



eunetha
EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

An analysis of HTA and reimbursement procedures in EUnetHTA partner countries: Annex 2 Case studies

Disclaimer: EUnetHTA is supported by a grant from the European Commission. The sole responsibility for the content of this document lies with the authors and neither the European Commission nor EUnetHTA are responsible for any use that may be made of the information contained therein.

Contents

Contents.....	2
Case study 1: Collaborative HTA by the Spanish Network of HTA agencies, Spain ..	4
Context	4
The Spanish Network.....	4
Working Practices.....	5
Coordination functions	5
Topic selection	6
Allocation of work.....	6
Production of Assessments.....	7
Decision making.....	8
Case Study 2: HTA at the Spanish Medicines Agency, Spain.....	8
Context.....	8
Working practices.....	8
Use of EUnetHTA reports	10
Case study 3: Collaborative HTA of non-pharmaceutical health technologies in Italy	10
Context:	10
Agenzia sanitaria e sociale regionale - regione Emilia-Romagna (ASSR RER)	11
Universita' Cattolica Del Sacro Cuore (UCSC - Gemelli)	12
Agenzia Nazionale per i Servizi Sanitari Regionali (Agenas)	13
La Rete Italiana di HTA (RIHTA).....	13
Developments in the procedures for the assessment of non-pharmaceutical health technologies	14
Case Study 4: Use of EUnetHTA assessments at the agency for Quality and Accreditation in Health Care and Social Welfare (AAZ), Croatia.....	15
Context	15
Working Practices.....	16
Use of EUnetHTA assessments	17
Challenges and solutions.....	18
Drivers to support use of EUnetHTA products.....	19
Case study 5: Collaborative assessments between Rijksinstituut Voor Ziekte- en Invaliditeitsverzekering (RIZIV), Belgium and Zorginstituut Nederland (ZIN), the Netherlands.....	20
Context:	20
Rijksinstituut Voor Ziekte- en Invaliditeitsverzekering (RIZIV).....	20
Zorginstituut Nederland (ZIN).....	21
The BENELUXA collaboration	22
Working Practices.....	22
Coordination.....	22
Topic selection	23
Allocation of work.....	23
Production of Assessments.....	23
Advice	24
Challenges.....	24
Case Study 6: Involvement of Hauptverband der Österreichischen Sozialversicherungsträger (HVB), Austria in the BENELUXA collaboration	26
Context	26

EUnetHTA WP7 research and analysis activity 1: Annex 2 Case studies

Working Practices- Pharmaceuticals	26
Use of EUnetHTA assessments	27
Involvement in BENELUXA collaboration	27
Challenges and solutions.....	27
Language.....	28
Timelines	28
Confidentiality status.....	28
Case study 7: Use of EUnetHTA assessments at the National Institute of Pharmacy and Nutrition (NIPN), Hungary	30
Context	30
Working Practices.....	30
Use of EUnetHTA assessments	31
Challenges and solutions.....	32
Drivers to support use of EUnetHTA products	33
Case Study 8: Use of EUnetHTA assessments by the Scottish Health Technologies Group, Scotland	34
Context	34
Working Practices.....	34
Use of EUnetHTA assessments	35
Adaptation process	36
Condensing the EUnetHTA assessment document	36
Removing interventions that were not appropriate to the Scottish context.....	37
Adding national context information	37
Adding economic evidence	37
Updating clinical searches	37
Challenges and solutions to using EUnetHTA products	38
Drivers to support use of EUnetHTA products	39
Case study 9: The use of EUnetHTA assessments by the HTA unit of the Finnish Medicines Agency, Finland	40
Context	40
Working Practices.....	40
Use of EUnetHTA assessments	41
Adaptation process	42
Challenges and solutions to use of EUnetHTA products	42

Case study 1: Collaborative HTA by the Spanish Network of HTA agencies, Spain

Context

Healthcare in Spain was originally centralised but became decentralised between 1980 and 2000. Each region (17 Autonomous Communities and 2 Autonomous Cities) is now responsible for providing their own healthcare and setting their own health budget. The National Health System is coordinated by the Inter-territorial 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 very comprehensive, both in the extension of coverage and the scope of services included and must be provided and guaranteed by the regions. The regions can widen this common portfolio of services (complementary regional 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.

Since 2006 there has been formal collaboration in HTA among the Spanish regions. The first initiative was named Agencies and Units for Health Technology Assessments (AUnets) and already provided information for the ICNHS. In 2012 the ICNHS agreed to provide a legal framework for this collaborative work, and renamed it Spanish Network of Agencies for Health Technology Assessment and Services of the NHS. At this point, the existing cooperative work meant that many of the needed shared procedures were already in place in the Network. Changes that have occurred since 2012 include formalisation of the topic selection process to better cater the needs of the Committee for Provision, Insurance and Financing (integrated by political representatives from all regions) and agreement to further develop common methodologies, templates and guideline process for the entire Network. In the last few years there has been increased work to improve homogeneity and quality. Besides, the tools for additional evidence generation for non-medical technologies have been widened. The Spanish Ministry of Health has introduced “monitoring studies”. These allow for “controlled” adoption of the new technology, (acknowledging the uncertainty due to insufficient evidence) conditional on the results collected during the study. These “monitoring studies” connect HTA agencies with scientific societies, national experts, Regional Health Authorities and Hospitals to design and conduct “specific registries” for one to two years.

The Spanish Network

The Spanish Network of HTA Agencies is a collaboration of eight HTA agencies working together to produce national HTA of non-pharmaceutical medical

technologies in Spain. 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 Commission for Provision, Insurance and Financing (including representatives from each of the regions in Spain) by consensus, signed off by the Inter-territorial Council and the Ministry of Health makes the final decision through a legal instrument. These reports also can be useful to help regional decision making.

The Spanish Network conduct approximately 40 health technology assessments per year. The reports are produced using shared methodologies, templates and through mutual recognition of each agencies' work. Reports can be completed by a single agency, but may also be carried out jointly. For example, joint working practices have been developed between the Galician (Avalia-t) and the Canary Islands (SCS) agencies, where Avalia-t completes the REA part of the report and the SCS completes the economic evaluation and budget impact analysis. Methodological work and the resulting documents (handbooks, reports, etc) are shared among all network members. The shared approach means that the format of the HTA reports delivered to the Ministry of Health is identical regardless of which agency produces it. Reports contain relative effectiveness assessment, cost analysis, organisational, ethical and social factors (EUnetHTA checklist is used). Depending on the request and timeframes, the assessment may contain cost effectiveness analysis.

The corresponding regional governments fund each of the HTA agencies. Additionally, in the framework of the Spanish Network, an Annual Work Plan is established, that includes specific health technology assessments assigned to the different regional agencies. The Ministry of Health allocates specific funds to finance this Annual Plan.

Working Practices

Coordination functions

The Deputy Directorate of Quality and Cohesion, from the Ministry of Health, holds the permanent Secretariat of the Spanish Network. The tasks of the Secretariat are: elaborate the annual work plan and monitor its accomplishment, allocate work and resources to agencies so that the agreed work plan can be completed. Also it facilitates communication between agencies, through an online platform where working documents and published final reports are shared within the members of the Network and face to face meetings where the strategic lines of the Network, at national and international level, are designed. In order to disseminate the activities of the Network a web platform has been established (<http://www.redets.msssi.gob.es>). Additionally, the Permanent Secretariat holds the representation of the Spanish Network together with the presidency of the Network.

Besides the permanent Secretariat, there is a governing body, the plenary, where the directors of the agencies sit under a rotating presidency. Every year one of the Spanish Network agencies holds the presidency and another agency the vice-presidency. Strategic discussions and reporting on the development of the work plan takes places at the plenary that meet at least twice a year. The responsibilities of the president and vice president are to monitor the work timeline and ensure it is proceeding as planned, facilitate the coordination among the regional agencies and the Secretariat and holds the representation of the network alongside the permanent Secretariat. It also entails the task of organising the Network annual conference

The annual conference provides the opportunity for the personnel of the agencies to come together for networking and exchange of information through a scientific approach. These conferences include working meetings and internal workshops, and also sessions open to the public with the aim of disseminating the Network activities.

Topic selection

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 (army personnel, certain civil servants and justice personnel), 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 Commission. The prioritisation process is transparent and systematic although certain flexibility is allowed and a topic which may not score highly, can still be chosen for assessment if it is considered very relevant for the NHS. Approximately 70 topics are proposed each year and of those, about 40 are included in the annual HTA plan and distributed equitably among the agencies depending on their work burden.

From 2016 on, the Spanish Network is using a systematic priority scoring tool (PriTec Tool), in order to support this prioritisation process. This tool was initially developed by one of the regional agencies (Avalia- t)¹ and has been adapted for use at the national level. The tool is applied by the Committee for Provision, Insurance and Financing. In a meeting of this Committee, the scoring is revealed and discussed and consensus is reached on the topics chosen for assessment.

Allocation of work

The chosen topics are included in the annual work plan by the plenary of the Network and signed off by the Inter-territorial Council. The Spanish Ministry of Health allocates budget for the work and specifies a timetable for completion of the

¹ <http://www.pritectools.es/index.php?idioma=en>

assessment. The Secretariat of the Network sends the annual list of priorities to the Plenary and agrees on the final work plan. The discussion within the plenary leads to final allocation of tasks on the basis of the agencies' capacity, previous involvement and specialisations as well as eventual matching priorities from their region. The final distribution is even across agencies, accounting for the estimated workload entailed by each product. Each agency completes approximately a similar number of topics per year. The nature of the assessment required is agreed between the Spanish Ministry of Health and the agencies.

Each year a series of work slots are held free for unforeseen topics that may require assessment at a short notice (for example from ministerial departments and patient associations). This is important in case new evaluation needs come up during the year where a response to decision makers is required and that have to be included in that annual work plan.

Production of Assessments

Reports are produced by each agency individually and there is mutual recognition of reports between agencies and shared methods and templates. The agencies in the Spanish Network share the work to develop guidelines and tools to support their processes. The development of shared guidelines is included in the annual work plan and carried out collaboratively between the agencies.

The reports are prepared by the agencies, who normally identify and collect the evidence themselves rather than relying on evidence from industry. Clinical experts are included in the HTA process. There are currently discussions about how the Spanish Network may handle evidence from industry. Although currently there is no formal process for including other stakeholders in the development of the reports, the Spanish Network is in the process of developing a common framework for communicating with and involving stakeholders. This includes a proposal about how to involve patient groups and users in HTA. In relation to this issue, a recent conference on patient and public engagement on HTA was organised by the Spanish Network of Agencies in April 2017". The content of the reports completed by the Spanish Network depends on the question they are asked to address. They will include relative effectiveness assessment and organisation and ethical and social issues using the checklist available from EUnetHTA. Cost- analysis will include the information that is required to make decisions about budget impact. Cost effectiveness is sometimes included if requested and may entail "ex novo" analysis.

The Spanish Network has developed a series of shared methodological guidelines including procedural aspects such as topic identification and selection, presentation of data and quality control of HTA, and methodological aspects such as developing search strategies, quality assessment of studies and analysing results. Also, the HTA Network has designed a communication plan and there is a permanent working group to implement it.

Decision making

The assessment reports include advices and recommendations for the Inter-territorial Council, but they are not binding.

The Committee for Provision, Insurance and Financing (a committee within the ICNHS) reviews the information in the assessment and by consensus makes a proposal to update the common portfolio of services, weather to include, to remove or to modify the conditions/indications for provision of the service/technology. The Ministry of Health is responsible for final approval, through a legislative measure.

Case Study 2: HTA at the Spanish Medicines Agency, Spain

Context

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) is the Spanish Medicines Agency which is part of the Spanish Ministry of Health, Social Services and Equality. As part of its remit it produces health technology assessments of medicinal products called therapeutic positioning reports. Therapeutic positioning reports identify the therapeutic value of a product compared to alternatives. The reports provide advice to the DG Pharmacy to inform national pricing and reimbursement decisions. The reports also provide advice to the 17 regional health authorities about procurement and selection of medicinal products and to other decision makers at a healthcare level (hospitals, prescribers, etc.) about the use of medicinal products.

AEMPS produce approximately 50 therapeutic positioning reports each year. Reports produced by AEMPS include clinical effectiveness. The process is completed sequentially where clinical effectiveness information is compiled and an economic assessment is performed after price setting. Because AEMPS is a medicines agency supporting licensing of medicines, they have access to the regulatory documents that underpin the marketing authorisation procedure. AEMPS use these documents to complete the assessment of therapeutic effectiveness themselves without using additional evidence, unless significant evidence exists outside the regulatory submission identified by the organisation itself, provided by the marketing authorisation holder, or other stakeholders involved in the procedure (including scientific societies and patients associations).

Working practices

AEMPS normally provides HTA for all new products and indications with a positive opinion by the CHMP. Because they are a medicines agency they have access to information about which medicinal products are currently being assessed. They also do assessments for other medicinal products at the request of pricing and reimbursement authorities and, only occasionally, for products that do not follow centralised procedures.

AEMPS initiates the assessment process which usually starts when the CHMP opinion is granted and continues for approximately 6 to 8 months. It is possible for AEMPS to initiate an assessment before CHMP opinion, but because of the uncertainties in the regulatory information and discussion before opinion is granted, this is not a usual or preferred option.

The therapeutic positioning reports are developed and adopted by consensus within the Co-ordination Group for Therapeutic Positioning (GCPT). The GCPT support the topic selection, prioritisation (if required), scoping and work allocation process. 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 DG Pharmacy (part of the Ministry of Health), responsible for price and reimbursement decisions at national level, is also part of the GCPT although it does not have an active role in the development of reports and mainly participate as an observer. The scope of the assessment is agreed by the GCTP before it is carried out.

The assessments produced by AEMPS include a single intervention that is compared to one or more comparators. However AEMPS has flexibility to draw on comparator products when making advice (for example when advising a treatment is used in a particular position in the treatment pathway after or before other treatments).

The therapeutic positioning reports have two parts; the first part is an assessment of therapeutic effectiveness, the second part includes economic considerations (cost effectiveness and/or budget impact). AEMPS will mainly use the regulatory documents that it holds for the intervention under assessment and the comparators to support the assessment of therapeutic effectiveness unless additional significant evidence exist that may change the therapeutic positioning of the medicinal product. The therapeutic positioning reports consider legal, ethical and patient issues and these are explicitly stated in the reports only when considered particularly relevant for the medicinal product being assessed.

AEMPS prepare the first draft reports themselves, using assessors from the clinical evaluation teams. They usually receive the contribution of external clinical experts as well. The first draft is then reviewed by usually 2 regional health authorities who will agree with AEMPS on a draft to be reviewed by stakeholders (patient associations, scientific societies and the Marketing Authorisation Holder of the medicinal product). 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 and to allow price competition downstream.

The report at this stage supports national pricing and reimbursement decisions undertaken by DG Pharmacy, together with any other tools DG Pharmacy consider relevant in the decision making process, such as economic information, that may be provided by companies to the DG Pharmacy for price and reimbursement negotiation in the subsequent steps of the procedure. However, economic information is never provided or used to establish the therapeutic value of the medicinal product. Once the Ministry of Health has made its pricing and reimbursement decision, an economic assessment is carried out by the regional health authorities forming the GCPT to complete the positioning report and is shared internally among GCPT participants to support subsequent procurement decisions. The final therapeutic positioning of the medicinal product will consider both the therapeutic effectiveness and the economic considerations and will be incorporated at this stage in the report. These final conclusions are expected to be followed by the regional health authorities and other decision makers at a healthcare level in the exercise of their competences.

Use of EUnetHTA reports

AEMPS are a new organisation in EUnetHTA and do not have experience of using EUnetHTA assessments, the broad remit and number of reports AEMPS complete means there will be overlap with the EUnetHTA assessment topics. The contents of EUnetHTA assessments overlap with the contents of an AEMPS assessment, and the two stage process whereby clinical effectiveness is completed first before economic assessment is similar to how EUnetHTA REA assessments are likely to be used in some countries. However, the process by which AEMPS produce their assessments (i.e. primarily using regulatory evidence and without MAH involvement in evidence submission) differs from that used by EUnetHTA and the process of assessment also starts earlier than EUnetHTA assessments would be available.

Case study 3: Collaborative HTA of non-pharmaceutical health technologies in Italy

Context:

In Italy, for medical devices there is a national database of medical devices in circulation in Italy, but currently there is no national-level decision making about pricing and reimbursement. Decisions about purchasing non-pharmaceutical health technologies are made either at a regional level or at a hospital level. The Ministry of Health commissions the Agenzia nazionale per i servizi sanitari regionali (Agenas) to carry out national level HTA² and horizon scanning³ in collaboration with regional HTA agencies, to provide evidence to support regional and local decision making

² <http://www.agenas.it/aree-tematiche/hta-health-technology-assessment/attivita-hta/report-hta>;

<http://www.agenas.it/aree-tematiche/hta-health-technology-assessment/attivita-hta/altri-documenti-hta>

³ <http://www.agenas.it/aree-tematiche/hta-health-technology-assessment/hs-horizon-scanning/report-hs>

about resource allocation. However, there is no formal process for taking HTA information in consideration during decision making processes.

There are 21 regions in Italy, some of these have HTA units within the regional health authority. In some regions there are also local HTA units based within hospitals and in Lombardy there is a network of hospitals producing HTA that is coordinated at a regional level. Some regions maintain their own formularies and lists of available products which are applied across the region, while in other regions the decision making is at a local level. The extent to which HTA informs decision making varies between regions and hospitals. A recent survey carried on by Agenas on HTA in the regions shows that only in one of them are the results of regional HTA formally binding for decision making⁴. The Italian Network for HTA (RIHTA) was established in 2009, this manages assessment activities, supports capacity building and expertise and facilitates information exchange between regions. In January 2017 the National Center for Health Technology Assessment in Italy was established in the context of Istituto Superiore di Sanità. The mission of the Centre is to improve quality, standards and value for money and to integrate HTA principles and methodologies into practice for planning public health services at all levels.

Agenzia sanitaria e sociale regionale - regione Emilia-Romagna (ASSR RER)

ASSR RER is the HTA agency of the Emilia Romagna region. It provides an HTA function for hospitals within 14 health trusts across the region. In the Emilia Romagna region each health trust maintains its own list of medical devices that can be used. To include a new medical device on the list a request is sent to a local decision making committee (Commissione Aziendale Dispositivi Medici, CADM). There is also a regional decision making committee (Commissione Regionale Dispositivi Medici CRDM), but their advice is not binding on the local health trusts. Both committees are among a range of stakeholders who can request HTA from ASSR RER. The intention to purchase high cost technologies must be notified by the local health trust to a regional group (Gruppo Regionale Tecnologie Biomediche, GRTB). GRTB is another stakeholder who may request HTA from ASSR RER.

ASSR RER produces HTA to support decisions about medical devices and high cost technologies. The guidance it produces informs acquisition and use rather than pricing and reimbursement. Regional legislation is in place that advises that an assessment has to be carried out on certain products before they are entered on lists allowing their use. However, it is not mandatory to follow the advice. Non-pharmaceutical medical technologies may be assessed when the technology is very expensive, controversial, likely to be disruptive and where there is a risk of there being variation in practice if an assessment is not carried out. ASSR RER produces approximately 3 HTAs per year⁵.

⁴ Publication ongoing

⁵ http://assr.regione.emilia-romagna.it/it/servizi/Indice_A...Z/H/hta/pubblicazioni-hta

ASSR RER work in a relatively reactive manner receiving topics as they are submitted rather than producing an annual work plan. Topics for assessment can come from the health trusts in the region, clinicians, local and regional policy bodies, and from industry. People submitted assessment requests must also complete an outline proposal. The HTA Unit supports them to do this. The proposal reflects the scope for the possible assessment and is sent to the decision maker who then decides on the most appropriate way forward from one of 3 options (1) stop the assessment, (2) carry out a full or multi technology assessment and (3) carry out primary evidence generation.

ASSR RER carries out its own assessments. Initially it identifies whether the assessment is being undertaken elsewhere. If it isn't being carried out or the assessment is not sufficiently overlapping, then an assessment is initiated. Medical devices are normally assessed as a short report⁶, these are approximately 10-20 pages long and focus on the health problem and current use of technology, description and technical characteristics of technology, clinical effectiveness and safety, but also include information about economic (costs and budget impact), organisational, legal and ethical issues. High cost technologies are subject to a complete HTA using the EUnetHTA CORE model and guidelines and are subject to external peer-review before publication.

Universita' Cattolica Del Sacro Cuore (UCSC - Gemelli)

The HTA Unit in the Agostino Gemelli University teaching hospital is part of the Universita' Cattolica Del Sacro Cuore. It has been involved in the production of HTA since 2001. It produces HTA for medicinal products and other medical technologies (medical devices, medical equipment and diagnostic tests) to inform decisions about procurement, budgeting, pricing (where possible) and use of medical technologies in clinical practice within the specific context of the University Hospital. As part of the process of budgeting, it works with clinicians not only to support introduction of new technologies but also to identify areas for disinvestment to ensure that additional costs are managed. The HTA unit carries out approximately 50 assessments of medical devices and 30 assessments of pharmaceuticals each year.

The work of the HTA Unit strongly relates to budget allocation and so there is advance planning of assessments so that the HTA produced can be used to support investment and rationalisation of spending and disinvestment. Proposals for new technologies to be introduced are formally submitted to the HTA Unit by doctors within the hospital. Possible topics for disinvestment are identified by a working group who periodically reviews the hospital formulary and medical devices list.

When carrying out an assessment UCSC look for existing assessments before they carry out their own assessment. To guide this process they use the AdHopHTA

⁶ <http://assr.regione.emilia-romagna.it/it/servizi/pubblicazioni/short-report>

checklist⁷. For pharmaceuticals, they are mostly able to use and adapt existing assessments, but for other medical technologies they more often have to develop their own assessment. The HTA that they produce can include information for all the domains of HTA, but only includes ethical, legal, and social information if needed. Economic information includes cost and budget impact. The reports include a recommendation about whether the technology should be introduced and if it is recommended if restrictions or conditions should be applied. The reports produced by the HTA unit inform a decision maker which is a committee within the University Hospital, reports are disseminated internally.

Agenzia Nazionale per i Servizi Sanitari Regionali (Agenas)

Agenas is a national HTA organisation established in 2007. Agenas is responsible for supporting the regions to promote, plan, evaluate and manage the introduction of new technologies using HTA and disseminating to the regions the results of studies and HTA made nationally. Agenas coordinates the RIHTA network (see below).

Agenas produces HTA that informs the appropriate use of medical devices and procedures. The Ministry of Health commissions the Agenas to carry out national level HTA assessments⁸ and horizon scanning reports⁹. The assessments provide evidence to support regional and local decision making about resource allocation. Five to six topics are assessed as HTAs each year and 3 horizon scanning reports are produced each year. Agenas also produce systematic reviews.

Some of the HTA is completed by Agenas acting on their own, but the majority of the HTA is carried out collaboratively with regional agencies as part of the RIHTA network (see process for HTA described below).

La Rete Italiana di HTA (RIHTA)

Since 2010 there has been a voluntary HTA network in Italy 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. Regions take part in the network in different ways depending on their capacity.

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

⁷ <http://www.adhophta.eu/>

⁸ <http://www.agenas.it/aree-tematiche/hta-health-technology-assessment/attivita-hta/report-hta>;

<http://www.agenas.it/aree-tematiche/hta-health-technology-assessment/attivita-hta/altri-documenti-hta>

⁹ <http://www.agenas.it/aree-tematiche/hta-health-technology-assessment/hs-horizon-scanning/report-hs>

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 supporting development of 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 manual¹⁰ 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.

The 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 are subject to public consultation before being finalised and are published on the Ministry of Health and Agenas websites. The advice in them is not mandatory.

To support data exchange between regions, the EUnetHTA POP database is used to record ongoing projects within regions. For some hospital-based organisations there can be issues of confidentiality that affect their ability to share documents.

Developments in the procedures for the assessment of non-pharmaceutical health technologies

Since the creation of the HTA Network and the establishment of the EU directive on cross boarder healthcare, Italy have been developing a mechanism to support further cooperation in HTA between the national, regional and local agencies. They are looking to build on the positive experiences of the voluntary network to further develop synergies in HTA and bring together capacity across agencies.

A law has now (2015-2016) been established that supports cooperation in HTA. This includes mention of the use of EUnetHTA tools and products.

The law establishes a national steering Committee “Cabina di Regia” that includes representation from the MoH, AIFA, Agenas and 4 regional representatives. The regional representatives are chosen by the regional assembly as being able to represent the interests of the regions. The Committee is tasked to define priorities for assessment in line with European guidelines (for example EUnetHTA guidelines), promote and coordinate the activities of assessment, validate the methodology for assessment, manage publication, dissemination and evaluation of the assessments,

¹⁰ http://www.agenas.it/images/agenas/hta/Manuale_procedure_HTA.pdf

promote their use by the regions and health agencies so as to inform decisions on the adoption and introduction of medical devices and the disinvestment.

Proposals for topics received by the Ministry of Health will be assessed by the Steering Committee. Topics that are prioritised will be those that meet the prioritisation criteria and which come from groups of regions or the national committee for healthcare. Prioritisation criteria include the potential impact on the healthcare pathway, any ethical and social implications (particularly in regard to quality of life and sustainability of care), potential organisational impact, potential economic or financial impact, technical relevance of the technology in the healthcare pathway, uncertainty in effectiveness and epidemiological significance.

The selected topics will then be allocated to regional agencies or other public or private units. Assessments will be completed collaboratively and the network will have a common approach and share methods and objectives. The reports will be appraised by the Steering Committee and will produce recommendations that will be mandatory for the system. There will be input into the assessment from all regions (e.g. through consultation) but the decision will be taken by consensus at the Steering Committee. The recommendations from the reports will feed into the central procurement Committee and the Commissione Nazionale LEA (the Committee for healthcare) to support definition of the minimum basket of health care.

Annual activity on health expenditure will be monitored with regions providing information about expenditure and consumption so that the implementation of the recommendations in the reports can be monitored.

A strategic paper has now been released by the Steering Committee in order to be adopted by the national government and Regions in accordance with a formal Agreement. The next step will be to define the initial reports, these reports will act to pilot the process. Following the pilot an annual work plan will be developed which will include both assessments and also training, capacity and methodological requirements. According to this paper Agenas will coordinate the assessment production for the national HTA program on medical devices.

Case Study 4: Use of EUnetHTA assessments at the agency for Quality and Accreditation in Health Care and Social Welfare (AAZ), Croatia

Context

The Agency for Quality and Accreditation in Health Care and Social Welfare (AAZ)¹¹ has 3 strands of work: quality, accreditation and health technology assessment (HTA) at national level. The HTA department produces HTA on the whole range of health technologies from different life cycles, as STA or MTA to support decision

¹¹ <http://aaz.hr/hr>

making following a request from the Croatian Health Insurance Fund (CHIF), The Ministry of Health or hospital managers.

The HTA department produces approximately 8 MTAs per year which can be pharmaceutical or non-pharmaceutical health technologies, including international EUnetHTA reports (as authors or co-authors). Approximately 65% of the reports are for non-pharmaceutical medical technologies, but almost all reports are in the form of MTAs so a large number of pharmaceutical products have also been assessed. Reports can include relative effectiveness assessment (REA) only or full comprehensive assessment (but without primary full economic analysis).

Decisions about the reimbursement of pharmaceutical and non-pharmaceutical medical technologies is carried out by CHIF. CHIF do not produce assessments, instead they appraise evidence that is provided by a company when the company submits for reimbursement. HTA in Croatia is not currently mandatory within decision-making process, therefore CHIF do not have to use HTA or request HTA from AAZ and CHIF will use AAZ in situations where they require further information to inform their decision. Examples where AAZ were asked to support the decision making include the new drugs for hepatitis C where multiple drugs came to market in quick succession and were associated with a high budget impact, long acting insulins and pharmaceuticals for lung cancer where again the introduction of the treatments was associated there was significant budget impact. The same was true for the Ministry of Health request for an assessment of Particle Beam Radiation Therapies for cancer.

Working Practices

AAZ does not select the topics that it assesses at the national level. Topic requests come from the Ministry of Health, CHIF or hospital managers. For pharmaceutical assessments AAZ must deliver their report 1 month after the request and this is defined in the ordinance on reimbursement on pharmaceuticals. For non-pharmaceutical health technologies, the timeframes for assessment are not defined by law and AAZ can negotiate the best timing for the report with the decision maker requesting the assessment. AAZ have created a topic proposal form¹² which agencies submitting requests may use to describe the topic and research question that they want AAZ to address in the HTA.

At the moment, stakeholders are not involved in the scoping process (that is deciding on the PICO to be addressed in the assessment), but recognising the importance of appropriate stakeholder involvement and EUnetHTA practice, this is planned to be introduced in the near future.

The reports produced by AAZ are approximately 70 pages long and include information about the condition, the technology, clinical evidence, cost and a

¹² <http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/podnosenje-zahtjeva>

summary of published cost effectiveness evidence. For non-pharmaceutical medical technologies relevant information about organisational, legal and ethical issues will also be added to the report. The type of information added is based on a shorter adapted version of the assessment elements in the EUnetHTA HTA Core Model. Cost-effectiveness evidence based on national primary analysis is not mandatory for decision making in Croatia but published cost effectiveness evidence is included in the reports to raise awareness of the value of health economic information and provide supportive information for decision making. Issues about transferring cost-effectiveness evidence from other jurisdictions is included in the report.

Where possible the assessment will make use of existing HTA assessment either created by EUnetHTA or another national agency. When AAZ is asked to complete an assessment, they will identify whether an assessment has already been completed. Where an assessment is identified that has a relevant scope this will form the basis of the AAZ assessment. AAZ will make the following adaptations to the assessment for use in the Croatian context:

- Update literature searches to identify and include any new clinical evidence and ongoing studies.
- Add epidemiological information such as patient numbers, morbidity and mortality in Croatia
- Add information about the technologies available in Croatia.
- Add information about costs of relevant technologies in Croatia.
- Add any additional information required such as a summary of cost effectiveness evidence and organisational or legal issues.

AAZ must translate any information taken from an existing report into Croatian because the language of assessment must legally be Croatian.

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.

Reports are published on the AAZ website¹³

Use of EUnetHTA assessments

AAZ have used EUnetHTA assessments in 2 ways:

- Summaries of evidence from EUnetHTA assessments, with the original reports in an appendix or with a link to the complete EUnetHTA assessment

¹³ <http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/baza>

- Use of relevant information from an assessment for use in a related assessment

For EUnetHTA assessments regardless of whether AAZ have been involved, AAZ prepares a summary and assessment elements B0001¹⁴ and A0020¹⁵ of the EUnetHTA assessment in Croatian that will be published on the AAZ website^{16,17} along 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 the additional information required for the Croatian decision making context 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.

AAZ were able to make use of information from a EUnetHTA assessment for use in a national assessment in a different area. AAZ were asked to do an assessment of Endovascular abdominal aortic aneurysm (AAA) repair, and were able to use the information about the Health problem and current use of technology (CUR domain of the HTA CORE model) from the EUnetHTA assessment of Abdominal Aorta Aneurysm Screening (AAA).

AAZ were able to use two EUnetHTA assessments (canagliflozin for the treatment of type II diabetes and ramucirumab in combination with paclitaxel as second-line treatment for adult patients with advanced gastric or gastro-oesophageal junction adenocarcinoma), for which the EUnetHTA assessment was available before company application for reimbursement at a national level. Both reports were used to demonstrate to the main decision-makers in Croatia (MoH and CHIF) the importance of HTA and the challenges that need to be overcome at a national level to introduce a sustainable and mandatory HTA process within reimbursement/investment or disinvestment decision processes.

Challenges and solutions

AAZ does not choose the topics that it assesses at national level and the decision makers do not have to ask AAZ for HTA, the use of HTA is not mandatory for decision making in Croatia. This means that there is no certainty that a topic AAZ will be asked to assess will be one that EUnetHTA also assesses. The lack of mandatory HTA 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 and for

¹⁴ What is this technology and the comparator(s)?

¹⁵ For which indications has the technology received marketing authorisation or CE marking?

¹⁶

http://www.aaz.hr/sites/default/files/HTA_Transkateterski_medicinski_proizvodi_za_lijecenje_odraslih_bolesnika_s_kronicnom_insuficijencijom_mitralne_valvule.pdf

¹⁷

http://www.aaz.hr/sites/default/files/HTA_Novi_oralni_lijekovi_za_lijecenje_bolesnika_s_hepatitisom_C_prijevod_HR.pdf

pharmaceuticals there is no ability to negotiate. These two factors mean that there are challenges when coordinating requests from national decision makers with EUnetHTA assessment topic selection 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 EUnetHTA is assessing and producing a translated summary of the of EUnetHTA assessments including additional information from assessment elements B0001 and A0020 (with links to or with original report in Appendix) so as to support awareness of the availability of the HTA. However, the lack of mandatory HTA in Croatia is the key barrier preventing the immediate use of EUnetHTA assessments in the Croatian national setting. In JA3 AAZ were requested to carry out an assessment of antibacterial sutures, because this was a non-pharmaceutical product they were able to negotiate the timeframes for the assessments and carry this out as a collaborative assessment. This means that the EUnetHTA assessment will be able to be adapted and used in Croatian decision-making.

Currently, HTA assessments must be written in Croatian. This means that EUnetHTA assessments will always require adaptation at least in terms of a summary in the Croatian language.

The legal framework for reimbursement specifies that companies must submit to CHIF and provide a submission of evidence that is then appraised. There is no ability for companies to request HTA from AAZ and for that to then be used by CHIF. This ability is envisaged for the new Ordinance on HTA which must be set out by the Croatian Minister of Health.

Drivers to support use of EUnetHTA products

AAZ have a methods guide¹⁸ that includes use of EUnetHTA assessments and use of other national assessments as a basis for carrying out their HTA. In addition identifying and using existing HTA reports is built into their procedures and ways of working. This means that if a EUnetHTA assessment is available then AAZ are able to make use of it. With increasing numbers of EUnetHTA assessments there should be more overlap with national priorities and AAZ will be able to use more of them in national adaptations of assessments for Croatian decision making.

Timing of assessment is rarely a barrier for national implementation in Croatia because pharmaceutical request for reimbursement is often delayed after launch. This means that when AAZ is asked to produce an assessment on a pharmaceutical, if there isn't a EUnetHTA assessment there is usually already a national assessment from a different HTA agency (e.g. NICE (with detailed evidence review group reports), HTA by CADTH, KCE, LBI...) that can be adapted.

¹⁸ http://aaz.hr/sites/default/files/hrvatske_smjernice_za_procjenu_zdravstvenih_tehnologija.pdf

Case study 5: Collaborative assessments between Rijksinstituut Voor Ziekte- en Invaliditeitsverzekering (RIZIV), Belgium and Zorginstituut Nederland (ZIN), the Netherlands

Context:

Rijksinstituut Voor Ziekte- en Invaliditeitsverzekering (RIZIV)

Rijksinstituut Voor Ziekte- en Invaliditeitsverzekering / Institut National d'Assurance Maladie Invalidite (RIZIV-INAMI) is the Belgian Healthcare Insurance agency¹⁹. It produces health technology assessments used to inform decisions about the reimbursement status of pharmaceutical and non-pharmaceutical medical technologies (including medical devices and also any other technologies that may be procured from a hospital or public pharmacy) in Belgium.

The role of RIZIV-INAMI is to coordinate and support (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 organisations²⁰. For pharmaceutical technologies, the decision maker who receives the advice from the Commission is the Minister of Social Affairs.

In Belgium the reimbursement process is initiated with a company submission. For new products and products with a claim of added value the submission can occur once a product receives CHMP positive opinion. Following submission RIZIV-INAMI staff prepare an assessment using evidence from the application and other sources. The assessment forms that basis of a proposal for reimbursement that is developed by the Commission for the Reimbursement of Medicines. For new products where there is a claim for added value the draft assessment will be sent to an external expert (for a procedure like peer review) as well as going to the Commission. The Ministerial decision is based on 5 criteria: added therapeutic value, price, budget impact, medical and social needs (place in the treatment pathway) and cost effectiveness, therefore assessments include clinical effectiveness and economic information. Cost effectiveness is carried out using the price proposed by the company and used when there is a claim of added therapeutic value. In the future new indications will also be subject to cost effectiveness analysis. The same member of RIZIV-INAMI staff will carry out all sections of the assessment.

HTA and pricing procedures occur in parallel. The procedure is tied to the 180 days in the Transparency Directive. RIZIV have 90 days to produce a final assessment

¹⁹ <http://www.inami.fgov.be/fr/Pages/default.aspx>

²⁰ Voting members; insurers, representatives of physician associations / pharmacist associations, academics / universities; Non-voting members; Ministry representatives, industry organisations, RIZIV representative

report, but before this provide a draft report to the company for their response. Therefore a draft report has to be prepared within 60 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 (taking into account additional advice from the administration of Finance and the Minister responsible for the Budget).

Zorginstituut Nederland (ZIN)

Zorginstituut Nederland (ZIN) is the National Healthcare Institute of the Netherlands²¹. ZIN has a number of tasks associated with healthcare of which HTA is one, and quality of healthcare another. In the Netherlands there is a law that indicates that to be reimbursed a technology must be of comparable effectiveness or greater effectiveness than the existing treatment. ZIN produces health technology assessments to inform decisions about the reimbursement status of pharmaceutical and non-pharmaceutical medical technologies (medical devices or non-hospital/outpatient interventions). The largest number of assessments produced by ZIN are for non-hospital pharmaceutical technologies. ZIN does not have to carry out assessments of all pharmaceutical technologies (e.g. not all drugs used in hospital) and will not assess generics.

For outpatient pharmaceuticals the company applies for reimbursement, for inpatient pharmaceuticals ZIN selects technologies for assessment and plans activity. For non-pharmaceutical health technologies requests for assessment can be received from a range of stakeholders²². The pharmaceutical assessment procedure usually starts after the marketing authorisation. Once the company submission is received ZIN prepares an assessment using evidence from the application and other sources to assess the technology. ZIN have 70 days (outpatient drugs) to prepare advice for the Ministry. The Ministry then has 20 days to make a final decision. The 70 days represents approximately 1 month to write a draft report that is then scheduled into a monthly Committee meeting for discussion before being amended. The assessment will then go through a stakeholder review before being reviewed again by the Scientific Committee. The management board of ZIN then issues advice to the Ministry of Health about the use of a technology and whether price negotiations should take place. ZIN does not take part in price negotiations, these are taken forward by the Ministry of Health. For some technologies, after the technical advice, the technology will go to a societal appraisal Committee where a societal perspective on the technology will be obtained (based on the data in the technical reports). In these situations their advice will also go to the management board at ZIN to develop the final advice to the Ministry of Health.

Assessments by ZIN include cost effectiveness analysis for pharmaceuticals where there is a claim for added value and the annual budget impact is predicted to be

²¹ <https://www.zorginstituutnederland.nl/>

²² However, ZIN is not obliged to comply unless the request comes from the health ministry.

higher than 2.5 million euros. The assessment will be completed at the same time as the REA but by different people. The assessment reports by ZIN include 3 parts: therapeutic assessment, cost effectiveness assessment and budget impact assessment. They will be reviewed by the Committee at the same time. Cost effectiveness is assessed with the official price given and part of the assessment will be whether it is cost effective and if price negotiations should take place. The reimbursement procedure is tied to the 180 days in the Transparency Directive.

The BENELUXA collaboration

Initially, a collaboration initiative has been developed by the Netherlands, Belgium and Luxembourg. Recently Austria has joined the initiative, which has been called the BENELUXA initiative.

There are 4 strands to the collaboration:

- Information sharing
- Horizon scanning
- HTA assessment
- Pricing and reimbursement, including joint negotiations

Agencies can make a choice as to which of these areas of collaboration they want to take part in. So far 1 collaborative pricing and reimbursement procedure (including assessment and preparations for joint negotiations) has been completed and another is ongoing (between Belgium and the Netherlands). Some more are being prepared. These collaborative projects are for pharmaceuticals.

The collaboration is carried out in the context of Belgium and the Netherlands having past and on-going experience of using each other's work in their assessments that means their Committees have a familiarity with the reports produced by the other agency. The collaborative approach works alongside and does not replace national processes or national legislation. Instead the agencies have found a middle ground where both can work collaboratively as part of a single procedure that then flows back to the national processes for reimbursement and pricing negotiations.

Working Practices

Coordination

The collaborative procedure requires not only existing scientific competencies but also the workforce needs to be expanded to include specialists for the coordination of timelines between the two agencies. This means that is necessary to plan in advance and to include project managers in the process to ensure that each stage of the assessment process is clearly defined with explicit due dates and the responsible

person identified. Each agency needs to know when they can expect what kind of document from who they will receive it and by when they must respond.

Topic selection

The collaboration is voluntary also for companies. When a company chooses to initiate a collaborative process, they submit simultaneously to both national processes separately in each country. A company is able to submit identical documents. For health economic assessment, the company has to provide a model relevant to both healthcare contexts. In the experience so far the company submitted a base model for the Netherlands and adapted it for use in Belgium.

Allocation of work

For the assessments completed so far RIZIV have led on the therapeutic assessment and ZIN the pharmaco-economic assessment and budget-impact, ZIN assess the appropriateness of the model for both healthcare contexts. This allocation of work arises because RIZIV do not consider cost-effectiveness in the same level of detail as ZIN and do not have dedicated pharmaco-economic assessors. Staff communicate with each other when writing the report to discuss what was being written.

For the assessments completed, companies are told which agency is doing which part of the assessment and if there are questions about pharmaco-therapeutic issues to go to RIZIV and if there are questions about pharmaco-economic issues to go to ZIN.

Production of Assessments

Before the assessment formally starts, the agencies hold a pre-submission meeting with the company to discuss the draft submission and whether the content is appropriate for the two countries or if further information needs to be added. In their national processes this stage is optional for ZIN but is mandatory for the joint process. For RIZIV in their national processes there is the possibility of a pre-submission meeting but this isn't normally based on a submission but rather on what company wants to discuss or their questions on what to include in the submission.

The completed joint report goes to their respective national Committees for review and adoption. For Belgium after the report is adopted it is sent to the company for a response and when the response is received teams from both the Netherlands and Belgium work on the amending the report, the amended report will then go back into the national procedures. In accordance with the Belgian process where for products with added value the report goes out to external review, RIZIV can ask ZIN to review the report, therefore once a report has been seen by the two national committees, ZIN sends it out to their stakeholder groups (industry, patients, scientific societies and insurers) thereby following their national procedures for stakeholder involvement.

The reports are written in the national templates of the agency completing that section of the report e.g. in the collaborative assessments so far Belgium receive a health economic assessment in the Dutch report structure and the Netherlands receive a medical-therapeutic assessment in the Belgian report structure. For cost-effectiveness although the Dutch template was used by ZIN, the report and narrative highlight where there are differences for the Netherlands and for Belgium so that sometimes there are separate sections for each country where information differs.

Advice

The joint report will include a conclusion that aims to reflect a shared conclusion. However, it is recognised that the assessment and/or appraisal frameworks for providing the advice differ between the agencies so could deviate. Experience so far has shown no real differences in agreement on added value.

Challenges

The joint procedure fits into the national procedures which in turn fit into the timelines required by the Transparency Directive. The differences in timings and roles between the two agencies, and the stringent timelines imposed by the Transparency Directive means there is little flexibility in the timings for each stage of assessment production. The timings for the joint assessment must be defined in advance and strictly adhered to so the joint assessment does not delay the national procedures. The following steps seek to minimise issues arising from the lack of flexibility in timings:

- early discussions with companies before they submit so they can minimise the risk of the information not being appropriate or sufficient.
- these assessment are given priority
- greater overall coordination of the joint process than the national processes 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 process has to occur so that the joint 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

For the joint process 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 joint procedure can take place. Collaborative working and information sharing outside of the joint process is more challenging because if a company submits at different times across countries then the procedures may not be synchronised and windows of HTA activity are less likely to overlap meaning that joint work may not be possible.

The Belgian procedure legally requires that assessments are written in a Belgian national language (French, Dutch, and German), therefore, until now, joint assessments with ZIN are produced in Dutch. Companies submitting for the joint procedure 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). In the long term it is hoped that it will be possible to move to producing reports in English, so that there is also transferability to more 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.

The collaborative procedure is voluntary so companies cannot be compelled to go through a joint procedure. The voluntary nature of the process can be a challenge in that companies may decide that they do not wish to go through the joint process. At the moment it is not possible to compel companies to go through a joint procedure. There needs to be time to demonstrate that the collaborative approach works.

Because the joint process fits in with national processes a therapeutic report written by RIZIV will be sent by ZIN to their stakeholder groups as part of their national review procedure. Companies can be nervous about this stage of the procedure as the report is still confidential, but it is going to a larger audience than in a national procedure with a potentially larger risk that information could be leaked. The use of the national report structures also means that stakeholder groups in the Netherlands will know if a collaborative assessment is being carried out because they will see the Belgian report structure. This hasn't resulted in significant issues, but has to be taken into account by companies when they choose the joint process.

When working as part of a national process, staff preparing assessments have a body of shared experiences developed from working with each other and their national Committee. Staff can be used to particular ways of working and writing reports. When taking part in a joint procedure these ways of working may no longer stand and can be questioned. The rationale for taking a particular position or making a particular conclusion must be more explicit and precise, so that the report writers are able to respond if question about how a statement was formulated. This process takes additional resources at the moment, but in long term this process will improve the clarity of the assessments (and therefore the transparency in the decision making process) produced will win time and efforts.

Case Study 6: Involvement of Hauptverband der Österreichischen Sozialversicherungsträger (HVB), Austria in the BENELUXA collaboration

Context

Hauptverband der Österreichischen Sozialversicherungsträger (HVB)²³ has legal responsibility for the management of the Austrian social security system. As part of this responsibility it produces health technology assessments that are used to inform its decisions about the inclusion of health technologies on a list of treatments available for reimbursement in Austria^{24,25}. The focus of HVB work is outpatient pharmaceuticals, some assessment activity also takes place for non-pharmaceutical outpatient interventions, but this is carried out less routinely. In general all pharmaceuticals products will be assessed for inclusion on the list; HVB produces over 300 assessments of pharmaceuticals per year that include clinical effectiveness information and economic information. Of these there will be 50-150 assessments of a new substance.

Working Practices- Pharmaceuticals

Companies initiate the assessment process by applying for reimbursement following receipt of marketing authorisation. The application is made directly to HVB. Once the application is received HVB staff prepare an assessment. The assessment is an independent evaluation of the technology based on the company evidence. As part of this HVB check the evidence provided by the company using other sources of evidence to identify if there is missing evidence from the company submission. HVB do not carry out their own systematic research as part of this process.

The evaluation completed by HVB has 3 components. The first is a pharmacological evaluation that includes the degree of innovation on a scale of 1-8 and identifies the appropriate comparators, the second is a medical therapeutic evaluation that identifies the added therapeutic benefit compared to the identified comparators. This is presented on a scale of 1-6. The third component is an economic evaluation that includes a calculation of the target price which is determined by the classification of added therapeutic value and prices of other available alternative treatments. The economic evaluation is performed after the medical therapeutic evaluation, but because of the constraints of the timelines both evaluations can go on in parallel.

As part of the assessment HVB identifies issues that affect inclusion on the list, the company then has the opportunity to respond to the issues and clarify uncertainties. This process can result in a modified application. The evaluation also includes

²³ <http://www.hauptverband.at/portal27/hvbportal/content?contentid=10007.693656&viewmode=content>

²⁴ treatments not on the list may still be reimbursed but this will only be in specialised conditions on an individual case basis

²⁵ <http://www.hauptverband.at/portal27/hvbportal/content?contentid=10007.693707&viewmode=content&portal:componentId=gtnf9b47759-1774-4391-bf98-34bdf6b3aff9>

proposed conditions for reimbursement e.g. if the drug will be made available only for a subgroup, who should be the prescriber and conditions for prescription. The (modified) application is then presented to an independent drug review board (that includes representatives from organisations such as the chamber of commerce, chamber of labour, chief medical officer, Austrian physician association, Austrian pharmacists association and social insurance system) who make a recommendation about whether the drug is included on the list of available treatments with the conditions offered by the company. HVB then make a decision based on the recommendation of the board which is then implemented by HVB.

Use of EUnetHTA assessments

Of the pharmaceutical assessments completed by EUnetHTA, there has been only limited overlap in the topics that have also been assessed by HVB. For example a number of the EUnetHTA assessments have been of hospital products which are not assessed by HVB. Canagliflozin for the treatment of type II diabetes was assessed as part of the HVB work programme and the scope of the EUnetHTA assessment overlapped with the HVB scope of assessment, but the EUnetHTA assessment was published too late for HVB to use it in their assessment procedures.

Involvement in BENELUXA collaboration

There are 3 areas of interest for HVB in the BENELUXA collaboration:

- Exchange of information
- HTA, Assessment analysis
- Price negotiations

The fourth strand of the BENELUXA collaboration focussing on horizon scanning is of less relevance to HVB, but a different Austrian organisation (LBI) is involved.

Currently, HVB acts as an observer in some aspects of the BENELUXA collaboration in order to get a better understanding of the different procedures and ultimately to align the processes so as to support collaborative working.

Challenges and solutions

The key challenges in taking part in collaborative assessment work are:

- Language
- Timelines
- Confidentiality status

For HVB these challenges all have a legal basis.

Language

HVB are bound by law to produce assessments in German and for companies to submit in German²⁶. In addition procedural documents emphasise that communication between negotiating parties shall be in German. Practically, if HVB is taken to court the documents supporting the assessment must be available and these must be in German, but can refer to literature in English. The BENELUXA collaboration currently undertakes assessment activity in Dutch because the Belgian agency requires assessments and submissions in one of the Belgian national languages and Belgium and the Netherlands have Dutch as a common language. It may also be possible to work in English but then assessments have to be translated to German and within the timelines (see section below) available for HVB to carry out an assessment there would be significant pressure to achieve this. It may also be possible to use parts of the assessment in English if these are referenced to or cited as an expert statement.

Timelines

The work of HVB like that of the other BENELUXA organisations is bound by the Transparency Directive. In Austria, to make a decision within 6 months (180 days), the decision of the independent review board must be given by month 5 which means that a first draft assessment should be completed by the end of month 2. Even though the assessment may still be subject to some further modifications following interactions with the company it needs to be mainly complete by the end of month 2. These timelines to produce a complete assessment are shorter than those of the other BENELUXA countries. Both RIZIV and ZIN produce a draft assessment in 60 and 70 days respectively, but then have national committee procedures and consultation processes before preparing the final assessment. The timing of the procedures for the assessment to go through before the decision is reached means that there is little flexibility to change the timing of the assessment phase meaning that collaborative work has to be planned very carefully in advance by participating countries.

Confidentiality status

In Austria documents relating to the reimbursement and pricing process are confidential. To take part in collaborative working, there would need to be agreement with the company involved that information can be shared with the other relevant organisations and groups involved in the collaboration e.g. for the BENELUXA collaboration this would mean the other BENELUXA HTA agencies, 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

²⁶ Article 8 of the Federal Constitutional Law states that German is the official language of the Republic without prejudice to the rights provided by federal law for linguistic minorities. German is the language for all governmental or public affairs.

who formulate the reimbursement proposal). For aspects such as price negotiations, this may be a particular challenge as information is sensitive.

Case study 7: Use of EUnetHTA assessments at the National Institute of Pharmacy and Nutrition (NIPN), Hungary

Context

The HTA Department in the National Institute of Pharmacy and Nutrition (NIPN)²⁷ produces reports that are used by the National Health Insurance Fund (NHIF) and Ministry of Human Capacities to make decisions about national reimbursement and pricing of pharmaceuticals and other health technologies.

The HTA Department produces approximately 200 outputs per year including 90-100 pharmaceutical reports, 90-100 reports about medical aids used by patients (for example hearing aids) and 4-5 healthcare technology reports about medical devices used by physicians in hospitals (for example medical devices associated with surgical procedures and diagnostic assessments). For all types of products companies submit for reimbursement to the NHIF who then send the company's submission of evidence to NIPN who reviews the submission. The pharmaceutical and healthcare technology reports produced by NIPN include a review of the company's submitted evidence of clinical effectiveness, cost effectiveness and budget impact, the reports for medical aids include a clinical overview and budget impact but not cost effectiveness (just comparing the prices and attributes of the devices).

Working Practices

All topics for assessment come to NIPN through NHIF. NHIF obtains the topics from companies submitting an application and submission of evidence for reimbursement. NHIF forwards submissions to NIPN within approximately 2 days of receipt of the application from the company. 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.

Following receipt NIPN reviews the evidence submission from the company and then provides a report to NHIF. 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. The review completed by NIPN is approximately 40-80 pages long (45% medical – 45% economic - 10% other). To meet the needs of the decision makers, NIPN also provide a short summary of the main points of the report and the conclusions of reports from other countries. In their review NIPN will check the appropriateness and robustness of the company's submission including checking the appropriateness of the proposed place in therapy, appropriateness of the included clinical evidence and a critical evaluation of the health economic evaluation (not for medical aids) and budget impact. The consistency of the clinical data with the cost

²⁷ https://www.ogyei.gov.hu/health_technology_assessment/

effectiveness modelling will also be checked. Currently companies do not have to provide the economic model at the time of submission and NIPN ask NHIF to request the model from the company. Later on in 2017, NIPN will start to receive the economic model as part of the submission at the start of the assessment phase. The review completed by NIPN focuses both on clinical and economic aspects (there are some important uncertainties - e.g. final price of a technology).

The nature of the assessment procedure means that the work of NIPN is single technology assessment. However, they are currently carrying out work on a multiple technology assessment.

The reports for medical devices contain a recommendation on the reimbursement of the technology (yes/no/under restrictions). From Q3 2017, the reports for pharmaceuticals will also contain a recommendation. The recommendation is made by NIPN with the involvement of the different departments across the organisation including regulatory and pharmacovigilance colleagues. These reports are then sent back to NHIF who formulate an initial decision. 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 are allowed from submission to initial decision by NHIF and then a subsequent 90 days allowed from initial decision to final decision. The timeframes for assessment and decision making are defined by the transparency directive.

Use of EUnetHTA assessments

In their national procedures NIPN used the EUnetHTA reports for canagliflozin for the treatment of type 2 diabetes mellitus and ramucirumab in combination with paclitaxel as second-line treatment for adult patients with advanced gastric or gastro-oesophageal junction adenocarcinoma to support their national assessments.

For the other EUnetHTA assessments, it was not possible to use the EUnetHTA assessment because it was too late (in the case of the pharmaceutical assessments of sorafenib and hepatitis C) or the company did not request reimbursement from NHIF (in the case of all non-pharmaceutical assessments and also pharmaceutical assessments of vorapaxar and zostavax).

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 of the company submission (e.g. in the case of canagliflozin NIPN's assessment questioned the non-inferiority of the product based also on the joint assessment) 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.

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. Over time with the production of more EUnetHTA assessments that have a consistent scope with the NIPN national assessment, having a EUnetHTA assessment may make the NIPN review process easier.

Challenges and solutions

An issue for NIPN is timing of the availability of the EUnetHTA assessment. Submissions from NHIF can be received shortly after marketing authorisation and are quickly passed to NIPN for their review. NIPN then have a very short period of time in which to complete the review and this time period cannot be negotiated. For pharmaceuticals the EUnetHTA procedure where a final assessment is available 1 month after marketing authorisation is received would be timely for NIPN.

For non-pharmaceutical reports the amount of time NIPN have for their review is shorter than for pharmaceuticals and there is no predictability as to when a company may submit for reimbursement. Therefore although NIPN complete a large number of medical device reports, coordinating the use of EUnetHTA outputs with national assessment activities is challenging. This is because they do not know in advance if a topic is to be assessed and then once a topic is sent to NIPN a report is required in 15 days (medical aids) and 30 days (healthcare technologies). For example they are reviewers for the ongoing EUnetHTA assessment of non-invasive prenatal testing, but they were asked to provide a national report last year, for other non-pharmaceutical EUnetHTA assessments no national report was requested.

The remit of NIPN is to critically review company submissions and EUnetHTA assessments are used to support the NIPN review procedure. For NIPN to get most use out of a EUnetHTA assessment the following features would be supportive:

- General consistency between the national submission and EUnetHTA assessment in terms of the question addressed and evidence included
- The comparators need to include those relevant in Hungary
- The outcomes need to be presented in the EUnetHTA assessment in a way which supports their use as inputs in the economic evaluation, so that these could be used for sensitivity analyses if relevant
- Full consideration of possible patient subgroups (those that are particularly relevant from a Hungarian perspective include ones that may be used to limit budget impact where a treatment is cost effective but the budget impact is high, or groups for whom a treatment is particularly cost effective)

For non-pharmaceutical health technologies the topics that NIPN are asked to assess are not predictable. Healthcare technologies can be any non-pharmaceutical technology used by a physician in a hospital where a company has chosen to submit for reimbursement to the general NHIF reimbursement fund. Examples of completed topics include non-invasive prenatal screening and INR technologies used for anti-coagulation monitoring. However, companies can also submit these topics to the NHIF hospital fund in which case NIPN will not review the submission. The lack of predictability combined with short timelines for completing their review – limits the ability to make use of EUnetHTA assessments and to support EUnetHTA topic selection procedures. However, in general, topics for EUnetHTA assessments that would be valued from a Hungarian perspective are:

- High cost
- High uncertainty
- Limited evidence base

Drivers to support use of EUnetHTA products

Although NIPN do not know in advance which topics they will be asked to assess, the number of assessments done each year means that there is likely to be significant overlap with the EUnetHTA assessments for pharmaceuticals. In addition, within the constraints of comparators changing NIPN would be able to comment on aspects of the PICO to maximise the likelihood of an assessment being relevant from a Hungarian perspective. For medical devices there are more difficulties in overlap because of the volume of non-pharmaceutical products that come to market and there can be more difficulties in defining the PICO, particularly the comparators and population. Doing this in advance of an assessment starting would generally be more challenging for NIPN than for pharmaceuticals.

NIPN have a remit to review company submissions which means they do not produce assessments that stand alone from the company submission. However, there are no restrictions on the evidence sources they can use in their review, so if a EUnetHTA assessment is available, NIPN can use it to support their review process and use the data from the EUnetHTA assessment in sensitivity analyses.

NIPN have recently updated their methods guide for pharmaceuticals (Professional healthcare guideline on the methodology of health technology assessment) and in doing this have referred to EUnetHTA guidelines and tools. A methods guide for medical device assessments will be completed in the future. The methods guide will be made available in Hungarian and English. The use of shared methods supports use of the data from EUnetHTA assessments in their reports.

Case Study 8: Use of EUnetHTA assessments by the Scottish Health Technologies Group, Scotland

Context

The Scottish Health Technologies Group (SHTG) is part of Healthcare Improvement Scotland (HIS). It produces mainly rapid reviews, which are used to develop national advice for Scotland about non-pharmaceutical health technologies. The advice developed by the SHTG Committee is non-mandatory but decision makers within Scotland (that is, health boards, government and national committees and individual clinicians) are required to consider the advice produced.

SHTG produce approximately 25 HTA related outputs per year including horizon scanning outputs, evidence notes²⁸, and innovative medical technology overviews²⁹. The majority of these outputs are evidence notes (rapid reviews). Both evidence notes and innovative medical technology overviews (IMTOs) include a summary of the clinical and cost effectiveness evidence. In addition, IMTOs include brief consideration of organisational and patient issues. Companies provide evidence for an IMTO but do not submit evidence for an evidence note. SHTG horizon scanning outputs are lists of English language HTA reports from other jurisdictions that include clinical and cost effectiveness evidence³⁰, they are used to stimulate decision makers to consider topics for referral and assessment in Scotland.

Working Practices

SHTG have an open topic referral process, whereby anybody can refer a topic for assessment. However, the majority of topics come from national or regional planning committees. Topics referred are assessed against criteria for appropriateness including the:

- likely national impact (either in terms of resources consumed or released),
- whether the topic is aligned with Scottish priorities,
- whether there is an answerable research question,
- whether there is evidence available that can answer the research question, and

²⁸ See

http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg/evidence_notes.aspx

²⁹ See

http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg/shtg_publications/imto.aspx

³⁰

http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg/hta_current_evidence.aspx

- whether the production of guidance at this time has an opportunity to make an impact on healthcare.

Topics that are assessed as meeting the criteria are worked up into a topic exploration which is an initial 1/2 page document that describes the topic, the possible research question and an initial indication of the quantity and quality of available evidence. This document is taken to an evidence review committee (ERC) meeting. At this meeting the person who referred the topic provides a brief presentation focusing on the PICO aspects, and SHTG presents their exploratory work. Public partners are present at this meeting. The meeting informs the decision to carry out further work on the topic.

Topics that are referred are subject to an initial scoping stage which clarifies the research question and whether the topic is suitable for an evidence note or other evidence review product. After this the specified work is completed by the research team and undergoes an internal quality assurance process. The ERC then prepare a draft advice statement based on the evidence product. Companies and other stakeholders including clinical experts, peer review the evidence product using a structured set of questions before it goes to the ERC for the formulation of draft advice. There is an internal quality assurance process before the SHTG evidence product is sent for peer review.

The scientific committee that finalises the advice based on the SHTG evidence product is comprised of 27 members including representatives of health boards and health professional groups within NHS Scotland; industry representatives; academic experts and public partners. Board representatives are nominated by the Chief Executive of the health boards. To support the process of developing advice statements from Evidence Notes, the SHTG members receive the evidence note, the peer review comments and the draft advice statement. Stakeholders have the right to challenge the advice produced by the SHTG, but to date this has not happened.

The process from topic referral to production of advice ideally takes approximately 6 months, and is dependent on availability of Committee slots, other topics being assessed and how quickly experts provide feedback and agreement on the research question. SHTG do not have formal timelines and targets for guidance production.

Use of EUnetHTA assessments

SHTG adapted 2 products from the EUnetHTA JA2 into SHTG evidence notes^{31, 32}. The two EUnetHTA assessments adapted were transcatheter implantable devices

³¹ http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg_-_evidence_notes/evidence_note_61.aspx

³² http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg_-_evidence_notes/evidence_note_58.aspx

for mitral valve repair in adults with chronic mitral valve regurgitation³³ and endovascular therapy using mechanical thrombectomy devices for acute ischaemic stroke³⁴.

As members of the EUnetHTA JA2 joint production work package SHTG received a list of possible topics that were being considered for an assessment by EUnetHTA. SHTG sought feedback from clinicians on the appropriateness of these topics.

When the final EUnetHTA assessment became available SHTG went through a process of adapting the EUnetHTA assessment and using it as the main source of evidence for a SHTG evidence note. The evidence note developed from the EUnetHTA assessment was able to fit into routine SHTG quality assurance procedures including consideration by the evidence review committee, internal review and peer review prior to being sent to the ERC for formulation of draft advice. The committee received the same documents that they would have received if SHTG had developed the evidence product without the EUnetHTA assessment. The evidence product looked like a standard SHTG evidence note but was clearly labelled as being adapted from the EUnetHTA assessment. The scientific committee also received peer review comments and the draft advice statement as they would in the standard process.

Adaptation process

The adaptation process included:

- Condensing the EUnetHTA assessment document
- Removing interventions that were not appropriate to the Scottish context
- Adding national context information
- Adding economic evidence
- Updating clinical searches

Condensing the EUnetHTA assessment document

The EUnetHTA assessments were approximately 100 pages long and included only relative effectiveness assessment. In contrast SHTG evidence notes are approximately 18 pages long and include both relative effectiveness assessment and cost effectiveness evidence. It was not considered feasible to give the Committee the whole EUnetHTA assessment, therefore SHTG went through a process of summarising the evidence so that it was in a format that could be given to the

³³ <http://www.eunethta.eu/outputs/5th-pilot-rapid-assessment-wp5-ja2-strand-b-transcatheter-implantable-devices-mitral-valve-r>

³⁴ <http://www.eunethta.eu/outputs/6th-pilot-rapid-assessment-wp5-ja2-strand-b-endovascular-therapy-using-mechanical-thrombecto>

Committee. Each component of the EUnetHTA report was considered relevant (with the exception in one assessment of two of the interventions (see issue below)), so the SHTG process condensed and summarised the whole EUnetHTA report, rather than removing some sections of the EUnetHTA report while leaving others. This process meant that the product viewed by the Committee looked the same as if it had been an evidence product prepared by SHTG.

Removing interventions that were not appropriate to the Scottish context

The EUnetHTA assessments were multiple technology assessments. Feedback from clinicians in Scotland suggested that two of the three health technologies included in the EUnetHTA assessment (mitral valve repair) were not sufficiently well developed for a SHTG evidence note to add value at the point that SHTG were completing their assessment. Therefore, SHTG removed from the assessment the interventions that were not relevant to the Scottish context.

Adding national context information

To formulate its advice the scientific committee require epidemiological information and background information on the Scottish clinical context. The information needed was not available in the EUnetHTA assessment and had to be added. This information included estimates of population size and clinical information about centres carrying out the procedure associated with the medical device.

Adding economic evidence

All SHTG evidence notes include a review of the cost effectiveness evidence. SHTG therefore had to develop searches to identify economic evidence and then perform a review of that evidence. The process of including economic evidence meant that searches for the economic evidence needed to be developed, and the literature reviewed. For one adaptation (mitral valve repair) the EUnetHTA assessment identified no comparative studies using 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 study one arm of which, given had been (correctly, given the EUnetHTA inclusion criteria) excluded from the EUnetHTA assessment. This meant that the excluded data had to be described 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. Where economic analyses are based on studies which are tangential to the main body of clinical evidence this will require an additional step of checking and ensuring transparency around any potential discrepancies.

Updating clinical searches

Because the research team had to run searches for the economic evidence, they also chose to update the clinical searches. Updating searches was not straightforward as the EUnetHTA searches had to be amended to reflect different

interfaces used for searching. For one HTA (thrombectomy) the SHTG adaptation of the EUnetHTA assessment took place a year after the original EUnetHTA searches were run and the SHTG searches identified 12 further systematic reviews. that. These reviews were mainly based on the same primary evidence as had been included in the EUnetHTA assessment, but in some cases included different sub group analyses or raised different issues. This issue highlights the speed at which evidence can accrue when a new technology becomes available and the dilemma for HTA agencies between providing up-to-date evidence summaries and an efficient use of resources.

Challenges and solutions to using EUnetHTA products

The absence of economic evidence in the EUnetHTA assessments led to the key concern about how easy it would be to go from the clinical evidence in the EUnetHTA assessment to the health economic evidence required in a SHTG evidence note and whether a review of economic evaluations would be sufficient or if on the basis of the EUnetHTA assessments they would be required to carry out de novo economic modelling which the agency has limited capacity to complete. For these adaptations this concern was unfounded. However, for one evidence note SHTG was required to add in a study arm to the clinical effectiveness section of the report, as the economic evidence that was available, was based upon this. It was also noted that the evidence for both assessments was relatively straightforward and consistent, and that in instances where the evidence was more variable adding the cost effectiveness evidence to the clinical effectiveness may be more challenging.

SHTG carried out further work to update the clinical searches, but in hindsight the additional information gained by updating the clinical searches was not considered to have added enough value to justify the resources used, and so would probably not be routinely carried out in the future.

It was not considered possible to use the EUnetHTA assessment without adaptation because of need to provide contextual and economic evidence to support the formulation of advice. Providing the whole EUnetHTA assessment and adding the other relevant sections was not considered possible because the EUnetHTA assessment document is much longer than the Committee is expected to use for advice formulation. SHTG decided it would not be possible to use the EUnetHTA executive summary instead of the evidence note, because a greater level of detail was required for the evidence note, and there was a need to add in epidemiological and economic information. Using their standard document format provided familiarity which the committee value. The EUnetHTA reports were noted to be similar in length from other HTA reports that SHTG are used to summarising.

Drivers to support use of EUnetHTA products

SHTG have flexibility in and responsibility for their topic selection process. This allowed them to take the lists of proposed topics received from EUnetHTA, to gather feedback and initiate the process of considering a topic for assessment.

SHTG identified no legal or procedural restrictions to using EUnetHTA assessments. Their legal framework is high level and not directive of the procedures they follow. Advice is not mandatory and not covered by a funding stream which can give SHTG more flexibility in their assessments, though there is a right to challenge advice.

SHTG have standard operating procedures for the completion of Evidence Notes, IMTOs and HTAs. These refer to the use of secondary sources of evidence and therefore the use of EUnetHTA assessments as a source of evidence is covered within existing standard operating procedures. The adaptation of the EUnetHTA assessment could follow the SHTG routine quality assurance processes which meant that any deviations from standard operating procedures and best practice would be flagged.

The use of EUnetHTA assessments instead of alternative sources does not constitute a large change to routine working practice. SHTG Evidence Notes use secondary sources like EUnetHTA assessments whenever possible in their work and do not request and use company submissions. Thus, there is familiarity with the working practices required to use a EUnetHTA assessment and adapt them.

For both the EUnetHTA assessments SHTG was a dedicated reviewer and therefore had had the chance to provide input into the EUnetHTA assessment. The agencies who were the lead authors of the evidence note were both experienced in HTA and known to SHTG, this supported fostering trust in the EUnetHTA assessments being adapted and more generally in using future EUnetHTA products. In addition, SHTG local clinical experts had been expert reviewers on the EUnetHTA work, so this gave a degree of assurance about the quality of the work and its relevance for Scotland.

Case study 9: The use of EUnetHTA assessments by the HTA unit of the Finnish Medicines Agency, Finland

Context

The HTA unit of the Finnish Medicines Agency³⁵ (FIMEA) produces mainly rapid reviews for single indications of new hospital medicines. These reports support decision making about use by hospitals. By special request (for example from the national pricing board) they may also carry out assessments of outpatient pharmaceuticals including single and multiple technology assessments. The reports produced by FIMEA include a conclusion on added value of the technology given the clinical effects observed and expected costs. These conclusions are non-mandatory. The HTA unit works separately from the regulatory department and the two units don't currently share information. Clinical experts used by the regulatory department can also be used by the HTA unit.

FIMEA produce approximately 10 reports per year³⁶. The reports include an assessment of clinical effectiveness and also costs and budget impact analysis. The reports are written in Finnish with a Swedish and English abstract³⁷, but language is not legally mandated. FIMEA completes the HTA themselves, but companies are asked to provide evidence. The evidence requested is mainly focussed on the clinical evidence e.g. completed and ongoing clinical trials, and subgroup analysis. In addition the company is asked for information about budget impact and any budget impact models available.

Working Practices

The responsibility of choosing topics for assessment rests with FIMEA. The topic selection process starts with the list of CHMP positive opinions. From this list inpatient medicines will be selected and new active substances and major variations to licensed indications prioritised. Hospital districts can be asked about topic prioritisation if needed. The assessment will usually start immediately after topic selection, but may be delayed if a company decide not to launch immediately after marketing authorisation is granted, but in Finland this rarely happens (average time between marketing authorisation and launch for a hospital medicine is approximately 60 days).

The assessment is completed by FIMEA normally starting soon after the time of CHMP opinion and with the aim to produce a draft report within 2 months e.g. at the time of marketing authorisation. Internal or external clinical experts will be involved in developing the assessment. The assessment would normally make use of primary clinical studies because working before marketing authorisation it is not expected

³⁵ http://www.fimea.fi/web/en/development/therapeutic_and_economic_value_of_medicines

³⁶ http://www.fimea.fi/kehittaminen/hoidollinen_ja_taloudellinen_arvo/arvioinnit

³⁷ As an example see:

http://www.fimea.fi/documents/160140/1454401/2016_14_Reslitsumabi+vaikean+eosinifilisen+astman+hoidossa.pdf/13722b81-b522-4c76-bf0b-8d3a9f8035da

that there will be secondary research available. The assessment will include conclusions about the pharmaceutical based on the clinical and economic profile, these conclusions are developed by the FIMEA staff. Before publication the report will be sent to the company for comments, once the company has commented it will be published on the website and there will be a public consultation. Comments received are published alongside the report on the FIMEA website.

The FIMEA assessment process is fairly flexible with the exception of the timings for assessment where they aim to start after CHMP positive opinion, so a report can be published as soon after marketing authorisation as possible. A key challenge for FIMEA lies in the appraisal and decision making process. Currently there is no national decision making process for hospital medicines. However, the Council for Choices in Health Care in Finland (COHERE)³⁸ is planning to make first recommendations for new hospital medicines during 2017. The recommendations will be based on assessment reports produced by FIMEA in addition to statements from other stakeholders.

Use of EUnetHTA assessments

FIMEA used the following EUnetHTA reports in their national assessments:

- Ramucirumab in combination with Paclitaxel as second-line treatment for adult patients with advanced gastric or gastro-oesophageal junction adenocarcinoma
- Rapid relative effectiveness assessment of new pharmaceuticals for the treatment of chronic hepatitis C

The assessment of ramucirumab was an assessment that had been prioritised by FIMEA for completion as part of their normal work³⁹. As a reviewer for the EUnetHTA assessment FIMEA had access to a draft of the EUnetHTA report that they could then use 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.

The report for hepatitis C was not part of FIMEA routine work and was completed following a request by the Council for Choices in Health Care to report on the impact in Finland (in terms of clinical effects and costs) of introducing the different the hepatitis C pharmaceuticals under different treatment decisions⁴⁰.

³⁸ <http://palveluvalikoima.fi/en/frontpage>

³⁹ http://www.fimea.fi/documents/160140/1153780/29643_uusi_KAI_4_2015.pdf/0b6f071f-0381-43bf-a075-9a9663f9f7a1

⁴⁰ http://www.fimea.fi/documents/160140/1153780/KAI+7_2016.pdf/cdc1d453-f4c3-4456-b06f-db2173f56680

In both instances data from the EUnetHTA assessment was used to support the process of creating the national assessment and the final product created by FIMEA looked like a standard FIMEA product.

Adaptation process

The adaptation process for ramucirumab 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, 30% economic evidence and 10% other aspects. To create their national assessment FIMEA went through a process of summarising 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. This means that sections of the EUnetHTA report did not tend to be removed, rather each were summarised. Summarising the EUnetHTA assessments was not perceived as challenging as long as the relevant information is easy to find. However, for the EUnetHTA assessment of hepatitis C treatments the length of the report and appendices meant that relevant information could be difficult to read and not always easy to identify.

A larger selection of subgroup analyses were included 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.

Challenges and solutions to use of EUnetHTA products

The biggest challenge for FIMEA is the timing of the availability of EUnetHTA reports relative to marketing authorisation (that is, a FIMEA assessment starts after CHMP positive opinion and aims to publish a draft report at marketing authorisation, whereas a EUnetHTA report becomes available approximately 100 days after CHMP positive opinion). The adaptation of ramucirumab was only possible because FIMEA were reviewers of the EUnetHTA report and accessed a draft to use in their report. If a draft version of the EUnetHTA assessments could be made available for

EUnetHTA WP7 research and analysis activity 1: Annex 2 Case studies

EUnetHTA partners this would support greater use among partners who are expected to start assessment before marketing authorisation is granted.

The information in EUnetHTA reports about use of technologies in other countries and relevant policies is useful. However, EUnetHTA reports would provide further added value if they went beyond the clinical studies and incorporated elements that are needed for economic evaluation such as extrapolation. These features of the EUnetHTA report could then be used by FIMEA to develop the economic sections of their report. Likewise EUnetHTA reports would provide greater value if they included economic information as this is always included in FIMEA reports and could support the agency's analyses. The inclusion of indirect comparisons and network meta-analyses is useful. However, sufficient information about the literature review and methods of analysis needs to be included to allow the approach to be reviewed.

The period of notice that a EUnetHTA assessment is going to be completed can be short and the lack of predictability in topic selection means that it is difficult to plan to use a EUnetHTA assessment and adjust accordingly. If EUnetHTA could produce an advance work plan so that agencies knew which assessments were to be completed before they started this would support greater use.

In their reports FIMEA provide a concluding statement about whether the differences in clinical effectiveness seen are of value given the costs whereas EUnetHTA assessments provide only a collection of the evidence, meaning that FIMEA still have to develop and consider the implications. A report from EUnetHTA that includes a clinical effectiveness conclusion would be of value to FIMEA.