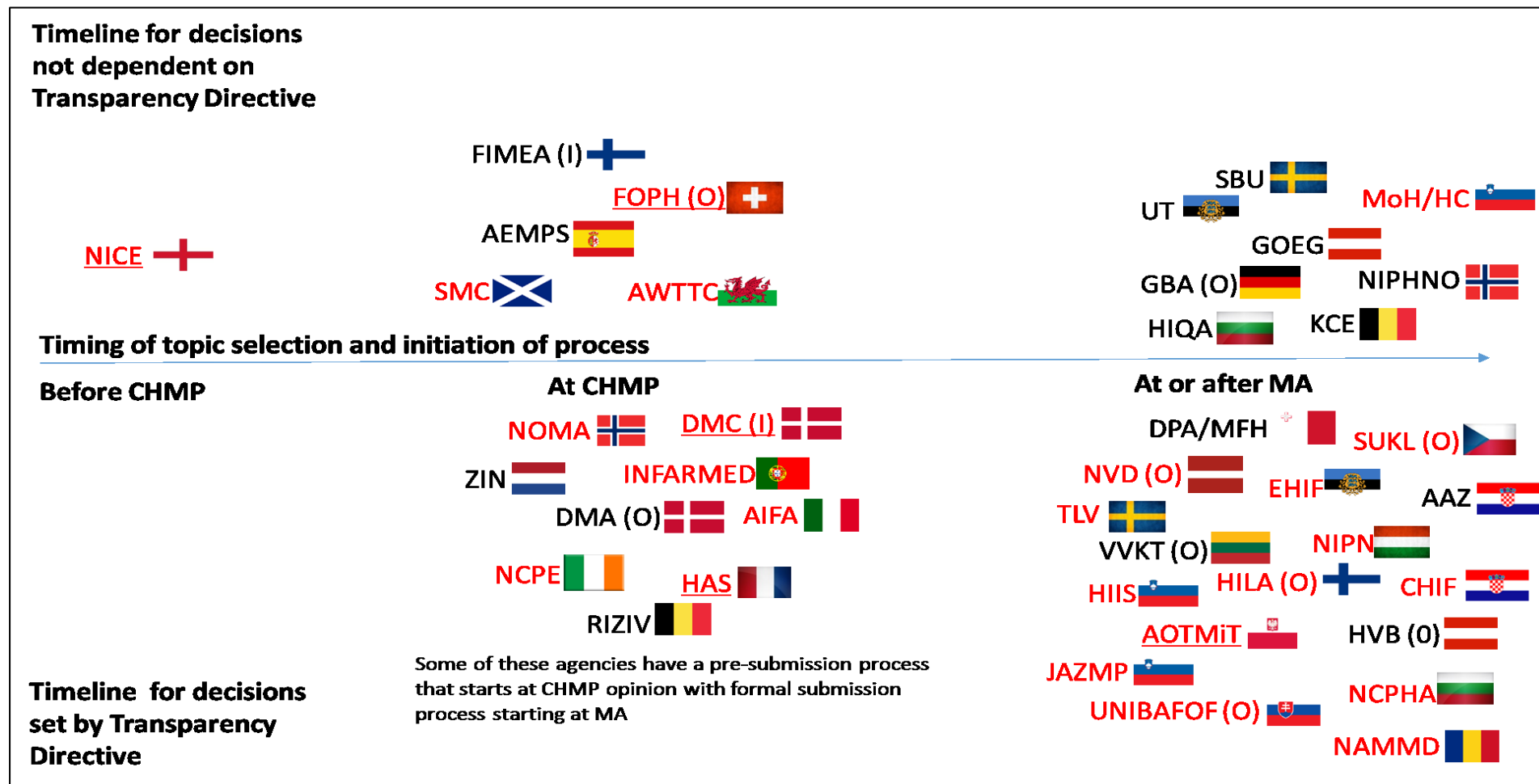
For non-pharmaceutical health technologies the introduction of a technology is often more diffuse and without a single specific time point at which a technology comes to market across Europe. In addition there is greater variation in when a product will become a national priority for assessment and a larger proportion of assessments are initiated by national organisations rather than industry. Because of this diffuse pathway, criteria of timeliness are fundamental to the topic selection and prioritisation procedures so that EU non-pharmaceutical HTAs are timely for the largest number of agencies interested in the topic.

Non-pharmaceutical health technologies - completion

For non-pharmaceutical HTAs more procedures have a longer timeframe for assessment or evaluation (figure 38), the timings also tend to have slightly more flexibility for negotiation. For implementation the key issue is therefore to identify as part of topic selection and prioritisation the point at which collaborative HTA will fit with national priorities and be most valuable.

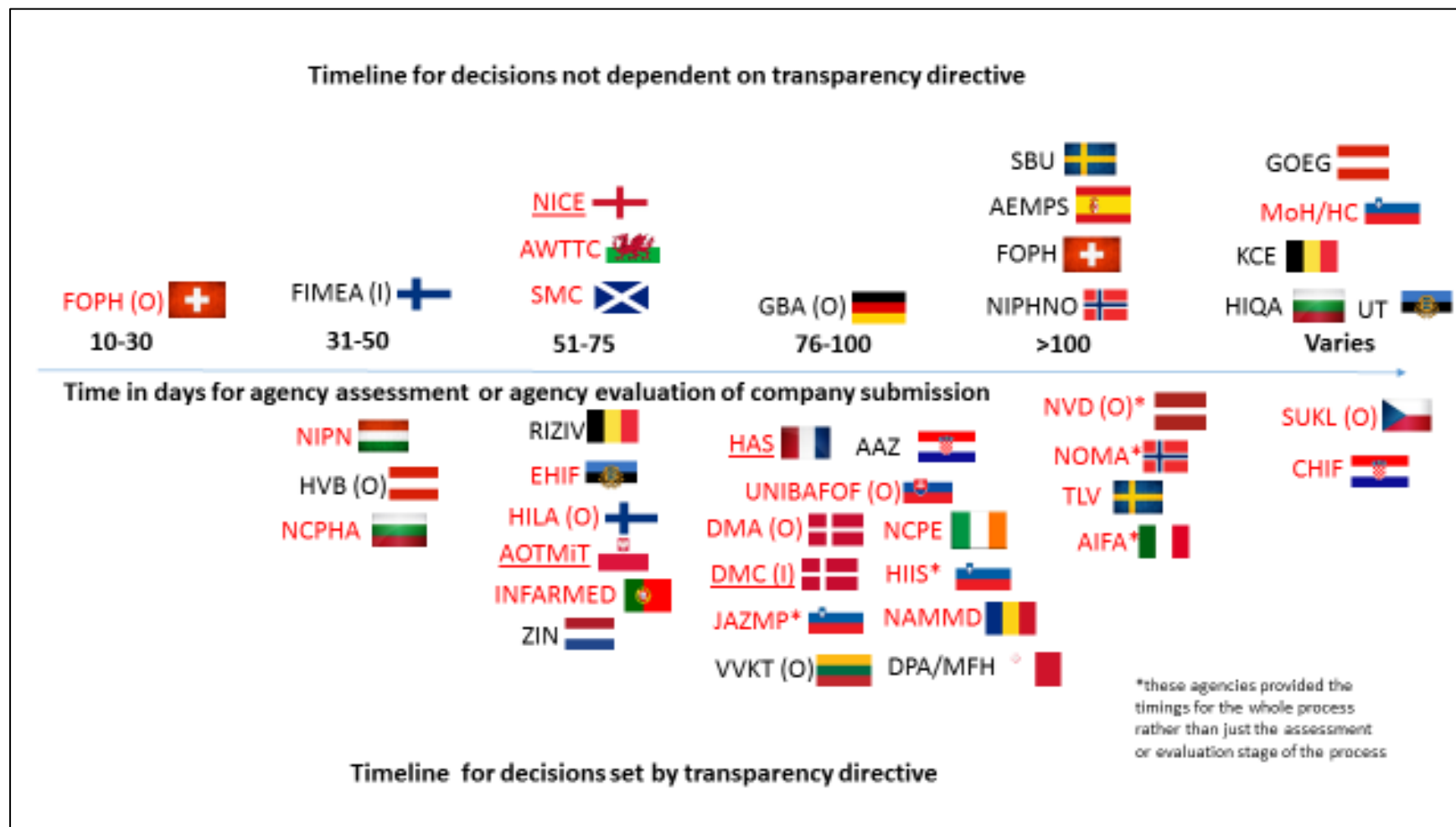
There is a small group of agencies working in a similar paradigm to those working on pharmaceuticals, who evaluate industry submissions as part of an application for reimbursement and for whom there is a very short timeframe to complete an evaluation. This is not flexible and this combination of factors will make national implementation challenging in these countries because there also tends to be low predictability as to the topics that will need assessment and when it will be required.

Figure 36: timing of initiation of the pharmaceutical procedure versus whether the procedure is governed by the Transparency directive (89/105/EEC)



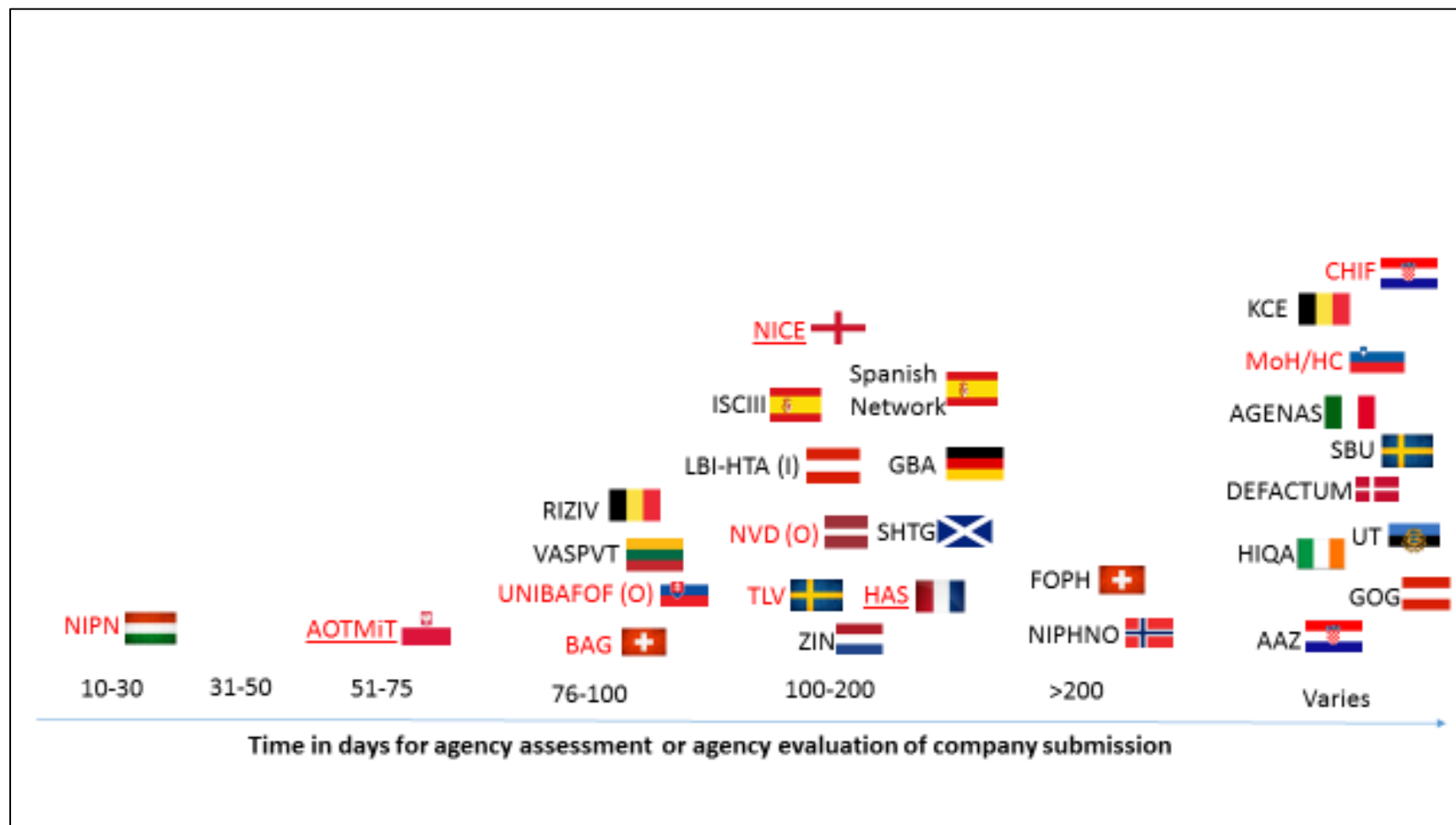
Key: Black = agencies creating own REA assessment; Red = agencies appraising industry submission and evaluating this rather than creating own REA assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only

Figure 37: Days received to create an assessment or evaluation of industry submission – pharmaceuticals



Key: Black = agencies creating own REA assessment; Red = agencies appraising industry submissions and evaluating this rather than creating own REA assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only

Figure 38: Days received to create an assessment or evaluation of industry submission – non pharmaceuticals



Key: Black = agencies creating own REA assessment; Red = agencies appraising industry submissions and evaluating this rather than creating own REA assessment; Red underline = mixture of approaches depending on programme. (I) Inpatient only (O) outpatient only

Recommendations to support timing of joint assessment

Key implementation challenge	Recommendations for centralised cooperation	Recommendations for agencies
<ul style="list-style-type: none"> HTA agency may not be responsible for starting the procedure HTA occurs at the start of any decision-making procedure Variation in launch dates and availability across Europe Variation in when non-pharmaceutical health technologies become a national priority in different countries For pharmaceuticals, some agencies start their procedures before marketing authorisation is granted, while others cannot For pharmaceuticals, inflexible and short timeframes for completing assessments defined by procedural and legal requirements of pricing and reimbursement 	<ul style="list-style-type: none"> Explicit consideration of timeliness of the assessment as part of scheduling and topic prioritisation Coordinate with industry to identify launch plans across Europe Develop timelines for EUnetHTA assessment for pharmaceuticals that allow effective implementation. <ul style="list-style-type: none"> Ideally joint assessment is available at the time of CHMP positive opinion. At the latest joint assessment is made available at the time marketing authorisation If this timetable for completion is not feasible, implementation would be supported by having a final report available at the point of marketing authorisation with a draft report available to agencies at the time of CHMP positive opinion 	<ul style="list-style-type: none"> Use HTA cooperation to put in place mechanisms for predicting and developing a better understanding of when assessments might be requested Work with decision-makers and users of HTA to understand whether for certain topics there might be flexibilities in timing that could allow agencies to maximise use of collaborative HTA

Chapter 8: Use of HTA to inform decision making

Key messages

- HTA is frequently part of a larger formal procedure to inform reimbursement decisions. This procedure requires procedural rigour, transparency and availability of documents in case of challenge.
- Almost all countries provide advice, recommendations or opinion to support the decision maker (97% and 95% for pharmaceuticals and non-pharmaceutical health technologies, respectively).
- In only a minority of countries is the advice or recommendations statement the sole responsibility of the HTA agency (25% and 36% for pharmaceuticals and non-pharmaceutical health technologies, respectively).
- Assessments inform a range of decisions. Most commonly these are reimbursement (97% and 91% for pharmaceuticals and non-pharmaceutical health technologies, respectively) and for pharmaceuticals also pricing decisions (69%).
- Decision makers receive a range of documents that accompany the advice. The complete HTA report is the most commonly provided document for both pharmaceuticals (61%) and non-pharmaceutical health technologies (91%). However, for pharmaceuticals the industry submission of evidence (57%) is also likely to be provided.
- Countries have governance procedures that guide the inclusion of HTA in formal decision-making and support rigour and accountability of the procedure. If collaborative HTA is to be used as an alternative to national HTA then it must meet the governance requirements within MS

Description of how HTA is used to inform decision making

Provision of opinion, recommendations or advice to support the decision maker

Almost all countries have a procedure where opinion, recommendations or advice is given to support the decision maker for both pharmaceuticals (28 out of 29 countries; 97%) and non-pharmaceutical health technologies (21 out of 22 countries; 95%).

For pharmaceuticals, the Czech Republic (SUKL) do not make advice or recommendations. SUKL issue a decision themselves within a legally binding document. In the case of lawful appeal, it is reviewed by the Ministry of Health who can either confirm or annul the decision, in cases of annulment the decision is re-evaluated. For non-pharmaceutical health technologies Norway (NIPHNO) indicated

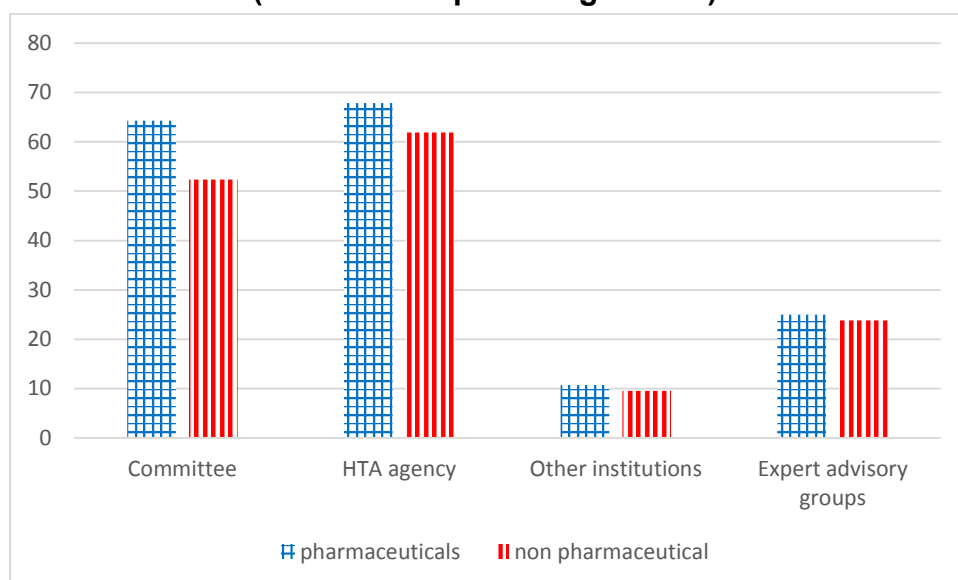
that the HTA unit does not provide advice directly. Decision makers may read the conclusions as a kind of advice, but it is not explicitly written as advice.

The provision of advice is not always across all programmes and agencies within a country, for example in England (NICE) provide guidance for decision makers in all programmes except for MIBs and Evidence Summaries. In Sweden, TLV technical staff make recommendations to the decision maker however SBU does not.

Among the regional agencies, all provide advice and recommendations to the decision maker with the exception of ASSR-RER in Italy.

The provider of opinions and advice

Figure 39: Party providing advice, recommendations or opinion to inform the decision maker (% countries providing advice)



Key: pharmaceuticals data for 28 countries producing advice, non-pharmaceutical health technologies data for 21 countries producing advice. Agencies coded multiple categories so data may add up to more than 100%.

For pharmaceuticals 18 out of 28 countries (64%) indicated that advice is made through a Committee, 19 out of 28 countries (68%) indicated the advice is made by the institution producing the HTA. Where the institution producing or evaluating the HTA also produces the recommendations or advice, 7 (25% of the total 28) indicated that they do this alone with the other 12 indicating that it is done either in consultation with or alongside advice and recommendations obtained from external experts, stakeholders or committees (figure 39 and case study 18).

For non-pharmaceutical health technologies 11 out of 21 countries (52%) indicated that the advice is made through a Committee, 13 out of 21 countries (62%) indicated that the advice is made by the institution producing the HTA. Where the institution making the HTA report produced the recommendations or advice, 8 countries (38%

of the total 21) indicated that they did this alone and 5 indicated that it was done either in consultation with or alongside advice and recommendations obtained from external experts, stakeholders or committees.

Case study 18: The role of Committees in providing advice at RIZIV in Belgium

Rijksinstituut Voor Ziekte- en Invaliditeitsverzekering (RIZIV) coordinates and supports (technically and legislatively) the decision-making procedures for the reimbursement of health technologies. This includes organising meetings and supporting the Committee that is charged with providing advice about the reimbursement of health technologies to the decision maker (for pharmaceuticals the Committee who makes the advice is known as the Commission for the Reimbursement of Medicines). The Commission includes healthcare providers, insurers, academics, Ministry representatives and Industry organisations. For pharmaceutical technologies, the decision maker who receives the advice from the Commission is the Minister of Social Affairs.

The HTA prepared by RIZIV forms the basis of a proposal for reimbursement that is developed by the Commission. RIZIV have 60 days to prepare a draft report that is then sent to the company for their response (the total time to produce a final assessment report is 90 days). There is then a subsequent 60 days for the Commission to develop the final reimbursement proposal. Finally, the Minister will take a decision on reimbursement within 30 days.

Criteria used to formulate recommendations and advice

For pharmaceuticals 24 countries out of 29 (83%) have criteria to guide advice formulation. In 5 countries (18%) the presence of criteria varies depending on the agency or programme in which the topic is considered. For non-pharmaceutical health technologies 15 countries out of 22 (68%) have criteria, 4 countries (18%) do not and in 3 countries (14%) it varies depending on the agency or programme in which the topic is considered. Agencies do not always provide recommendations or advice, therefore not all agencies or programmes within a country will have criteria to support formulation of recommendations and advice. For example, in Austria HVB and LBI-HTA have criteria, whilst GOEG does not. In England criteria are available for DAP, MTEP, IP, TA, and HST but not MIBs and Evidence Summaries. In Finland criteria are available for HILA but not FIMEA. In Lithuania, criteria are formulated for VVKT but not for VASPVV.

Of the agencies reporting their criteria, the most frequently mentioned were efficacy, relative effectiveness, cost-effectiveness, safety, innovation, and budget impact. Criteria reported as 'other' include price and level of reimbursement, legal issues, market potential, pricing policy in other countries, applicability and comfort, etc.

Among the regional agencies, criteria most frequently include clinical or healthcare system benefits and ethical, social, legal and political aspects (Spain, Technology

appraisals in AQuAS, OSTEBA, SCS, UETS Madrid). In addition, one programme (Lifecycle technology assessment; OSTEBA) also mentioned potential risks, costs and economic impact.

Publication status of the advice

For pharmaceuticals, the status of the advice to the decision maker is public in 12 out of 28 countries (43%), public but with confidential information removed in 9 countries (32%) and confidential in 4 countries (14%). In 2 countries (7%) the status varies depending on the agency or programme making the advice.

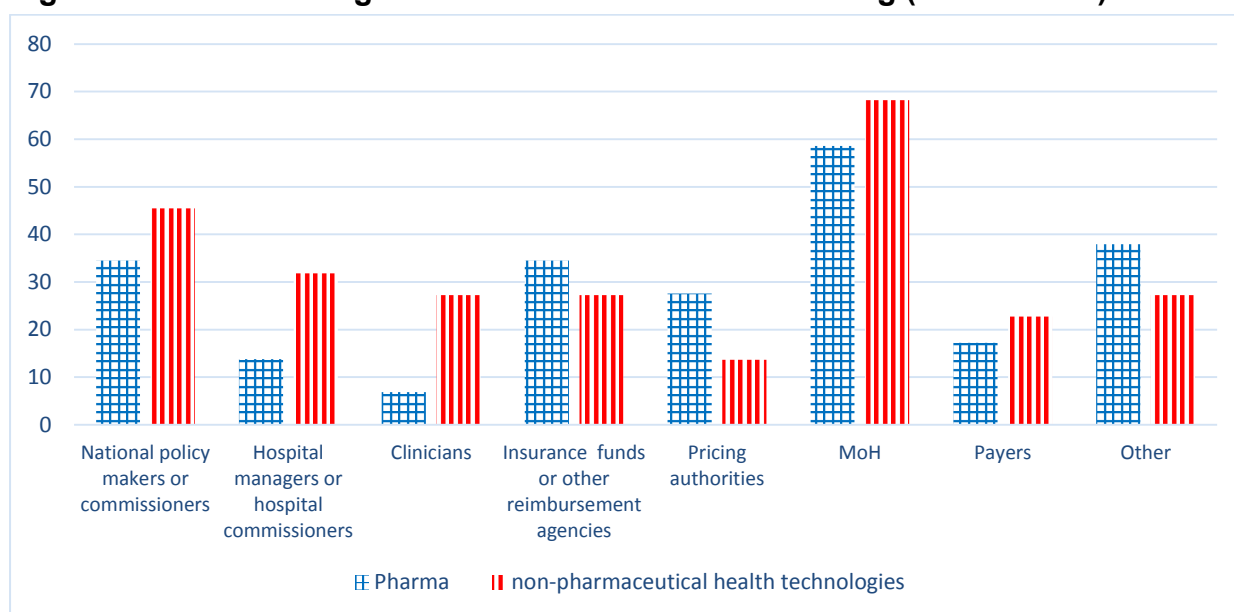
For non-pharmaceutical health technologies, the status of the advice to the decision maker is public in 10 out of 21 countries (48%), public but with confidential information removed in 4 countries (19%) and confidential in 4 countries (19%). In 3 countries (14%) the status varies depending on the agency or programme making the advice.

Decision making

Who uses the assessment for decision making

For both pharmaceuticals and non-pharmaceutical health technologies, in the majority of countries assessments are used for decision making by the Ministry of Health (57% and 68%, respectively) or national policy makers and commissioners (34% and 45%, respectively). For pharmaceuticals, assessment also informs pricing authorities (28%) and insurance funds (34%) whilst for non-pharmaceutical health technologies, assessments are more likely to inform clinicians (27%) and hospital managers (32%). 'Others' using assessments for decision making include other government agencies and regional authorities (figure 40). Regional agencies identified a similar group of decision makers including most frequently national policy makers or commissioners, hospital managers and commissioners, clinicians, MoH and payers.

Figure 40: Parties using assessments for decision-making (% countries)



Key: pharmaceuticals N=29, non-pharmaceutical health technologies N=22. Agencies coded multiple categories so data may add up to more than 100%.

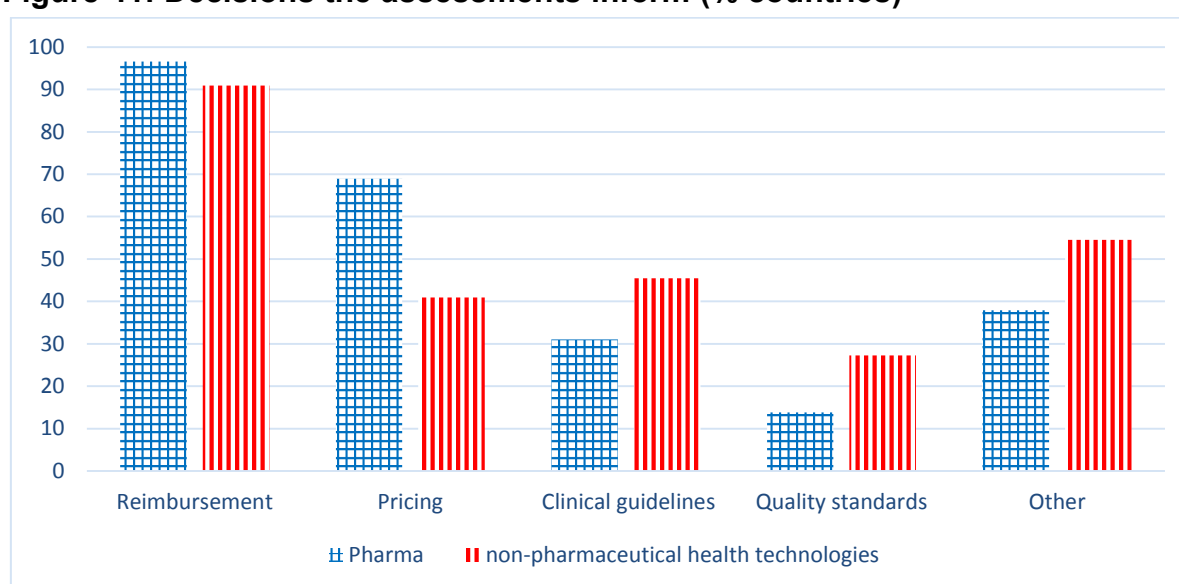
What decision does the assessment inform?

In the majority of countries the HTA informs reimbursement of pharmaceuticals (28 out of 29 countries; 97%) and non-pharmaceutical health technologies (20 out of 22 countries; 91%). For pharmaceuticals countries frequently use assessments to inform pricing (20 out of 29 countries; 69%). A smaller proportion of countries use assessments to inform pricing of non-pharmaceutical health technologies (9 out of 22 countries; 41%) (figure 41).

Assessments are not only completed to inform reimbursement and pricing decisions. For non-pharmaceutical health technologies almost half of countries (10 countries; 45%) use assessments to inform clinical guidelines and just under a third (6 countries; 27%) to inform quality standards. For pharmaceuticals there is less use of the assessments outside of pricing and reimbursement; just under a third indicate that assessments may inform clinical guidelines (9 countries; 31%) and a small proportion indicating that they may inform quality standards (4 countries; 14%).

Among the regional agencies the assessments inform decisions about reimbursement and quality standards, as well as clinical practice and organisational issues. Other decisions the assessments inform include advice for national, regional or local policy strategy and setting, investment and disinvestment, commissioning, budget decisions, information on restriction of the product and treatment eligibility and product impact.

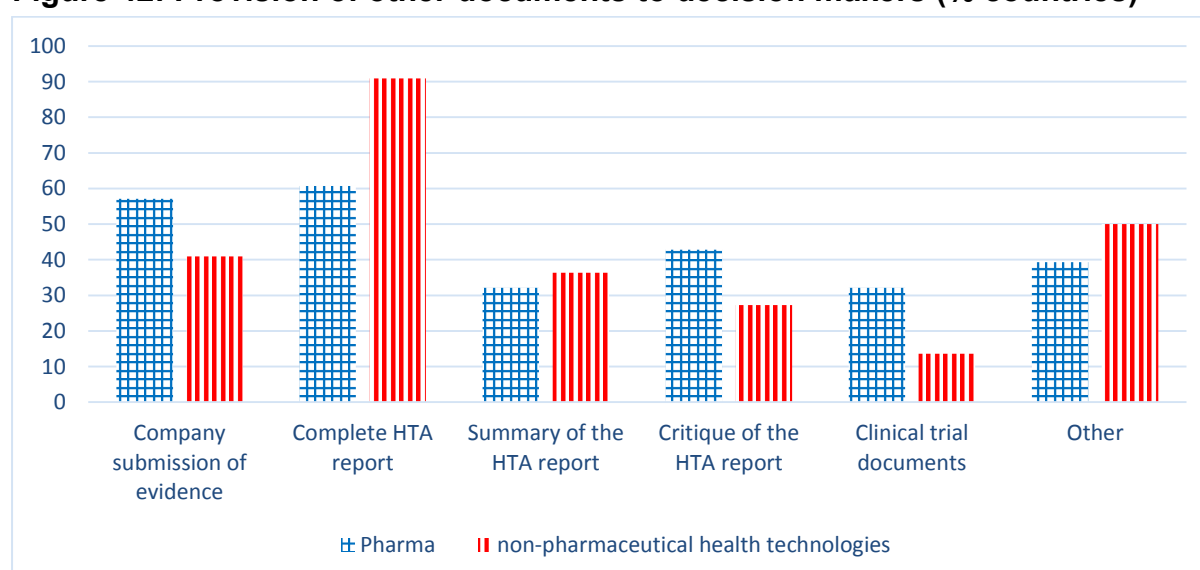
Figure 41: Decisions the assessments inform (% countries)



Key: pharmaceuticals data for 29 countries, non-pharmaceutical health technologies data for 22 countries. Agencies coded multiple categories so data may add up to more than 100%.

Documents provided to decision makers

Figure 42: Provision of other documents to decision makers (% countries)



Key: 28 countries for pharmaceuticals (Romania NA) and 22 countries for non-pharmaceutical health technologies. Agencies coded multiple categories so data may add up to more than 100%.

The complete HTA report is the most commonly provided document for both pharmaceuticals (61%) and non-pharmaceutical health technologies (90%). However, for pharmaceuticals the company submission of evidence (57%) is equally likely to be provided. Critiques or reviews of the HTA report include the HTA team's response (with added new non-confidential evidence, further analysis or correction) to the HTA report and summaries collected via external peer review procedure or public or stakeholder consultation.

'Other' documents include specific diagnostic/interventional procedure guidance, horizon scanning reports, statements from patient experts/clinical experts/social insurance institution, rapid review assessment, clinical value assessment, prioritisation framework for decision, responses to specific questions addressed to the technology manufacturer, patients' organisation submissions and key references. Clinical trial documents were more commonly provided in assessment of pharmaceuticals than non-pharmaceuticals (32% versus 14% of countries) reflecting the differing evidence bases usually available.

In Spain all 6 regional agencies provide the complete HTA report to the decision maker, additionally Avalia-t provides the review of the HTA report and AQuAS the summary of the HTA report. In Italy ASSR-RER provides HTA reports for high cost technologies and short reports for medical devices. Veneto provides information sheets, rapid HTA, re-assessments or guidance depending on the type of advice required by the decision maker.

Publication status of other documents made available to the decision maker

For pharmaceuticals, the publication status of other documents made available to the decision maker is public in 9 out of 28 countries¹⁸ (32%), public but with confidential information removed in 5 countries (18%) and confidential in 9 countries (32%). The publication status of documents varies by programme or agency in 4 countries (14%).

For non-pharmaceutical health technologies, the publication status of other documents made available to the decision maker were public for 9 out of 22 countries (41%), public but with confidential information removed in 5 countries (24%) and confidential in 3 countries (14%). The publication status of documents varies by programme or agency in 4 countries (19%).

Not all agencies or programmes within a country necessarily release documents given to the decision maker. For example, in Switzerland documents used in the pharmaceutical and medical device procedures are confidential but those for the HTA programme public. In Sweden SBU release documents publically, but TLV remove confidential information first and in Austria documents are confidential for HVB but made publically available by GOEG and LBI-HTA.

All regional agencies release documents presented to the decision maker.

Use of information from other jurisdictions relating to advice/recommendations

Twenty countries out of 29 (69%) use information from other jurisdictions as part of the procedure for producing recommendations or advice for pharmaceutical

¹⁸ Romania answered not applicable

assessments and 15 out of 22 countries (68%) report using information from other jurisdictions as part of the procedure for producing recommendations or advice for non-pharmaceutical health technology assessment.

The documents used include recommendations and advice from other agencies and the list of countries and agencies used is similar for advice and recommendations as for assessment. Additional countries were mentioned by Poland to include AWTTC (Wales), TLV (Sweden) and NCPE (Ireland). LBI-HTA in Austria indicated that they report the recommendations on the technology from other countries as part of the description of the technology.

Analysis of advice and decision making procedures

The decision-making frameworks used to create advice vary between countries. Some countries make advice on the basis of relative effectiveness, efficacy or safety but often other factors are also taken into account such as cost effectiveness, innovation and budget impact. Agencies may make judgements about each of these factors before coming to an overall decision, but not always.

The role of different organisations in making the advice varies. Although a minority of agencies formulate advice themselves, in the majority either the HTA agency will produce draft advice that is then debated by an advisory group or Committee, or in other instances the HTA won't include advice and this is developed independently by a Committee or another organisation. Therefore for many agencies the creation of advice to inform decision making is a multi-organisation activity.

From an implementation perspective there is a risk that if (1) an agency produces advice using an independent Committee rather than as part of the HTA procedure, or (2) the agency does not formulate specific recommendations about relative effectiveness or (3) the HTA agency does not agree with the advice provided, the agency is less likely to use the collaborative HTA because it is not seen as fit for purpose. For the group of agencies who do produce advice themselves, the provision of advice in collaborative HTA may support additional resource savings and efficiencies in national assessment, though it is likely that the agency would still have to identify whether they agreed with the advice before they included it in their national report. In addition, these possible resource savings would have to be offset against the additional time required for the collaborative HTA to produce robust advice acceptable to MS. If providing advice meant extending the length of time an assessment takes, then the loss of implementation because the report was no longer timely may not offset additional efficiency gains from providing advice.

Accountability and governance

Collaborative HTA will for many countries be used as part of a formal reimbursement and/or pricing procedure. This is particularly the case for pharmaceuticals, but also the case for some non-pharmaceutical assessments. If collaborative HTA is to be

used within a national procedure as an alternative to national documentation, then the collaborative HTA procedure must satisfy national procedures in terms of governance and the agency's accountability to the national procedure. If agencies cannot ensure that documentation used in their national procedure is sufficiently transparent and procedurally robust in the event of a challenge then the collaborative HTA is unlikely to be used meaningfully in national contexts.

Given existing procedures, the collaborative HTA is usually not the only document that an agency is likely to require to ensure that there is sufficient accountability to their national procedures. The documents provided to decision makers are generally similar for pharmaceuticals and non-pharmaceutical health technologies and for national and regional agencies. The documents provided are most frequently:

- Complete HTA report
- Company submission of evidence (for some agencies this is the HTA report)
- Summary of the HTA report
- Critique or review of the HTA report

For these agencies documents such as the company submission of evidence, other stakeholder evidence received and consultation documents will have to be available to agencies and decision makers for scrutiny and use if there is an appeal or court case. They may also need to be available for national stakeholder or public consultation exercises. This is particularly the case for company submissions of evidence where for over half the countries carrying out pharmaceutical assessments the decision maker receives the company submission of evidence.

Ensuring accountability of procedure is not necessarily the same as making documents public, for some agencies it would be sufficient if supporting documents could be shared but not made public. However, if documents are not made public and are not available for national scrutiny then the EU procedure may not have sufficient transparency to satisfy countries. If countries are going to use collaborative HTA as an alternative to national HTA then collaborative HTA has to include sharing of documents not just with authors and reviewers of the collaborative HTA, but also those who will use the collaborative HTA in their national procedures. This will require negotiation with agencies and stakeholders providing evidence and comments as part of the collaborative HTA procedure.

Recommendations for Advice and Decision making

Key implementation challenge	Recommendations for centralised cooperation	Recommendations for agencies
<ul style="list-style-type: none"> • HTA in many cases feeds into a formal procedure for which the national agency has accountability and which requires governance procedures to be in place. • The creation of advice to decision makers is often a multi-stakeholder activity taking a variety of decision making criteria into account • For some agencies supporting documents must be published to support transparency and to be part of stakeholder and public consultation. • For some agencies all supporting documents must be available for use in the case of challenge • For some agencies authorship and conflicts of interest of people and organisations involved in the assessment need to be published 	<ul style="list-style-type: none"> • Increase the accountability and transparency of the collaborative HTA procedure so that when using collaborative HTA agencies have sufficient procedural rigour to use it as an alternative to national HTA, to include: <ul style="list-style-type: none"> ○ Publishing and making available documents underpinning the assessment ○ Transparency of the assessment procedure including authors and stakeholders involved and conflicts of interests 	<ul style="list-style-type: none"> • Identify the supporting documents that are required to meet the terms of any national governance procedures, including: <ul style="list-style-type: none"> ○ The availability status required (public or available for use in case of challenge) ○ The language in which they must be available • Identify other procedural aspects such as conflicts of interest and declarations of authorship that would be required to use collaborative HTA as an alternative to national documentation

Chapter 9: Reassessment procedures

Key messages

- As new evidence and information about a health technology emerges, reassessment performs a vital function in ensuring that decisions and re-evaluations of decisions are appropriately made.
- The majority of countries carry out reassessments (89% and 82% for pharmaceuticals and non-pharmaceutical health technologies, respectively). However, reassessment procedures are not in place across all agencies in a country and may not always be frequently used.
- For pharmaceuticals there is greater use of MTA for reassessment (50%) than for initial assessment (38%). As with initial assessment the most common approach to reassessment is an assessment of clinical effectiveness and economic information (over 80% of countries).
- For non-pharmaceutical health technologies there is use of both STA and MTA for reassessment and no single common approach to reassessment
- Reassessment can be triggered (1) automatically after a set period of time (2) following identified changes to the technology, evidence base or clinical practice, and (3) at the direct request of a stakeholder or decision maker for example MoH, payers, providers or industry.
- Although reassessment may be challenging to coordinate so as to maximise implementation, it is an area where agencies may have more control over timing and planning of the work. It may therefore offer an opportunity for meaningful use of collaborative HTA and potentially relevant topics could be explored as part of topic selection and prioritisation procedures.

Description of reassessment procedures

Presence of a reassessment procedure

For pharmaceuticals, 26 out of 29 countries (90%) carry out reassessments, a similar proportion of countries 18 out of 22 countries (82%) carry out reassessments for non-pharmaceutical health technologies. Not all agencies in a country have reassessment procedures for example in Austria reassessment is completed by HVB and LBI-HTA but not GOEG. In Finland by HILA but not FIMEA.

A small number of countries indicated that they have a legal or procedural basis for carrying out reassessments but do not or do not often carry them out (for example, Hungary, NIPN; Belgium, KCE), others indicated that they do reassessments but that the procedure isn't established (for example, Norway NIPHNO, Spain AEMPS, ISCIII and the Spanish Network; Sweden, SBU and Malta, DPA/MFH). Slovenia and

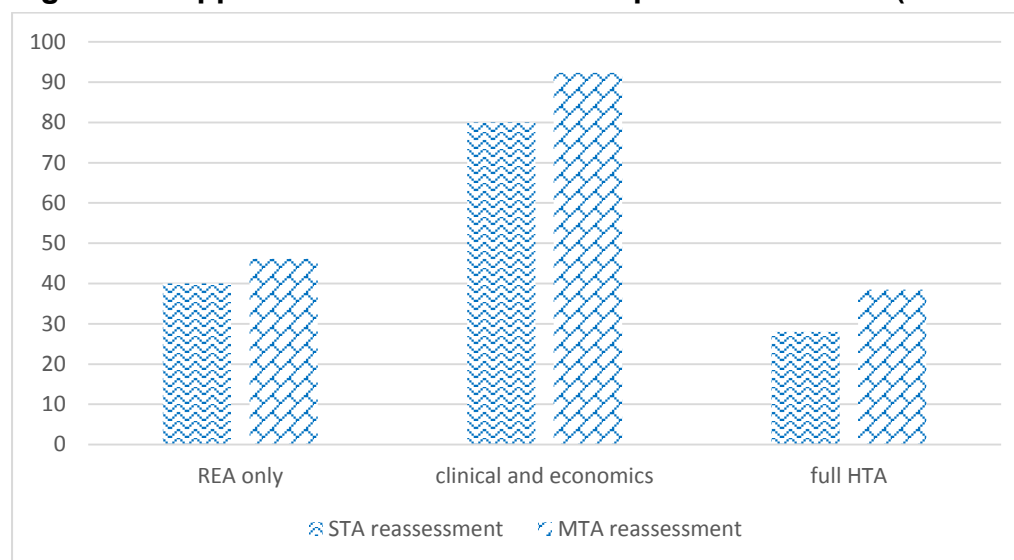
Romania indicated that reassessments are carried out but use the same procedures as initial assessments and are considered a new assessment.

Approach to reassessment of pharmaceuticals

Twenty-five out of 26 countries (96%) carry out reassessment using STA and 13 out of 26 countries (50%) carry out reassessment as MTA.

The majority of reassessments include clinical effectiveness and economic information as for initial assessments. As with initial assessments the majority of countries adopt a single approach, but some have flexibility to use different approaches depending on the topic or the agency carrying out the assessment (figure 43).

Figure 43: Approach to reassessment of pharmaceuticals (% countries)

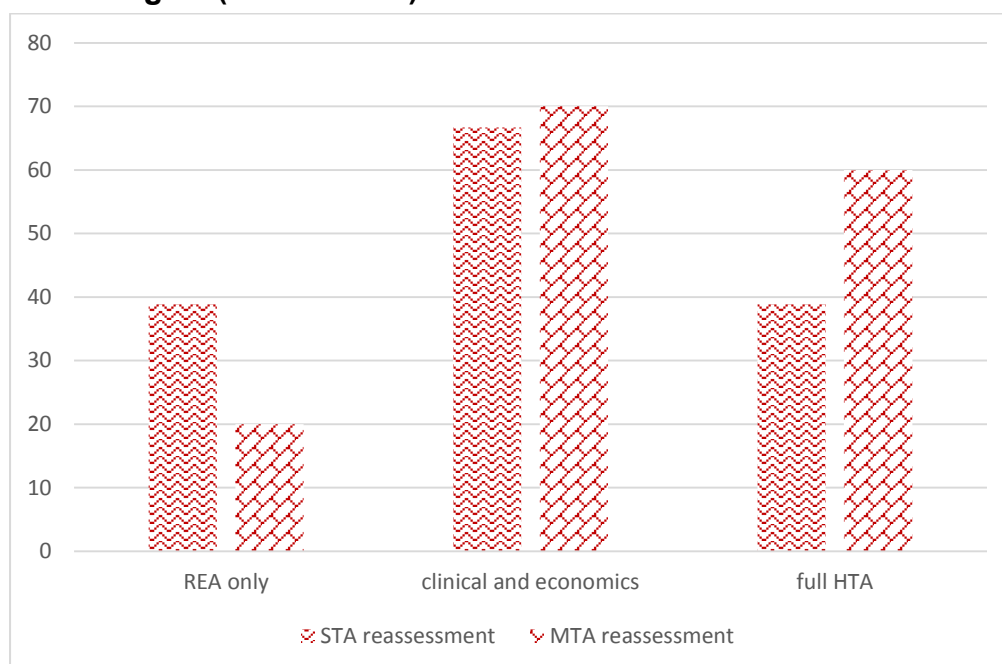


Key: data for STA reassessment = 25 countries; MTA reassessment = 13 countries. Agencies coded multiple categories so data may add up to more than 100%.

Approach to reassessment of non-pharmaceutical health technologies

All 18 countries who reassess non-pharmaceutical health technologies use STA and in 10 out of 18 countries (56%) reassessments can use MTA.

In contrast to pharmaceutical reassessments, no single approach to reassessment dominates, reassessments of non-pharmaceutical health technologies can include REA only, clinical effectiveness and economic information and full HTA.

Figure 44: Approach to reassessment of non-pharmaceutical health technologies (% countries)

Key: data for STA reassessment = 18 countries; MTA reassessment = 10 countries. Agencies coded multiple categories so data may add up to more than 100%.

Criteria for reassessment

For both pharmaceuticals and for non-pharmaceutical health technologies, there are 3 main instances when reassessment occurs (1) routinely after a set period of time (2) following identified changes to the technology, evidence or clinical practice and (3) at the direct request of a stakeholder or decision maker for example MoH, payers, providers or industry. Sweden (TLV) mentioned that reassessment occurs mainly but not solely as a result of sales volume or budget impact information. In addition, Italy (AIFA) indicated that reassessment can be triggered as part of a renegotiation procedure of the reimbursement terms.

For countries where reassessment occurs within a set amount of time this is usually a maximum of 3-5 years. For example in the Czech Republic and in Denmark (DMA) reassessment is done at least once every 5 years. In Switzerland the price of pharmaceuticals is re-evaluated after 3 years of the initial price setting. In Wales recommendations made after 1 October 2011 are reviewed within three years or in light of significant new information and on the production of any relevant NICE publications. However, the period before re-assessment could also be shorter, for example in Slovenia (JAZMP), the price is valid for up to a year after which a new application and assessment is needed. In addition, Austria (HVB) indicated that their assessments could include a recommendation for temporary inclusion on their reimbursement list after which reassessment is required. Switzerland also indicated

that reimbursement may be granted for a limited time after which reassessment may be necessary (coverage with or without evidence development).

In some countries a period of time is stipulated after which a review is considered, but the review may not occur unless it was felt that evidence also suggested the assessment needed to be revised. For example, in England guidance normally has a review period of 3 years after which the guidance is reviewed to see whether a reassessment is needed. In Ireland guidelines are subject to a formal 3 yearly review cycle and if important new evidence emerges HTA may be revised. In Scotland for non-pharmaceutical health technologies there is a 2 yearly review if new evidence is felt to materially alter the existing advice statement.

In some instances reassessment was carried out when certain criteria were identified, in these instances the main triggers for reassessment were: changes in the technology, changes in the evidence base and changes in clinical practice. Austria (HVB), England (NICE), Estonia (UT), Latvia (NVD) Portugal (INFARMED) and Spain (AEMPS) all mentioned some or all of the following factors as possible triggers for a reassessment: new evidence of safety or efficacy, changes in price or pack size of the technology, changes in pricing of the comparator, changes in the indication of the technology, changes in clinical practice and budget impact.

In other cases the trigger for reassessment was a request from another organisation for example Austria (HVB) at the request of the marketing authorisation holder, Lithuania (VVKT) if requested from the appeal committee, in Malta on the MoH request and in Denmark (DEFACTUM) at the request of the hospital provider.

Approach to reassessment in regional agencies

Among the regional agencies all agencies indicated that they carried out reassessments for one or more of their HTA programmes.

In Italy both agencies (ASSR-RER and Veneto) carry out reassessment for non-pharmaceutical health technologies. For ASSR-RER reassessment as an MTA may be done if a new medical device is introduced. Veneto described no reassessment criteria but indicated reassessment would be completed as an STA.

Among the Spanish regional agencies the approaches to reassessment can include STA or MTA and the reasons for the reassessment are varied:

- AETSA indicated that emergent technology reports of non-pharmaceutical health technologies are reassessed if new data or evidence becomes available.
- UETS Madrid indicated that technology appraisals of non-pharmaceutical health technologies need to be updated every 5 years.

- SCS indicated that reassessments of non-pharmaceutical technology appraisals could be done, but are not done normally.
- Avalia-t and OSTEBA both indicated that reassessments of lifecycle technology assessments can be carried out when there are potentially obsolete technologies.
- Avalia-t also stated that reassessment may be carried out when the use of a health technology is conditional on real world data collection.

Analysis of reassessment procedures

As new evidence and information about a health technology emerges, reassessment performs a vital function in ensuring that decisions and re-evaluations of decisions are appropriately made.

There is a variation in reassessment procedures across the different countries. Some agencies have mandatory periods after which a product must be reassessed, other agencies reassess only if evidence emerges that may change the decision. Other agencies do not have established reassessment procedures. Reassessment practices within countries could be improved if opportunities to reassess existing collaborative HTA and to carry out collaborative HTA of established health technologies (that are likely to have been subject to initial national HTA) become part of HTA collaboration.

From an implementation perspective it may be challenging to maximise national implementation of a reassessment given the diverse range of situations when reassessment may take place. However, because reassessment activity is more likely to be planned activity, flexible and known in advance, collaborative reassessments could result in more meaningful implementation albeit in a smaller group of countries. For some technologies where the publication of evidence makes a significant change to the added value of the technology or an MTA is required because it is known that a number of new technologies are coming to market in close succession a collaborative reassessment of existing technologies could be of value. Indeed a collaborative reassessment could add greater value than an initial collaborative STA assessment because of the larger volume of evidence likely to be available and the potential need to incorporate multiple technologies as interventions which can challenge agency expertise and resources.

Topics for reassessment could be handled using similar topic selection procedures as proposed for non-pharmaceutical initial assessments. That is any call for topics can include possible reassessment topics, these would be selected and prioritised based on the agreed criteria, agreed by MS and scheduled as part of an annual work plan.

HTA collaboration could also support improved reassessment practices within countries by including recommendations about when a reassessment may become necessary given the evidence available and ongoing clinical studies.

As products become more established evidence of use and effect becomes more local and available from a wider range of sources meaning that the level of local adaptation required for a collaborative HTA reassessment may be greater than for an initial collaborative HTA. Evaluation of the amount of adaptation required for a collaborative reassessment versus an initial assessment may be required to ensure the collaborative HTA adds value and for which technology types it adds value.

Recommendations for reassessment procedures

Key implementation challenge	Recommendations for centralised cooperation	Recommendations for agencies
<ul style="list-style-type: none"> • The timeframe for reassessments varies from 1 year to 5 years • When a reassessment is due, some agencies consider whether a reassessment is needed but may not carry out a reassessment if it is felt the decision would not change • Some agencies do not have established reassessment procedures, and some agencies have them but rarely use them. 	<ul style="list-style-type: none"> • Reassessment activity could be included as an option in collaborative HTA topic selection because: <ul style="list-style-type: none"> ○ it is often planned HTA activity that is known in advance with more flexible timelines ○ the greater complexity and larger volume of evidence can challenge agency resources • Collaborative HTA should include a recommendation about when a reassessment might be required given ongoing studies and other technologies in the area • Include recommendations in initial assessments about when a reassessment may be required 	<ul style="list-style-type: none"> • Including reassessment information in the POP database will allow agencies to capitalise on joint HTA activity and sharing data between countries where overlapping activity is scheduled

Chapter 10: Stakeholder involvement

Key messages

- Stakeholder involvement can help to ensure that all relevant and important issues are taken into account, that the reporting in an HTA is accessible, and transparent.
- All countries involve stakeholders in their procedures. For 4 countries the procedure for stakeholder involvement isn't formally defined for all agencies or programmes.
- For both pharmaceutical and non-pharmaceutical health technologies the most common stakeholder groups involved are industry, clinical or professional groups and payers (all involved in over 80% of countries).
 - Industry tends to be involved throughout the assessment procedure for pharmaceuticals, but is less extensively involved in assessments of non-pharmaceutical health technologies.
 - All countries involve clinical experts in their procedures.
 - Payers are most frequently involved at the advice and decision-making phase (85% and 70% for pharmaceuticals and non-pharmaceutical health technologies, respectively).
- Over 60% of countries involve patient experts in one or more of their HTA procedures. For pharmaceuticals, patient experts tend to be more frequently engaged in the later stages of the assessment as part of the review of the draft report and during advice and decision making.

Description of stakeholder involvement procedures

Stakeholder involvement procedures

For pharmaceuticals, almost all countries, 27 out of 29 (93%) have a procedure for involving stakeholders within at least one agency in the country. Two countries (Romania and Slovakia) indicated that there is no established procedure for stakeholder involvement. However, both indicated that stakeholders are involved.

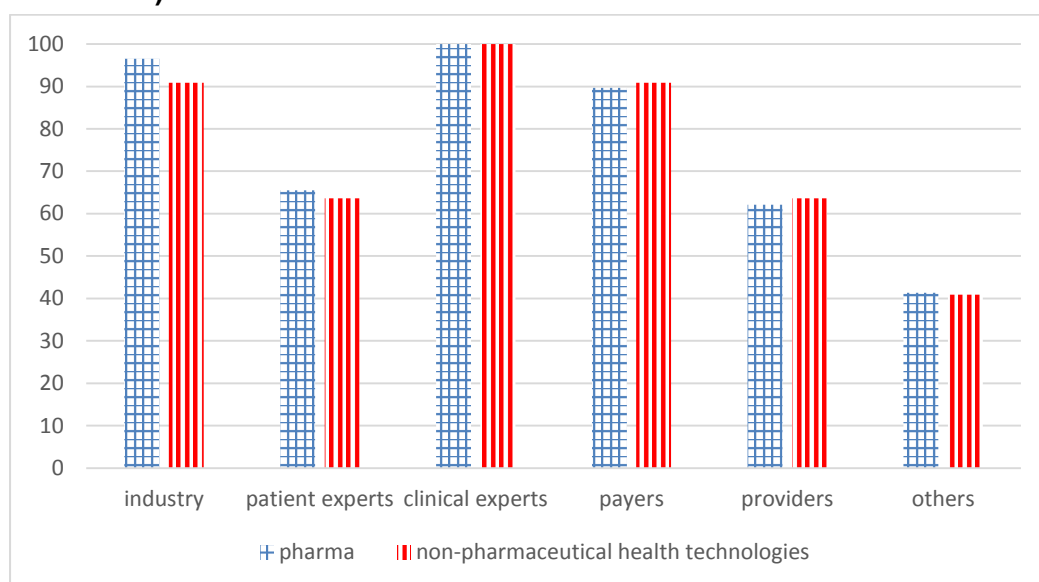
For non-pharmaceutical health technologies, 19 out of 22 countries (86%) have a procedure for stakeholder involvement. As for pharmaceuticals, the countries without a procedure (Lithuania, Slovakia and Hungary) indicated that stakeholders are involved in the assessment procedure.

The majority of the regional agencies (6 out of 8) indicated that there is a procedure for stakeholder involvement. Although two regional agencies indicated that they did not have a stakeholder procedure (Veneto and avaluat), they also indicated that stakeholders are involved in the assessment procedure.

Stakeholder groups involved

The most commonly included stakeholder groups for both pharmaceuticals and non-pharmaceutical health technologies are industry, clinical experts and payers. Patient experts and providers are also included in a majority of countries but less frequently than the other groups (figure 45).

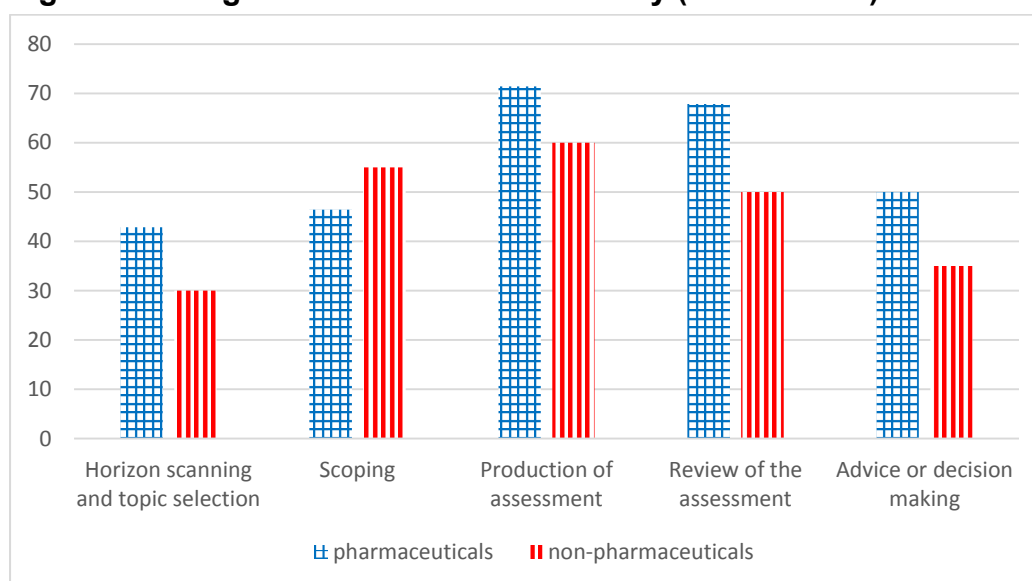
Figure 45: Stakeholder groups involved in the assessment procedure (% countries)



Key: N=29 countries pharmaceuticals N=22 countries non-pharmaceutical health technologies. Agencies coded multiple categories so data may add up to more than 100%.

Industry involvement

In 28 out of 29 countries (97%) there is industry involvement in the assessment procedure for pharmaceuticals and 20 out of 22 countries (91%) there is industry involvement in the assessment procedure for non-pharmaceutical health technologies. In countries where there is more than one agency or programme, involvement may differ between programmes or agencies. In Austria LBI-HTA and HVB but not GOEG involve industry and in Lithuania VVKT involves industry but VASPVT does not.

Figure 46: Stage of involvement of industry (% countries)

Key: N=28 countries involving industry for pharmaceuticals N=20 countries involving industry non-pharmaceutical health technologies. Agencies coded multiple categories so data may add up to more than 100%.

For pharmaceuticals, industry is most frequently engaged in the production of the assessment (20 out of 28 countries; 71%) and the review of the assessment (19 out of 28 countries; 68%) (figure 46). When the assessment starts industry often provides data, supporting materials, evidence or the synthesis of evidence and, if requested, submits additional documentation to support the production of the assessment. Once the draft assessment is available, industry may review the draft assessment and sometimes also the draft guidance or decision.

For non-pharmaceutical health technologies industry is most frequently involved in the production stage (12 out of 20 countries; 60%). Additionally, industry is frequently involved in the scoping stage (11 out of 20 countries; 55%) and review of the assessment (10 out of 20 countries; 50%). The nature of the involvement is similar as for pharmaceutical assessments.

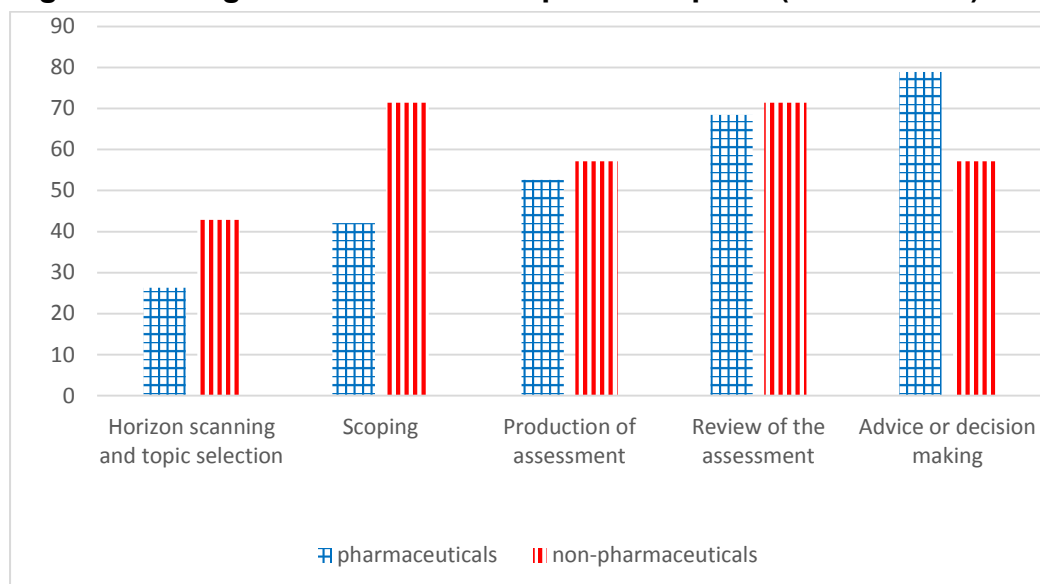
Among the regional agencies, one agency from Italy (ASSR-RER) and 2 from Spain (SCS and OSTEBA (OSTEBA for lifecycle technology reports only)), stated that they engage with industry during the assessment procedure. One agency involves industry in horizon scanning (33%), 3 involve industry in scoping (100%), one in the production of the assessment (33%) and one in the review of the assessment (33%).

Patient involvement

For pharmaceuticals, 19 out of 29 countries (66%) involve patient experts in the assessment procedure for pharmaceuticals. For non-pharmaceutical health technologies, 14 countries out of 22 (64%) involve patient experts. In countries where more than one agency or programme is involved in the stakeholder

procedure, involvement status may differ between programmes or agencies. For example, in England patient experts are involved in all pharmaceutical programmes except for Evidence Summaries.

Figure 47: Stage of involvement of patient experts (% countries)



Key: N=19 countries involving patient experts for pharmaceuticals N=14 countries involving patient experts for non-pharmaceutical health technologies. Agencies coded multiple categories so data may add up to more than 100%.

For pharmaceuticals patient experts are most likely to be involved in the advice and decision making (15 out of 19 countries; 79%) and review of the assessment (13 out of 19 countries; 68%)) (figure 47). For the assessment of non-pharmaceutical health technologies patient experts are most frequently involved in scoping (10 out of 14 countries; 71%) and review of the assessment (10 out of 14 countries; 71%).

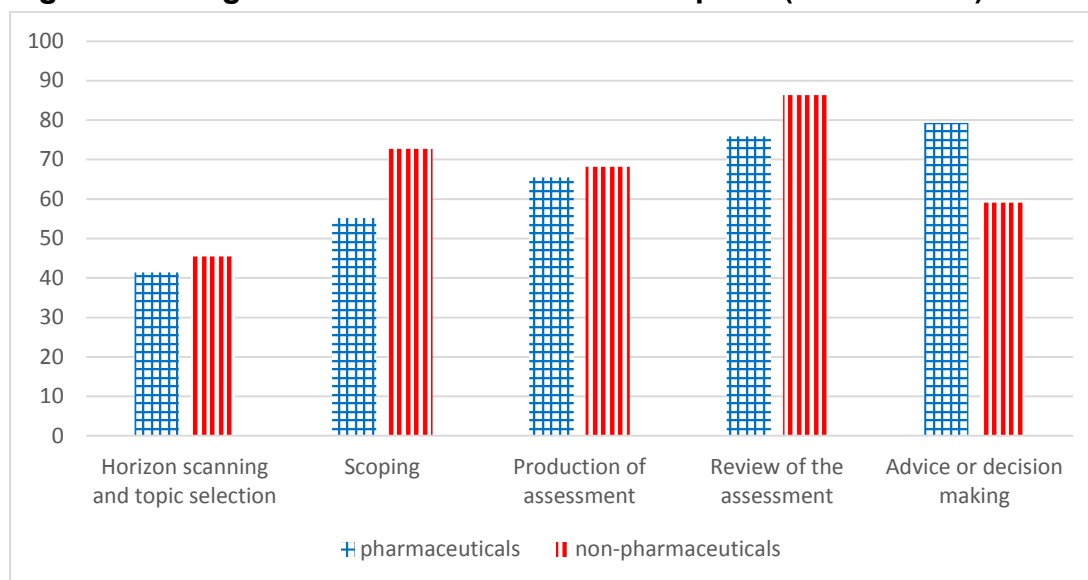
Patient experts take part in the review phase mainly by reviewing and commenting on the report. Additionally patient experts can be involved in advice or decision making by: attending the Reimbursement Committees or Advisory Committees and through consultation in price negotiations. The role of patient experts in the scoping and production of the assessment is to provide information, data and evidence. Additionally, patient experts can be involved in reviewing scoping documents or attending expert workshops.

In total 6 regional agencies (1 Italian and 5 Spanish) involve patient experts in the assessment procedure. Considering the stage of the procedure, 3 agencies involve patient experts in horizon scanning and topic selection (50%), 4 in scoping (66%), 2 in the production of the assessment (33%) and 3 in the review of the assessment (50%) and 2 in advice and decision making (33%).

Clinical expert involvement

All countries engage clinical experts (e.g. clinical specialists providing expertise about the disease or the technology) in their procedures. G-BA noted that in Germany they do not engage clinical experts in the assessment procedure on a regular basis, only in a few instances.

Figure 48: Stage of involvement of clinical experts (% countries)



Key: N=29 countries involving clinical experts for pharmaceuticals N=22 countries involving clinical experts for non-pharmaceutical health technologies. Agencies coded multiple categories so data may add up to more than 100%.

For pharmaceuticals clinical experts are most likely to be engaged in advice and decision making (23 out of 29 countries; 79%) and the review of the assessment (22 out of 29 countries; 76%) (figure 48). For non-pharmaceutical health technologies, clinical experts are most likely to be engaged in review of the assessment (19 out of 22 countries; 86%) and scoping (16 out of 22 countries; 73%).

During the assessment procedure clinical experts are involved in providing evidence and data, by giving opinion, advice and feedback or being part of the working committee in charge of producing the assessment. Additionally clinical experts may review the evidence submitted by industry, the draft report, the final report or the guidance; discuss the documents with the report authors; give their opinions on clinical evidence; are consulted on assumptions made in the model; and advise on the choice of comparators. Clinical experts may also be involved in medical ethics issues evaluation. During the advice and decision making phase clinical experts may be involved: as members of reimbursement committees or advisory commissions; by attending the Committee meeting to provide input/opinion to inform decision making and making recommendations based on the HTA report on whether reimbursement should be considered. During scoping clinical experts may be involved by providing

data or being consulted on questions such as relevant comparator, clinical value of the product, how the product is used in clinical practice, resource utilisation etc.

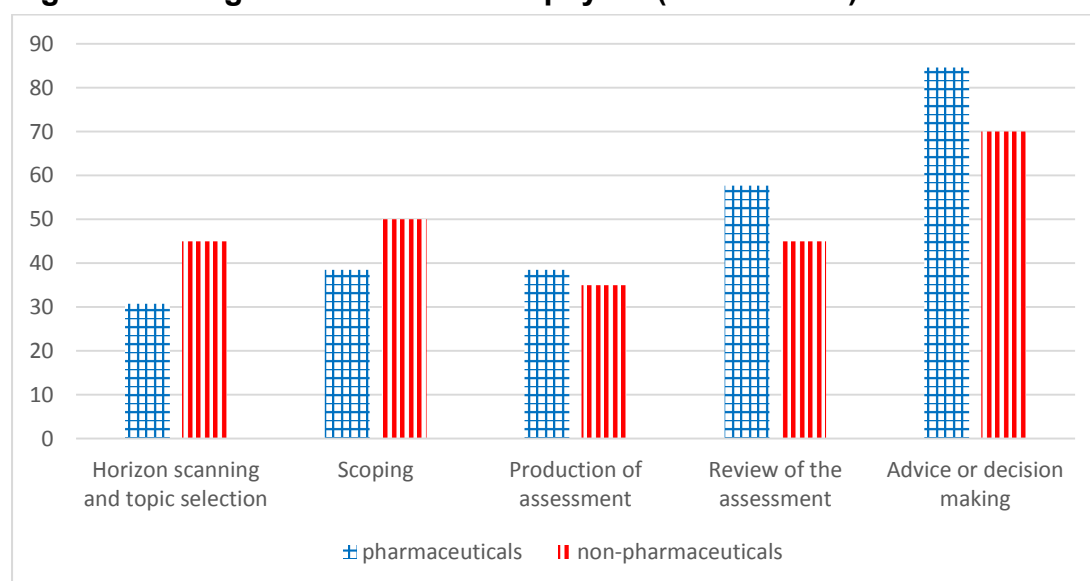
All 8 regional agencies involve clinical experts in the assessment procedure. Seven out of eight agencies involve clinical experts in horizon scanning and topic selection, scoping, review of assessment and advice or decision making. Six agencies indicated that they also involve clinical experts in the production of assessments.

In general, the pattern of involvement for clinical experts is similar to that of patient experts (e.g. a greater involvement towards the end of the assessment procedure). However, there are a larger percentage of countries engaging clinical experts at each stage.

Involvement of payers

Twenty-six out of 29 countries (90%) involve payers in their assessment procedures for pharmaceuticals (that is, reimbursement authorities, insurance funds and social security institutions). In total 20 out of 22 countries (91%) involve payers in the assessment of non-pharmaceutical health technologies. Not all agencies in all countries include payers in their procedures.

Figure 49: Stage of involvement of payers (% countries)



Key: N=26 countries involving payers for pharmaceuticals N=20 countries involving payers for non-pharmaceutical health technologies. Agencies coded multiple categories so data may add up to more than 100%.

Payers are most likely to be engaged in the advice and decision making (22 out of 26 countries; 85% and 14 out of 20 countries; 70% for pharmaceuticals and non-pharmaceutical health technologies respectively) (figure 49).

Payers can be involved in formulating the advice and decision: through participating/providing advice on access agreements; attending committee meetings

to inform decision making; being represented in the advisory commission. During the advice or decision making phase, payers (e.g. Health Insurance Institute, Corporate Pharmaceuticals Unit, and National Insurance Funds) may examine the impact of proposed price on public expenditure; the impact of potential market access schemes on the cost-effectiveness of the intervention; or verify the financial effects of adding new features on the organisations' budget.

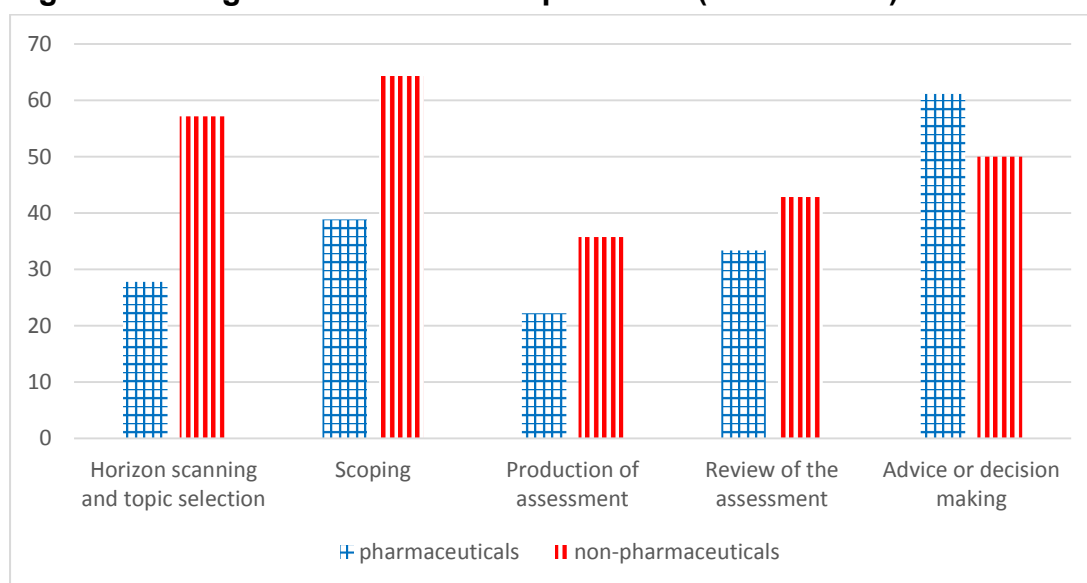
Specifically during horizon scanning and topic selection payers may suggest topics or propose new interventions/ technologies for assessment. The role of payers in the scoping stage and during the production of the assessment is to provide information, data and evidence. Additionally payers can be involved in reviewing the assessment report or attending reference groups, attending Committee meetings to approve advice or inform decision making, or being members of the reimbursement institutions with voting rights.

Seven out of 8 (88%) regional agencies involve payers in their procedures. Payers are most likely to be involved in horizon scanning, topic selection and scoping and less likely to be involved in production of the assessment, review of the assessment and advice and decision making.

Involvement of providers

Providers include hospital management and commissioners. In 18 out of 29 countries (62%) providers were involved in the assessment procedure for pharmaceuticals and in 14 out of 22 countries (64%) for non-pharmaceutical health technologies.

Figure 50: Stage of involvement of providers (% countries)



Key: N=18 countries involving providers for pharmaceuticals N=14 countries involving providers for non-pharmaceutical health technologies. Agencies coded multiple categories so data may add up to more than 100%.

For pharmaceuticals providers are most likely to be engaged in the advice and decision making (11 out of 18 countries; 61%). For non-pharmaceutical health technologies providers are more likely to be included in the earlier stages of topic selection (8 out of 14 countries; 57%) and scoping (9 out of 14 countries; 64%) (figure 50).

Providers can be involved in advice or decision making by: attending the Committee meeting to provide input into decision making or providing an evidence statement. Additionally pharmacy and hospital organisations may be on Committees. Providers may attend expert workshops or advisory group meetings to provide oversight to assessment and inform advice.

For the assessment of non-pharmaceutical health technologies providers can be involved in horizon scanning and topic selection by proposing and identifying topics for assessment; in some countries they can ask for evaluation of procedures to be reimbursed. Their role in scoping is to provide data and evidence and they can be involved in stakeholder groups. Providers can review documents and provide general consultation via peer review.

Seven out of 8 regional agencies (88%; one from Italy and six from Spain), involve providers during their assessment procedure. Providers were most likely to be involved in horizon scanning, topic selection and scoping and less likely to be involved in other stages.

Involvement of other stakeholder groups

12 countries indicated that they involve other stakeholder groups in pharmaceutical procedures and 9 countries indicated that they involve other stakeholders in their non-pharmaceutical health technology procedures.

Other stakeholders involved in the assessment procedure include academics or universities, other government organisations and regional representatives. A number of specialist experts were named as being part of the advisory committees including statisticians, economists, legal experts and other methodological experts.

These groups are most frequently engaged in the review of the assessment or advice and decision making stage. Involvement includes participating in Committee meetings and evaluating the company submission.

Analysis of stakeholder involvement

Stakeholder involvement in collaborative HTA can help to ensure that all relevant and important issues are taken into account and that the reporting in an HTA is accessible, and transparent.

As with quality assurance procedures:

- If stakeholder involvement in any displaced parts of national procedures are not part of the collaborative HTA procedure then collaborative HTA may not be perceived as a robust alternative to national procedures.
- Collaborative HTA does not need to replace all aspects of national stakeholder engagement practices. The procedure of adaptation and use of the collaborative HTA in decision making will allow agencies to incorporate stakeholder involvement into their work and some will have to do this as part of ensuring accountability of the larger procedure that HTA is part of.
- Stakeholder involvement must be balanced with the requirement for timeliness, if stakeholder engagement procedures lengthen the time required to complete an assessment, then this could adversely affect use if publication is delayed.

HTA collaboration can incorporate stakeholder involvement in two ways:

- directly incorporate stakeholder involvement (e.g. as part of the collaborative procedure a report is sent for stakeholder consultation)
- support national agencies to engage with national stakeholders to inform the collaborative HTA (e.g. supporting national agencies to liaise with national stakeholders about the appropriateness of a topic for assessment or a scope).

In general the pattern of stakeholder engagement in existing agency procedures varies for pharmaceuticals and for non-pharmaceutical health technologies meaning that a procedure that is fit for purpose for collaborative HTA may differ between technology types. Pharmaceutical HTA includes more stakeholder engagement towards the end of the procedures as part of reviewing the assessment and producing advice (aspects that may not be displaced by the production of collaborative HTA). Whereas for non-pharmaceutical health technologies, stakeholders are more likely to be involved throughout the whole procedure (and therefore more aspects may be displaced by use of collaborative HTA).

Topic selection, prioritisation and scoping

The nature of the stakeholder engagement required will vary depending on how MS are engaged in the procedure of topic selection, prioritisation and scoping. If collaborative HTA reaches out to all MS as part of this procedure, then the collaborative HTA cooperation could support national agencies to build national stakeholder involvement into their procedures to inform the collaborative HTA topic selection and prioritisation, rather than having to build in direct EU stakeholder involvement. If on the other hand, the topic selection, prioritisation and in particular scoping is contained within a small number of MS, then broad EU stakeholder

engagement is needed to generate a range of perspectives about priorities and relevant parameters for assessment.

For pharmaceuticals, industry would need to be involved to provide information about likely launch plans and timings across Europe. Given existing patterns of stakeholder involvement clinical experts would also need to be involved to support the identification of priority topics. For non-pharmaceutical health technologies, broader stakeholder engagement (to involve patient experts, clinical experts, payers, and providers) may be required so as to reflect existing patterns of national agency engagement. Given the diversity of non-pharmaceutical health technologies, a broader involvement of stakeholders may also be required to augment MS experience in this heterogeneous group of health technologies.

The development of a scope for collaborative HTA will require input that is likely to be specific to MS contexts. Therefore from the perspective of developing an appropriate scope for collaborative HTA that supports national implementation, stakeholder engagement where HTA collaboration supports MS to engage national stakeholders to provide comments on the scope for collaborative HTA may be more appropriate than trying to identify stakeholders who can provide an international perspective. However, international stakeholders may support the identification of outcomes for the assessment and global industry representatives are able to provide information about available evidence for the intervention of interest.

Assessment production and review

The production of the assessment is the place in the assessment procedure where national stakeholder involvement procedures are most likely to be displaced. However, agencies adapting assessments or using these to support evaluation may still choose to or be required to consult national stakeholders as they develop the national assessment from the collaborative HTA.

As with topic selection, either direct EU stakeholder involvement could be built into the procedure or MS could be supported to incorporate their own HTA quality assurance and stakeholder engagement procedures into their feedback on the collaborative HTA. For pharmaceuticals, industry and clinical experts are again the stakeholders most frequently engaged in the assessment production procedure. Involvement of industry is usually to provide evidence for the assessment and, if requested, additional documentation to support production. Clinical experts may directly inform the assessment production as it takes place, by providing opinion and responding to issues identified. For non-pharmaceutical health technologies a broader range of stakeholders are engaged during the production of the assessment to additionally include patient experts, payers, and providers.

Recommendations for stakeholder involvement

Key implementation challenge	Recommendations for centralised cooperation	Recommendations for agencies
<ul style="list-style-type: none"> If stakeholder engagement in any displaced parts of the national procedure is not part of the collaborative HTA procedure then collaborative HTA may not be perceived as a robust alternative to national procedures 	<ul style="list-style-type: none"> Develop clearly defined principles of stakeholder and expert involvement: <ul style="list-style-type: none"> At what point in the procedure national agencies should engage national stakeholders to inform the collaborative HTA Where and how stakeholders will be directly engaged in the HTA collaboration Where necessary develop resources that support national agencies to engage national stakeholders in the collaborative HTA procedure Work with stakeholders groups to define the methods of engagement in collaborative HTA procedures Include dedicated people in the HTA collaboration procedure to support patient involvement Quantify and share with MS any impact of adding stakeholder engagement procedures against a lengthening of the assessment procedure. 	<ul style="list-style-type: none"> Develop national procedures that allow relevant national stakeholders and experts to input into the topic selection procedures and the decision problem to be addressed in collaborative HTA

Chapter 11: Conclusion

The assessment of pharmaceuticals and non-pharmaceutical health technologies varies on important parameters, including:

- capacity to do HTA
- the function and content of HTA
- approaches used for assessment and evaluation
- availability of existing relevant structures (for example centralised regulation) that can support HTA activity

This means that (1) collaborative HTA requires different approaches to developing mechanisms for HTA cooperation depending on technology type, (2) some countries will require support to establish systems that use HTA to support decision making and (3) flexible implementation of joint HTA is required while systems develop.

Involvement in HTA cooperation

Topic selection

For pharmaceuticals, existing regulatory structures provide an opportunity to efficiently develop a predictable and timely topic selection system. Depending on the capacity of the collaborative HTA programme either all topics with certain characteristics (e.g. new products and major licence extensions) could be assessed or a set of topic selection criteria could be developed that could be applied by either all MS or those MS who consider only a subset of new marketing authorisations.

For non-pharmaceutical health technologies a different topic selection system must be developed. Currently, many agencies are reactive to requests from decision makers or applicants for assessment. This means that HTA collaboration that waits for MS to provide their topics for assessment is reacting to national HTA systems that are also reactive. Although HTA collaboration should include a function whereby MS can suggest topics for assessment, in a sustainable system this should not be the only topic selection function used. Non-pharmaceutical health technology topic selection should be forward-looking based on horizon scanning outputs to identify potentially important health care technologies in the pipeline. This would help ensure that collaborative HTA supports MS by not only by providing rigorous evidence to support decision making, but also to predict where priorities might arise in the future supporting national systems to become less reactive.

Scoping and project planning

Working with MS organisations about best possible timings and the scope of the assessment as part of topic selection will maximise the likelihood of developing relevant assessments. However, for all technology types, current procedures for scoping mean that MS will need to be supported to engage in early project planning.

As part of the support for MS, this should include supporting MS to include national stakeholders in the collaborative HTA scoping and project planning procedure.

Assessment and evaluation

Existing practices include both production of assessments and also evaluation of company submissions. It is important to clarify the output of pharmaceutical collaborative HTA in terms of whether it is an HTA or an evaluation of a company submission of evidence. These products and the documents that support them are not interchangeable and different skills and resources are required to carry them that will affect agency involvement in HTA collaboration.

If the collaborative HTA output is an HTA rather than an evaluation of a company submission, then agencies may be more comfortable authoring reports if they currently produce HTA. For pharmaceuticals, where a majority of agencies make most of their decisions on the basis of evaluations of company submissions, there may be particular issues with resources and expertise required to author reports. As part of capacity development and in order to maintain the sustainability of HTA collaboration agencies currently evaluating submissions should be supported to be part of authoring teams so as to allow a range of agencies to be involved in HTA collaboration.

Use of collaborative HTA

Different working practices define how an agency will use collaborative HTA (that is, to adopt or adapt it, or to use it to support evaluation). For agencies currently evaluating company submissions, clarity and agreement among MS is needed on whether the goal of using collaborative HTA is for it to be:

- an alternative to national submissions of REA (e.g. the collaborative HTA is used instead of an REA national submission)
- used in addition to national submissions of REA (e.g. the collaborative HTA is used to support evaluation of the national submission)
- incorporated into the national submission of REA (e.g. either the company's submission of evidence for the collaborative HTA or the collaborative HTA itself is submitted to the agency as part of the national submission)

All these options could be an outcome of HTA cooperation, but each affect the timing of when HTA is needed and the changes MS will need to make to their systems. Within current systems, the second of these is possible, the first and third will require procedural and often legal changes to be possible in many countries.

While MS HTA consistently uses REA, it is usually not the only area included in HTA. If collaborative HTA only includes REA, this affects MS use because other aspects of the HTA will need to be carried out locally.

For countries making use of REA and cost effectiveness analysis, clinical effectiveness information appears not only in the clinical effectiveness section of the report but also the cost effectiveness section of the report and in any health economic model provided. Cost effectiveness analysis is usually provided by Industry and agency work on clinical and cost effectiveness is undertaken in parallel because of restrictions to timing. To use collaborative HTA as an alternative to national REA there must be assurances that the inputs in the collaborative REA will be the same as in the national cost effectiveness analysis. Without such assurances collaborative HTA may only be used for sensitivity analysis and as additional to national clinical effectiveness information.

A second issue related to content of HTA is that countries may face particular challenges evaluating health economic information or examining wider issues such as patient, social, ethical and organisational issues. This can either be because of resource constraints on the agency or it could be that the information is not easily identifiable in the country (for example if it is a rare disease or particularly innovative health technology). Therefore in some instances an assessment may provide more added value if it is extended beyond REA, so that collaborative HTA is able to support agencies to better consider some of the wider issues. Such discussions are best built into topic selection procedures.

HTA is often the first part of a larger procedure to support reimbursement and/or pricing decisions. For pharmaceuticals this is commonly a pricing and/or reimbursement decision procedure that is governed by the Transparency directive (89/105/EEC). Collaborative HTA must fit with any procedural requirements set by the larger procedures in which HTA is going to be used.

For pharmaceuticals, it may be possible to liaise with Industry about launch plans to identify the most appropriate timing for collaborative HTA, but in the absence of such liaison to maximise use of collaborative HTA. It must at the latest be available at the time of marketing authorisation. A number of HTA agencies start work earlier than marketing authorisation and therefore require the report at the time of CHMP opinion, so in the long term collaborative HTA must work towards a system that runs in parallel with the regulatory timetable and an output is available at CHMP opinion.

For non-pharmaceutical health technologies, a key issue is identifying the best time to carry out an assessment for it to be of most value; the point at which technologies become national priorities for assessment varies. A discussion about timelines for production should take place as part of topic selection.

The role that HTA plays in supporting reimbursement and pricing decisions means that if collaborative HTA is to be used as an alternative to national HTA, then it must address the requirements from MS for rigour, transparency and governance. This means supporting and incorporating quality assurance and stakeholder engagement, ensuring transparency of procedures and involvement and facilitating availability of

supporting documents. This is required so that in the event of challenge MS are able to rely on the collaborative HTA procedures.

Re-use national, regional and local HTA information from other jurisdictions

Agencies frequently use HTA from other jurisdictions to support their assessment. HTA cooperation has the potential to support not just centralised cooperation to create collaborative HTA, but also better information sharing between countries so that for topics not subject to collaborative HTA, there is more efficient use of resources. This is particularly the case for non-pharmaceutical health technologies where the range of topics is wide, capacity to undertake assessment low and programmes may still be establishing. Adapting existing tools so that they become databases of sources of HTA information will be an important feature of information sharing as will working towards a system where documents produced in a shared language are made publically available.

Appendix 1: List of agencies providing information about HTA and reimbursement procedures

Country	Agency	Data provided in relation to technology type	EUnetHTA partner
Austria	Hauptverband der Österreichischen Sozialversicherungsträger (HVB)	Pharma (outpatient) MedTech (outpatient)	Yes
	Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA)	MedTech (inpatient)	Yes
	Gesundheit Österreich GmbH (GOEG)	Both	Yes
Belgium	Rijksinstituut voor Ziekte- en Invaliditeitsverzekering (RIZIV)	Both	Yes
	Belgian Health Care Knowledge Centre (KCE)	Both	Yes
Bulgaria	National Center of Public Health and Analyses (NCPHA)	Pharma	Yes
Croatia	Hrvatski zavod za zdravstveno osiguranje (Croatian Health Insurance Fund(CHIF/HZZO))	Both	No
	Agency for Quality and Accreditation in Health Care and Social Welfare (AAZ)	Both	Yes
Cyprus	Department of pharmaceutical services of the ministry of health Cyprus (MoH)	Pharma	Yes
Czech Rep	State Institute for Drug control (SUKL)	Pharma (outpatient)	Yes
Denmark	DEFACTUM (coordinates regional HTA activity)	MedTech	Yes
	Danish Medicines Agency (DMA)	Pharma (outpatient)	No
	Institute for rational pharmacotherapy (IRF)	Pharma	No
Estonia	Ministry of social affairs	Pharma	No
	Estonian health insurance fund (EHIF)	Pharma	No
	University of Tartu, Department of Public Health (UT)	Both	Yes
Finland	Finnish Medicines Agency (FIMEA)	Pharma (inpatient)	Yes
	Pharmaceuticals Pricing Board (HILA)	Pharma (outpatient)	No
France	Haute Autorité de Santé (HAS)	Both	Yes
Germany	Federal Joint Committee (Gemeinsamer Bundesausschuss - G-BA)	Both	Yes
Greece	National organisation for healthcare provision (EOPYY)	Both	Yes
	Institute of pharmaceutical research and technology (IFET)	Pharma	Yes
	National evaluation centre of quality & technology in health S.A. (EKAPTY)	MedTech	Yes
Hungary	National Institute of Pharmacy and Nutrition (NIPN)	Both	Yes
Ireland	Health Information and Quality Authority (HIQA)	MedTech	Yes
	National Centre for Pharmacoeconomics (NCPE)	Pharma	Yes
Italy	Agenzia Italiana Del Farmaco (AIFA)	Pharma	Yes
	Agenzia Nazionale Per I Servizi Sanitari Regionali (Agenas)	MedTech	Yes
	Agenzia sanitaria e sociale regionale - Regione Emilia-Romagna (ASSR-RER)	MedTech	Yes
	Regione veneto (Veneto)	MedTech	Yes
Latvia	The National Health Service (NHS / NVD)	Both (outpatient)	Yes
Lithuania	State Medicine Control Agency Lithuania (VVKT)	Pharma (outpatient)	Yes

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Country	Agency	Data provided in relation to technology type	EUnetHTA partner
	Valstybinė Akreditavimo Sveikatos Priežiūros Veiklai Tarnyba Prie Sveikatos (VASPVT)	MedTech	Yes
Malta	Directorate Pharmaceutical Affairs, Ministry for Health (DPA/MFH)	Pharma	Yes
Norway	Norwegian Medicines Agency (NOMA)	Pharma	Yes
	Norwegian Institute of Public Health (NIPHNO)	Both (inpatient)	Yes
Netherlands	Zorginstituut Nederland (ZIN)	Both	Yes
Poland	Agency for Health Technology Assessment and Tariff System (AOTMIT)	Both	Yes
Portugal	National Authority of Medicines and Health Products (INFARMED)	Both	Yes
Romania	National Drug Agency (NDA)	Pharma	No
Slovakia	Ministry of Health of the Slovak republic (MoH)	Both (outpatient)	Yes
Slovenia	Agency for medicinal Products and Medical Devices of the Republic of Slovenia (JAZMP)	Pharma	Yes
	The Health Insurance Institute of Slovenia (HIIS)	Pharma	No
	Health council (MoH HC)	Health programmes	Yes
Spain	Agencia Española De Medicamentos Y Productos Sanitarios (AEMPS)	Pharma	Yes
	Instituto De Salud Carlos III (ISCIII)	MedTech	Yes
	Agency for Health Quality and Assessment of Catalonia (AQuAS)	Both	Yes
	Andalusian Agency for Health Technology Assessment (AETSA)	Both	Yes
	Scientific advice Unit of the Galician Agency for Knowledge Management (AVALIA T)	Both	Yes
	Health Technology Assessment Unit (UETS Madrid)	MedTech	No
	Basque Office for HTA (OSTEBA)	Both	Yes
	Canary Islands Unit for HTA (SCS)	MedTech	Yes
Sweden	The Dental and Pharmaceutical Benefits Agency (TLV)	Both	Yes
	Swedish Agency for Health Technology Assessment and Assessment of Social Care (SBU)	Both	Yes
UK	National Institute for Health & Care Excellence (NICE)	Both	Yes
	Scottish Medicine Consortium (SMC)	Pharma	Yes
	Scottish Health Technology Group (SHTG)	MedTech	Yes
	All Wales Therapeutics and Toxicology Centre (NHS Wales) (AWTTC)	Pharma	Yes
Switzerland	Swiss Federal Office of Public Health (FOPH/BAG)	Pharma (outpatient) MedTech	Yes

Appendix 2: Data extraction form

Question	Response	Reference
General information		
Country		
Organisation(s)		
Type of Medical Technology	Pharmaceutical/Medical Device/Both	
Further information about the types of technology covered		
Location	Inpatient/outpatient/both	
Remit	National/Regional	
Definition of inpatient and outpatient used by the agency to assign products to processes (if there are separate processes for inpatient and outpatient)		
This is a description of an established process for involving HTA in reimbursement and/or pricing	Yes/No	
This is a description of an established process for creating HTA but it does not formally inform pricing and/or reimbursement	Yes/No	
References		
Procedural documents used to support the data extraction		
Legal documents used to support the data extraction		
General capacity information		
Total number of assessments carried out in a year		
Completion of single technology initial assessments	Yes/No	
If yes, insert number per year		
Type of assessment	REA only, clinical effectiveness and economics, full HTA	
Time taken to complete an assessment		
Completion of multiple technology initial assessments	Yes/No	
If yes, insert number per year		
Type of assessment	REA only, clinical effectiveness and economics, full HTA	
Time taken to complete an assessment		
Completion of single technology re-assessments	Yes/No	
If yes, insert number per year		
Type of assessment	REA only, clinical effectiveness and economics, full HTA	
Time taken to complete an assessment		

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Completion of multiple technology re-assessments	Yes/No	
If yes, insert number per year		
Type of assessment	REA only, clinical effectiveness and economics, full HTA	
Time taken to complete an assessment		
Number of technical staff completing assessments		
Overview of the process		
Organisation(s) responsible for topic selection		
Timing of the stage relative to regulatory procedures (if applicable)		
Organisation(s) responsible for scoping		
Timing of the stage relative to regulatory procedures (if applicable)		
Organisation(s) responsible for producing HTA		
Timing of the stage relative to regulatory procedures (if applicable)		
Organisation(s) responsible for reviewing HTA (where HTA provided by industry)		
Timing of the stage relative to regulatory procedures (if applicable)		
Organisation(s) responsible for providing advice and recommendations		
Timing of the stage relative to regulatory procedures (if applicable)		
Organisation(s) responsible for decision making		
Timing of the stage relative to regulatory procedures (if applicable)		
Horizon Scanning		
Is there a horizon scanning process?	Yes/No	
If yes, is this process carried out within the organisation responsible for completing the assessment or externally by a different organisation?	Internal/ External/ Both	
If external, which organisation is responsible? If yes, what is the horizon scanning process used for?	Workload planning/ topic selection/ Both	
If yes, what is the horizon scanning process used for?		
If yes, what sources are used to inform horizon scanning?	Information from regulators Media scanning Literature searches Direct contact with companies Clinical and technology experts Other (specify)	

If yes, when does this occur relative to regulatory timings?		
If yes, how frequently is horizon scanning carried out		
If no, how are possible topics notified to the agency?		
Topic selection		
Who chooses which topics are subject to assessment?	HTA agency Company/Industry Clinical or Medical Societies Patient groups Hospital providers Payer (social security / social insurance) Ministry of Health Other (specify)	
Are there eligibility criteria for assessment? e.g are there types of technology outside of the remit of the agency	Yes/No	
If yes, which topics will never be assessed or what are the criteria that topics must meet to be assessed		
Is there any further selection from the topics that are eligible for assessment?	Yes/No	
If Yes, what are the criteria or process used to further select the topics eligible for assessment?		
Is there any prioritisation of topics to be assessed?	Yes/No	
If Yes, what are the criteria or process used to prioritise the topics to be assessed?		
How far in advance of doing the assessment does the agency know that a topic will have to be assessed?		
When does topic selection occur compared to regulatory timeframes?		
How often does topic selection occur?		
Approximately how many topics go through the topic selection process each year?		
Scoping (e.g. the decision problem or question to be addressed in the assessment usually specified by PICO)		
Is there a process to define the scope or decision problem to be addressed in the assessment before the assessment process formally starts	Yes/No	
Who is responsible for defining the scope or decision problem of the assessment	HTA agency Company/Industry Clinical or Medical Societies Patient groups Hospital providers Payer (social security / social insurance) Ministry of Health Other (specify)	

Does the scope include PICO (population, intervention, comparators, outcomes) What other information to be included in the assessment is specified in the scope?	Yes/No	
What other information to be included in the assessment is specified in the scope?		
How many days or weeks is allowed for the scoping process?		
When does scoping occur compared to regulatory timeframes?		
When does scoping occur compared to when the assessment starts?		
Status of the scope	Public Confidential Public but with confidential information removed	
Language of the scope		
Status of scope contents	Mandatory Recommended Other (specify)	
Synthesis of evidence used in the assessment and decision making		
Which of these best characterises the overall process for producing the assessment that informs decision making?	Company (that is the MAH or the MAH representative) provides the HTA that is used in the assessment process Agency carries out its own HTA using evidence from company (specify agency) Agency carries out its own HTA and identifies the evidence to use itself (specify agency) Third party provides the HTA using evidence from company (specify third party) Third party provides the HTA and identifies the evidence to use itself (specify third party) Other – please describe	
Are there separate REA and economic assessments?	Yes/No	
If there are separate REA and economic assessments are these completed one after the other or are they completed at the same time	Completed one after the other Completed at the same time N/A (no separate assessment)	
Contents of REA or clinical effectiveness assessment	Review of published literature Review of unpublished literature Narrative review	

	Meta-analysis Indirect comparisons and mixed treatment comparisons De novo analysis by company De novo analysis by agency De novo analysis by third party Confidential information	
Language of the assessment		
If the agency completes the assessment itself, how many days or weeks is allowed for the assessment process?		
When does REA assessment occur compared to regulatory timeframes		
Status of the assessments	Public Confidential Public but with confidential information removed	
Information review		
If the synthesis of evidence used in decision making is provided by the MAH or its representative is there a separate review process of this evidence?	Yes/No	
Who reviews the assessment		
Contents of the review	Summary of the evidence provided Assessment of missing evidence Errors in submitted evidence Critique of internal validity of evidence submitted Critique of external validity of evidence submitted Further analyses Other – please describe	
If the review identifies limitations in the assessment provided is there a mechanism of interrupting or stopping the process and obtaining further information e.g. a stop the clock process	Yes/No	
Language of the review		
How many days or weeks is allowed for the review process?		
When does the review occur compared to regulatory timeframes		
Status of the review	Public Confidential Public but with confidential information removed	
Quality Assurance processes		

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Is there a quality assurance procedure in place to review the work completed by the HTA agency?	Yes/No	
Is the quality assurance procedure internal or external or both	Internal/External/Both	
If internal, who is involved in the quality assurance process		
If external, who is involved in the quality assurance process?		
At what stage(s) in the assessment process do the quality assurance procedures occur		
Advice and recommendations		
Are recommendations and advice made to support the decision maker?	Yes/No	
If Yes, who makes the recommendations		
In addition to advice and recommendations, which documents are provided to the decision makers?	Company submission of evidence Full HTA report Summary of the HTA report Critique of the HTA report Clinical trial documents Other – please specify	
Language in which the documents are provided?		
When is the advice and recommendations provided compared to regulatory timeframes		
Status of the advice	Public Confidential Public but with confidential information removed	
Status of the other documents presented to the decision maker	Public Confidential Public but with confidential information removed	
Decision making		
Who uses the assessment for decision-making? e.g. who is the decision maker	National policy makers or commissioners Hospital managers or hospital commissioners Clinicians Insurance funds or other reimbursement agencies Pricing authorities MoH Payers Other (specify)	
What decision does the assessment inform (choose all that apply)?	Reimbursement Pricing Clinical guidelines Quality standards (e.g. indicators and targets against which performance or service quality is assessed)	

	Other (please specify)	
When does the decision making occur compared to regulatory timeframes		
Legal and procedural issues		
Assessment criteria		
Are there criteria for assessment incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this in a legal and/or a procedural document?	Legal/Procedural/Both	
What are the criteria for assessment?		
Timeframe		
Can the assessment start before the pharmaceutical has received market authorization?	Yes/No	
Is the timeframe for assessment determined by the Transparency Directive?	Yes/No	
Are there other restrictions placed on the timeframe for assessment or when the assessment occurs	Yes/No	
If yes, what are these?		
If yes, are these restrictions legal and/or procedural?	Legal/Procedural/Both	
Language of assessment		
Is it a requirement that an assessment is written in the national/local language?	Yes/No	
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Confidentiality status		
Is the confidentiality status of the outcome incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this restriction legal or procedural?	Legal/Procedural/Both	
Is the confidentiality status of the documents supporting the outcome incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Acceptable data		
Are there restrictions to the types of study designs and evidence accepted	Yes/No	
If yes, what are these?		
Is this incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Are unpublished clinical data accepted?	Yes/No	
Is this incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Is a full clinical study report (CSR) needed or is a redacted version of the CSR sufficient?		

Are there any other prerequisites attached to the use of CSRs (e.g. only if they can be quoted)?		
Acceptable intervention		
Are interventions assessed for each indication the product is approved for or is the assessment only for the main indication?		
Is this incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Do interventions being assessed require regulatory approval?	Yes/No	
Is this incorporated in a legal act and/or guideline?		
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Acceptable population		
Does the assessment have to include the full indication for which the product has approval		
Is this incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Does the assessment have to include defined subgroup analyses	Yes/No	
If yes, what are these?		
Is this incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Acceptable comparator		
Is there a restriction in the choice of comparator (e.g. off label use, best supportive care)?	Yes/No	
If yes, please specify:		
Is this incorporated in a legal act and/or guideline?	Yes/No	
If yes, is this restriction legal and/or procedural?	Legal/Procedural/Both	
Other legal restrictions		
Are there any other legal restrictions that can act as a barrier for using EUnetHTA products or to using products from other jurisdictions in your country?	Yes/No	
If yes, please specify.		
HTA reassessment		
Is there a process of reassessment of initial decisions	Yes/No	
Criteria for reassessment		
Process used for reassessment, tick all that apply	Single Technology Assessment Multiple Technology Assessment	

	Relative effectiveness assessment only Assessment including both clinical effectiveness and economics Assessment including both clinical effectiveness and economics and legal, social and ethical issues (full HTA).	
Stakeholder engagement		
Is there a process for engaging with stakeholders while completing the assessment	Yes/No	
Is Industry involved?	Yes/No	
At what stage in the process?	Horizon scanning and topic selection Scoping Production of assessment Review of the assessment Advice or decision making	
How?		
Are patient experts involved?	Yes/No	
At what stage in the process?	Horizon scanning and topic selection Scoping Production of assessment Review of the assessment Advice or decision making	
How?		
Are clinical experts involved?	Yes/No	
At what stage in the process?	Horizon scanning and topic selection Scoping Production of assessment Review of the assessment Advice or decision making	
How?		
Are payers involved?	Yes/No	
At what stage in the process?	Horizon scanning and topic selection Scoping Production of assessment Review of the assessment Advice or decision making	
How?		
Are providers involved?	Yes/No	
At what stage in the process?	Horizon scanning and topic selection Scoping Production of assessment Review of the assessment Advice or decision making	

How?		
Are there any other stakeholders involved?	Yes/No	
Who?		
At what stage in the process?	Horizon scanning and topic selection Scoping Production of assessment Review of the assessment Advice or decision making	
How?		
Are stakeholders able to challenge the decision?	Yes/No	
Which stakeholder groups are able to challenge the decision?		
Information held		
<i>Agency produced information about horizon scanning and topic selection (for example summaries of evidence for or databases of emerging topics)</i>		
Type of information held		
Organisation who owns the information (complete only if more than 1 organisation is described in this form)		
Publication Type	Public Confidential Public but with confidential information removed	
Timing of publication		
Language(s)		
<i>Agency produced information relating to assessment (for example assessments, reviews, summaries of the evidence, scoping documents, workshop summaries, lists of stakeholders)</i>		
Type of information held		
Organisation who owns the information (complete only if more than 1 organisation is described in this form)		
Publication Type	Public Confidential Public but with confidential information removed	
Timing of publication		
Language(s)		
<i>Agency produced information relating to advice /recommendations and decision making (for example recommendations documents, presentations or slides from Committee meetings, minutes from decision making Committees)</i>		
Type of information held		
Organisation who owns the information (complete only if more than 1 organisation is described in this form)		
Publication Type	Public Confidential Public but with confidential information removed	
Timing of publication		
Language(s)		

<i>Other (for example databases of reports or databases of recommendations developed by the agency or to which the agency contributes)</i>		
Type of information held		
Organisation who owns the information (complete only if more than 1 organisation is described in this form)		
Publication Type	Public Confidential Public but with confidential information removed	
Timing of publication		
Language(s)		
Information Used		
<i>Information produced by other agencies used to support horizon scanning and topic selection</i>		
Information from other jurisdictions used in the assessment and decision making process		
Process in which the information is used (complete only if more than 1 process is described in this form)		
Agency owning the information used		
Language		
Comments		
<i>Information produced by other agencies relating to assessment</i>		
Information from other jurisdictions used in the assessment and decision making process		
Process in which the information is used (complete only if more than 1 process is described in this form)		
Agency owning the information used		
Language		
Comments		
<i>Information produced by other agencies relating to advice/recommendations and decision making</i>		
Information from other jurisdictions used in the assessment and decision making process		
Process in which the information is used (complete only if more than 1 process is described in this form)		
Agency owning the information used		
Language		
Comments		
<i>Other HTA information produced by other agencies</i>		
Information from other jurisdictions used in the assessment and decision making process		
Process in which the information is used (complete only if more than 1 process is described in this form)		
Agency owning the information used		
Language		
Comments		

Appendix 3: Questionnaire to support analysis

The responses to these questions will help WP7 develop the discussion and recommendations section of the report. The responses will not be made public. In section 1 there is a series of questions about the products and ways of working you value from the perspective of your agency. In section 2 there are a set of more general questions about recommendations for procedures for HTA collaboration from the perspective of EUnetHTA partners as a group given the range of working practices observed.

Section 1

Please respond from the perspective of **your agency**

Consultation question	Response
Assessments of what type of technologies would be of most value for your agency?	
For your agency to be best able to use EUnetHTA assessments how far in advance of the national assessment starting does topic selection and notification of assessment need to occur?	
Given your working practices would it be desirable or possible for your agency like to engage in the topic selection processes for EUnetHTA assessments? <i>Consider, would you like to be involved in topic selection procedures, and if so how? Are there other organisations or stakeholders in your country that EUnetHTA needs to involve in topic selection</i>	
Given your working practices would it be desirable or possible for your agency to be part of a process to define the question (e.g. PICO) to be addressed in a EUnetHTA assessment before your national assessment was initiated? <i>If desirable but not possible, please indicate if this is because of resource constraints or legal or procedural constraints or some other reason</i>	
For your agency to be best involved in producing EUnetHTA joint assessments are there changes to the working procedures for joint and collaborative assessments you would value?	
For your agency to be best able to use EUnetHTA assessments are there changes to the content you would make? <i>Consider the topic areas covered in a EUnetHTA assessment, depth of the content and also the nature of the assessment e.g. an HTA based on company submission</i>	
For your agency to be best able to use EUnetHTA assessments are there changes to the timings you would make?	

Consider when the EUnetHTA assessment is available for adaptation e.g. 100 days after CHMP positive opinion	
For your agency to be best able to use EUnetHTA assessments are there changes to the transparency of the assessment procedure you would make? <i>Consider the transparency of the process, of the report and of the evidence informing the report</i>	
For your agency to be best able to use EUnetHTA assessments are there changes to the quality management and assurance procedures you would make?	
For your agency to be best able to use EUnetHTA assessments are there changes to stakeholder involvement that you would make?	
Are there other points in the procedures for producing EUnetHTA assessments or developing other EUnetHTA tools and guidelines where your agency would like to be engaged? <i>Consider not just the joint assessment process, but also other areas such as template, tools and guideline development</i>	

Section 2

Please respond from the perspective of **EUnetHTA partners as a group**

Consultation question	Response
Given the range of working procedures across EUnetHTA partners, what recommendations would you make about EUnetHTA topic selection procedures?	
What recommendations would you make about project planning and scoping?	
What recommendations would you make about the production process for assessments?	
What recommendations would you make about quality assurance of EUnetHTA assessments?	
What recommendations would you make about stakeholder involvement in EUnetHTA assessments?	
What recommendations would you make about the nature of the products (assessments and other tools and guidelines) produced as part of HTA collaboration?	
Do any of your recommendations change considering the differences in working procedures among EUnetHTA partners for pharmaceutical and non-pharmaceutical assessment	

Section 3: other comments

Page reference	Comment