Een procedure voor de beoordeling van nieuwe medische hulpmiddelen

KCE reports vol. 44A

Federaal Kenniscentrum voor de gezondheidszorg
Centre fédéral d'expertise des soins de santé
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Voorwoord

Innovatie in de gezondheidszorg staat hoog op de politieke agenda in vele landen. Innovatie kan slaan op een individuele nieuwe technologie of product, maar ook op het zorgproces bvb. bij chronische patiënten. Het kan zelfs slaan op het gezondheidszorgbeleid. Onderliggend rapport is daar een klein voorbeeld van. RIZIV en KCE ontwikkelden een wetenschappelijk raamwerk dat in het kader van de bestaande regelgeving moet toelaten om veelbelovende mogelijks innovatieve implantaten, waarvoor klinische bewijzen voor de baten en veiligheid voor de patiënt nog ontbreken, meer doelmatig te introduceren.

Een snelle en toegankelijke verspreiding van innovatieve implanteerbare technologie kan enorme voordelen met zich meebrengen voor patiënten. De implantatenindustrie kent geen tekort aan nieuwe schitterende ideeën. Een deel daarvan stroomt uiteindelijk ook door naar de dagdagelijkse praktijk. Denk maar aan doorbraken als de hartstent en neurostimulatie voor tremor of pijn, de pacemaker, heup- en knieprothese, om er enkele te noemen.

Het overhaast en onbegeleid toelaten van nieuwe implantaten en invasieve procedures houdt anderzijds ook risico's in voor patiënt en ziekteverzekering zoals bleek uit een aantal HTA rapporten van diverse instellingen waaronder het KCE. Een meer beheerste introductie laat toe dat een experimentele technologie zijn leercurve in de beste omstandigheden en met de nodige kwaliteitsgaranties doorloopt en maakt hem toch reeds vroegtijdig toegankelijk voor een welbepaalde patiëntenpopulatie.

Ook internationaal groeit meer en meer het besef – zeker voor de invasieve hulpmiddelen – dat naar analogie met geneesmiddelen goede klinische studies nodig zijn die de meerwaarde bewijzen. Het zijn de vruchten van hoog-kwalitatief klinisch onderzoek die uiteindelijk leiden tot vooruitgang in de geneeskunde.

Nieuwe medische technologieën kunnen op korte termijn investeringen vergen, maar over enkele jaren andere kosten in belangrijke mate doen dalen. Dit sluit naadloos aan bij health technology assessmentonderzoek, waar kosteneffectiviteitsanalyse een obligaat deel van uitmaakt.

Nieuwe medische technologieën zoals implantaten lijken vaak hét voorheen onmogelijk geachte magische alternatief te bieden voor moeilijke of risicovolle behandelingen, als het ware science-fiction die werkelijkheid wordt. Of een nieuw implantaat nu wel science brengt voor de patiënt dan wel uiteindelijk fiction blijft, daartoe kan het onderliggende raamwerk een bijdrage leveren. Een klein land als België kan op internationaal vlak een innovatieve rol spelen bij de introductie én wetenschappelijk onderzoek van veelbelovende invasieve medische hulpmiddelen.

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Samenvatting van het Rapport

INTRODUCTIE

België heeft internationaal gezien een sterke positie wat betreft de introductie en de implementatie van 'emerging' technologieën. Hiermee gepaard gaande beschikt België over een uniek wettelijk kader dat de conditionele terugbetaling van nieuwe implantaten en invasieve hulpmiddelen mogelijk maakt, het zogenaamde artikel 35 categorie 5 van de medische nomenclatuur. Deze wetgeving biedt de mogelijkheid mogelijks innovatieve 'emerging' implantaten waarvan de klinische doeltreffendheid en veiligheid niet of nauwelijks zijn aangetoond op een beheerde manier te introduceren en te implementeren. De bestaande conventies, die een toepassing zijn van categorie vijf, vertonen echter een aantal tekortkomingen. De belangrijkste is het gebrek aan een duidelijk ontwerp voor het uitvoeren van wetenschappelijk onderzoek, wat evaluaties van klinische werkzaamheid, kosteneffectiviteit, patiënt- en organisatiegerelateerde kwesties belemmert op het einde van de conventie als een complement voor de vaak aanzienlijke investering van de ziekteverzekering.

Daarenboven kan de afwezigheid van een strikte reglementering voor technologieën zoals medische hulpmiddelen leiden tot het verspreiden van ongeëvalueerde technologieën. Dit kan aanleiding geven tot verkeerd gebruik van publieke middelen. Het huidige ongestructureerde 'vigilantie' systeem is bovendien problematisch voor de publieke verantwoording en kan leiden tot mogelijke veiligheidsproblemen.

Om tegemoet te komen aan een aantal van deze tekortkomingen werd in deze studie, uitgevoerd door het RIZIV en KCE, een structuur opgesteld voor een nieuwe procedure voor het beheerd introduceren van nieuwe medische implantaten en invasieve hulpmiddelen in categorie vijf.

METHODOLOGIE

Om het project af te bakenen werden de verschillende concepten omtrent nieuwe en 'emerging' technologieën verduidelijkt. Verder werd de huidige procedure voor het evalueren van geneesmiddelen kort beschreven en geplaatst tegenover de mogelijke nieuwe procedure voor het evalueren van nieuwe en 'emerging' medische hulpmiddelen. De beschikbare literatuur voor deze inleiding werd geïdentificeerd op basis van een zoekfunctie in Medline en de CRD HTA database.

De wetgeving op Europees niveau betreffende medische hulpmiddelen werd omschreven. Deze wetgeving focust zich hoofdzakelijk op CE marking. Op dit ogenblik is de Europese wetgeving in een herzieningsfase.

Bestaande procedures voor het identificeren, beoordelen en toezicht houden op nieuwe en 'emerging' technologieën in UK, Australië, VS, Canada, Nederland, Denemarken, Finland, Frankrijk en België werden in kaart gebracht.

SYNTHESE VAN DE BESCHIKBARE PROCEDURES IN VERSCHILLENDE LANDEN

De systemen in Australië en Het Verenigd Koninkrijk kunnen aanschouwd worden als de meest volledige. Een actief horizon scanning systeem is aanwezig, details van de fabrikant en het medisch hulpmiddel moeten geregistreerd worden, vroegtijdige beoordeling van nieuwe en 'emerging' technologieën worden uitgevoerd, een post-market vigilantie systeem dat verplicht is voor de fabrikant en vrijwillig voor gebruikers is aanwezig, en de mogelijkheid tot conditionele of voorlopige financiering bestaat. In de UK bestaat er een bijzondere 'Review Body'. Het Interventional Procedures Advisory Committee (IPAC), dat advies uitbrengt aan NICE betreffende de veiligheid en werkzaamheid in ideale omstandigheden van interventionele procedures, kan procedures doorverwijzen naar de Review Body voor verdere onderzoeken. Dit orgaan organiseert de data collectie en informeert bij hoogdringende gevallen NICE indien procedures gepaard blijken te gaan met een buitengewoon hoog aantal ongunstige gebeurtenissen.

De VS heeft ook een relatief vergelijkbaar en goed uitgebouwd systeem. Een post-market vigilantie systeem voor fabrikant en gebruiker (MAUDE) en voor consumenten en

gezondheidsverleners (MedWatch) is aanwezig. In tegenstelling tot het Europese systeem, vereist FDA's Premarket Approval, dat van toepassing is voor de meeste klasse III hulpmiddelen, het aantonen van de klinische werkzaamheid in algemene omstandigheden als een voorwaarde voor het op de markt brengen van een medisch hulpmiddel. Hoewel de Europese wetgeving vermeldt dat klinische data beschikbaar moeten zijn, gebeurt dit enkel in het kader van het proces van CE marking bij de evaluatie van de technische fiche door de aangemelde instanties. Verder is het twijfelachtig dat de aangemelde instanties, die vooral technische organen zijn, de competentie hebben om klinische werkzaamheid in algemene omstandigheden en veiligheid te beoordelen waar relevante klinische resultaten voor de patiënt noodzakelijk zijn in plaats van korte termijn surrogaat eindpunten.

In andere landen zijn gelijkaardige structuren in beperktere mate aanwezig. Verschillende landen hebben hun krachten gebundeld voor het uitoefenen van horizon scanning activiteiten, wat geresulteerd heeft in het oprichten van Euroscan. In België bestaat er geen compleet geïntegreerd systeem. Niettegenstaande vormen verschillende initiatieven van het RIZIV en ziekenfondsen, zoals het oprichten van een HTA instituut (KCE) en de wettelijke mogelijkheid tot conditionele terugbetaalbaarheid, een goede fundering voor het verder ontwikkelen van een geïntegreerd systeem.

VOORSTEL VOOR EEN NIEUWE PROCEDURE

Op dit ogenblik is de wetgeving betreffende de terugbetaling van implantaten en invasieve hulpmiddelen in een herzieningsfase. Er zijn echter geen wijzigingen aangebracht voor de terugbetaling van nieuwe en 'emerging' technologieën waarvoor de werkzaamheid in ideale omstandigheden en veiligheid niet of nauwelijks zijn aangetoond. De voorgestelde procedure kan dus het huidige wettelijke kader aanvullen.

Voorbereidende stap: Horizon scanning

Idealiter bestaat de eerste fase in een proces van beheerd opnemen van nieuwe en 'emerging' technologieën uit systematisch horizon scanning. Momenteel is er geen dergelijk gestructureerd proces aanwezig in België. De introductie van nieuwe technologieën is echter niet nationaal gebonden en er zijn reeds initiatieven genomen op Europees niveau (Euroscan, EUNetHTA).

Stap 1: Registratie en notificatie

Vooraleer nieuwe en 'emerging' technologieën op de markt komen zouden ze moeten worden geregistreerd. De huidige Belgische wetgeving legt de notificatie van CE gemarkeerde hulpmiddelen op. Dit kan voldoende zijn voor hulpmiddelen met een minimale impact. Voor nieuwe en 'emerging' technologieën met een grotere impact, zoals invasieve klasse III hulpmiddelen, zouden er eerst klinische studies betreffende de veiligheid voor de patiënt en klinische werkzaamheid in algemene omstandigheden aanwezig moeten zijn. Een register zou op Europees of nationaal niveau gecentraliseerd moeten worden en publiek toegankelijk zijn om transparantie te garanderen.

Stap 2: Beschikbaarheid van bewijsmateriaal

Om een 'emerging' technologie te kunnen categoriseren moet er een pre-evaluatie van de beschikbare bewijzen betreffende werkzaamheid in ideale omstandigheden en veiligheid van de technologie gebeuren door de nieuw opgerichte Commissie voor de Terugbetaling van Implantaten en Invasieve Medische Hulpmiddelen (CTIIMH). Aan de hand van een systeem dat de niveaus van bewijskracht weergeeft, kunnen technologieën gecategoriseerd worden als technologieën met 'goede of ten minste gemiddelde bewijskracht betreffende werkzaamheid in ideale omstandigheden en veiligheid', en 'zwakke (of geen) bewijskracht betreffende werkzaamheid in ideale omstandigheden en veiligheid'. In het eerste geval maakt de nieuwe wetgeving over de terugbetaling van implantaten een onderscheid tussen implantaten of invasieve hulpmiddelen zonder enige bewezen toegevoegde waarde (klasse II) en deze met een bewezen toegevoegde therapeutische waarde in vergelijking met andere bestaande therapeutische alternatieven (klasse I).

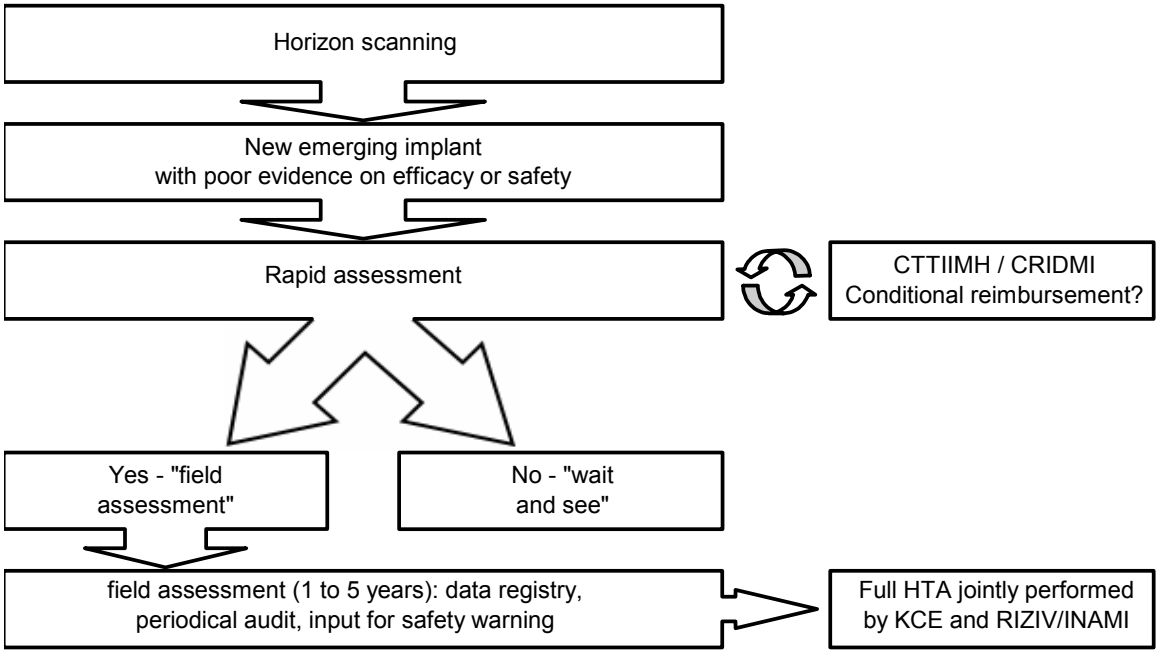
Indien er enkel zwakke klinische bewijzen beschikbaar zijn kan de technologie of het hulpmiddel in een begeleid proces ingevoerd worden. Om de strategie te bepalen moet een vroegtijdige

evaluatie met betrekking tot veiligheid en werkzaamheid onder ideale omstandigheden worden uitgevoerd. Indien men van oordeel is dat de 'emerging' technologie minder werkzaam is of indien er twijfels bestaan over de veiligheid, kan deze technologie (nog) niet beschouwd worden als 'emerging' en wordt er een 'wait and see' beleid gevolgd.

In het andere geval levert de evaluatie argumenten op voor een veelbelovende 'emerging' gezondheidstechnologie (mogelijks even doeltreffend en op zijn minst even veilig). Indien budgettaire middelen aanwezig zijn kan men overgaan tot conditionele terugbetaling.

Stap 3: Conditionele terugbetaling en wetenschappelijke evaluatie door praktijk evaluatie (ziekenhuis HTA)

In een voorbereidende fase en gekoppeld aan de vroegtijdige evaluatie worden het onderzoeksontwerp en de uitvoeringsformaliteiten besproken. Vervolgens bevat de evaluatiefase, gaande over een periode van normaal gezien één tot vijf jaar, het registreren van data en uitvoeren van tussentijdse evaluaties en mogelijke controles. Uiteindelijk wordt een volledige HTA uitgevoerd die de klinische effectiviteit onder algemene omstandigheden en de kosteneffectiviteit van de technologie beoordeelt.



Figuur: korte samenvatting van het belangrijkste onderdeel, stap 3, van het wetenschappelijke kader. Een uitgebreidere grafiek die ook alle bevoegde instanties en de nieuwe procedure voor de terugbetaling van klasse I en II implantaten bevat bevindt zich op pagina 35 van het wetenschappelijke rapport.

CONCLUSIES

Het implementeren van het in dit rapport ontwikkelde kader biedt de mogelijkheid om de sterke Belgische positie in Europa betreffende het begeleid introducteren en het in gebruik nemen van 'emerging' technologieën nog te versterken. De omschreven structuur is innovatief aangezien we geen gelijkaardige en goed uitgebouwde procedure hebben gevonden in andere landen. Verder is de procedure veelbelovend voor verschillende stakeholders/belanghebbende partijen aangezien het de budgettaire risico's beperkt en oogt op het voortbrengen van betrouwbare onpartijdige bewijzen aangaande klinische effectiviteit onder algemene omstandigheden en kosteneffectiviteit van de 'emerging' technologie.

1. Voor de fabrikant die innovatieve hulpmiddelen produceert met een 'toegevoegde waarde' kan het uitgewerkte kader verschillende voordelen bieden: het begeleid omnemen van procedures staat toe 'emerging' hulpmiddelen geleidelijk aan te introduceren op de markt en kan hierbij verkeerd gebruik en uitvoeringsproblemen vermijden; een (gedeeltelijk of volledig) door de overheid gesteunde klinische trial – ofwel gerandomiseerd of observationeel – en een HTA die leidt tot conclusies over de werkzaamheid onder algemene omstandigheden, kosten en mogelijks kosteneffectiviteit en organisationele- en patiëntgerelateerde aspecten.

2. Voor de overheid biedt dit kader significante voordelen. De procedure, en meer specifiek de vroegtijdige evaluatie, stelt de overheid in staat tijdig goed geïnformeerde beslissingen te maken die budgettaire problemen en het verkeerd gebruik van de publieke middelen verhindert.

3. De procedure verzekert patiënten dat 'emerging' technologieën geïntroduceerd worden in een 'state-of-the-art' omgeving en worden beoordeeld om hun veiligheid te beschermen. Bovendien kan een transparant registratie- en vigilantie systeem leiden tot makkelijker toegankelijke informatie over bestaande producten, procedures en mogelijke belangrijke veiligheidsproblemen.

Het gebruik van dit kader moet geëvalueerd worden, zowel op het output niveau als op het tijdsbestek, en na een aantal jaren mogelijks aangepast en geoptimaliseerd worden.

Scientific summary

Table of contents

1 BACKGROUND

Thanks to the technical evolution in medical science the number of new technologies, medical devices and techniques has been steadily increasing and is still expanding. New health technologies not only can offer solutions to strictly medical problems, they can also have secondary advantages such as the reduction of hospital length of stay, the improvement of quality and safety of care, the comfort of the patient, etc. But medical technological evolution is one of the major cost drivers of health care expenditure. As in other countries, the increasing expenses for new and emerging technologies are one of the main budgetary problems of Belgian health insurance. The reimbursement of technologies in the phase prior to adoption and usually before any reliable evidence exists on their clinical effectiveness and cost-effectiveness (i.e. an emerging technology) is a particular challenge in many health care systems. Decision makers responsible for funding health care need high quality and impartial information derived from rigorous assessments to make decisions in an environment of limited resources. On the one hand, a premature introduction of a medical technology in the system can lead to patient harms and inadequate use of resources. On the other hand, a too restrictive policy can hamper patient benefits and innovation.

Currently, there's already a regulatory base in the Belgian health insurance law for the conditional reimbursement of implants in Belgium.[1] The current application of this regulation, however, rarely involves a research design needed to prove the added value of the emerging technology. The current approach can also lead to budgetary failure or inappropriate use of resources. Moreover, the absence of sufficient regulation for technologies such as medical devices in general can lead to the diffusion of unevaluated medical technologies and possible safety problems.

Therefore, the aim of the current study is to set up a transparent and scientifically valid procedure in Belgium to evaluate medical devices early. Whilst early evaluations often fail to compare new and existing interventions, and may focus on physiological or biochemical outcomes rather than changes in clinical condition or quality of life, they can provide limited information on effectiveness which can be used to guide initial decisions on adoption and use. Complete health technology assessment should therefore be viewed as a continuous process over time, progressing from early 'indicative' studies to rigorous comparative analysis.

[1] Art. 35, §3, category 5 of the Belgian medical nomenclature

2 METHODOLOGY

Starting with a general description of the key concepts, this report provides an overview of the regulatory context for medical devices in developed countries at the European and international level, and of the current procedure for the assessment of pharmaceuticals in Belgium. A description of the existing procedures (if any) to identify, assess and monitor emerging medical devices is provided for the UK, Australia, the USA, Canada, the Netherlands, Denmark, Finland, France and Belgium. These countries were selected because of their relatively long HTA tradition and on the a-priori belief they could provide some insight to design a new procedure for Belgium. Further, this selection of countries ensures the coverage of the four biggest markets and leading health care systems of the industrialised countries (i.e. the USA, the UK, Canada and Australia). Based on those existing systems, this report tries thus to elaborate a new procedure for the assessment of emerging technologies in Belgium.

The available literature was identified through a search in Medline and the CRD HTA database. Furthermore, for each of the above-mentioned countries, information was collected from national and/or local government agencies, and from private agencies when relevant. In order to validate or add on to this information, contact was taken with one or more experts in the specific country. Experts were primarily questioned about three topics:

1. How do you identify emerging technologies in your country?
2. Do you have an established evaluation procedure for those emerging technologies?

If yes:

- Does this procedure pertain to both pharmaceuticals and medical devices?
- Do you have a system of conditional reimbursement?
- Follow – up during/after evaluation term?
- Registry of clinical trials?

If no:

- Do you plan to work on this issue?

3. Implementation and legislation

3 SCOPE AND DEFINITIONS

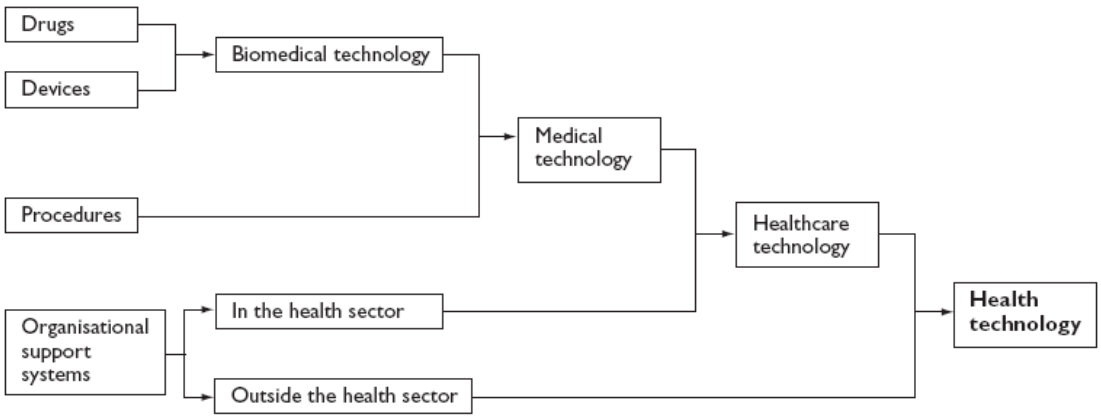
The key concepts on which this report is based are described in this section.

3.1 HEALTH CARE TECHNOLOGIES

In the 1970s, the US Office of Technology Assessment[2] defined the term "medical technologies" as "the drugs, devices, and medical and surgical procedures used in medical care, and the organisational and supportive systems within which such care is provided".

More recently, Liaropoulos[3] drew a schematic representation (figure 1) of the different definitions of biomedical, medical, healthcare and health technology:

Figure 1: Outline of the categories in health technology[3]



In 2005, a simpler and even broader definition has been provided by the European Network for Health Technology Assessment (EUnetHTA), where "health technology" is defined as the application of scientific knowledge in health care and prevention. Examples of health technologies are diagnostic and treatment methods, medical equipment, pharmaceuticals, rehabilitation and prevention methods, and organisational and supportive systems within which health care is provided.[4]

Such a broad definition is also adopted by The European Information Network on New and Changing Health Technologies (Euroscan) [5] where health care technologies encompass all methods used by health professionals to promote health, prevent and treat disease, and improve rehabilitation and long-term care. These methods include pharmaceuticals, devices, procedures, programmes, settings, and public health activities.

Within the current study, we seek to develop an assessment procedure for medical devices, i.e. only a subset of the health technologies. Pharmaceuticals are not considered here since a separate procedure for their evaluation already exists in Belgium (cfr. infra). The other two sub-categories, surgical procedures and organisational support systems, have also been discarded so far. This is mainly because Art. 35, §3, cat 5 of the medical nomenclature, the article from which the current study question came out, only deals with implantable medical devices. In the future, however, emerging surgical procedures

[2] Office of Technology Assessment. Assessing the efficacy and safety of medical technologies. Washington DC: National Academy Press, 1978.
[3] Liaropoulos L. Do we need 'care' in technology assessment in health care?, Int J Technol Assess Health Care. 1997;13(1):125–7.
[4] http://www.eunethta.net/
[5] http://www.euroscan.bham.ac.uk/index.htm

and organisational support systems could, from a scientific point of view, be assessed with a similar procedure as that for medical devices.

3.2 HEALTH TECHNOLOGY ASSESSMENT

According to EUnetHTA, health technology assessment (HTA) is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are patient focused and seek to achieve best value.

A similar definition is provided by INAHTA[6] that also defines technology assessment in health care as a multidisciplinary field of policy analysis studying the medical, social, ethical and economic implications of development, diffusion and use of health technology.

If should be strengthened however that the key components of health technology assessment are the assessment of the medical (safety, efficacy, effectiveness) and economic (cost-effectiveness) aspects of a technology.

3.3 MEDICAL DEVICES

Following the directive on medical devices (93/42/ECC) (cfr. infra), medical devices are defined as "any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception,

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means."

Examples of medical devices range from very simple ones such as thermometers and syringes to very complex devices such as defibrillators and CT scanners. Recently, some mixed or combination products emerged: drug-eluting stents, biologically engineered heart valves and catheters covered with antibiotics.

3.4 IMPLANTS

According to the European directive on medical devices (annex IX directive 92/42/ECC) implantable devices can be defined as any device which is intended:

- to be totally introduced into the human body or,
- to replace an epithelial surface or the surface of the eye,

by surgical intervention and which is intended to remain in place after the procedure. Any device intended to be partially introduced into the human body through surgical intervention and intended to remain in place after the procedure for at least 30 days is also considered an implantable device.

[6] http://www.inahta.org/inahta_web/index.asp

3.5 "EMERGING" AND "NEW" HEALTH CARE TECHNOLOGIES.

Banta and Luce[7] suggested that the life cycle of a technology consists of five stages:

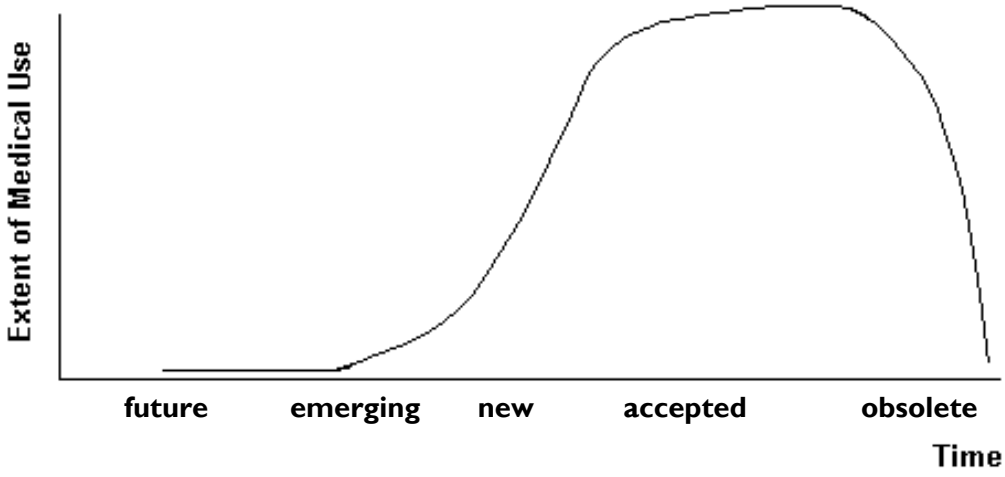
- Future: not yet developed
- Emerging: prior to adoption
- New: in the phase of adoption
- Accepted: in general use
- Obsolete: should be taken out of use.

Emerging technologies are technologies just about to be introduced to clinical practice. They comprise those technologies in the applied research stage. New technologies are technologies that have only recently been introduced to clinical practice. They comprise those technologies that should have passed the stage of clinical trials but are not yet extensively used.

Alternatively, the following definitions are provided by Euroscan:

Emerging technologies are technologies that are not yet adopted by the health care system (figure 2). Pharmaceuticals will usually be in phase II or phase III clinical trials or perhaps pre-launch. Medical devices will be prior to marketing, or within 6 months of marketing, or marketed but less than 10% diffused or localised to a few centres.

Figure 2: Stages in the technology life cycle



New technologies are technologies in the phase of adoption that have only been available for clinical use for a short time and are generally in the launch or early post-marketing stages.

Ideally, the assessment of a technology should be performed before its widespread diffusion, which is in the emerging phase of that technology. This requires however that some scientific evidence about the clinical efficacy and safety of the technology is available.

[7] Banta HD, Luce BR. Health care technology and its assessment. An international perspective. New York: Oxford University Press, 1993.

3.6 LEARNING CURVE OF HEALTH TECHNOLOGIES

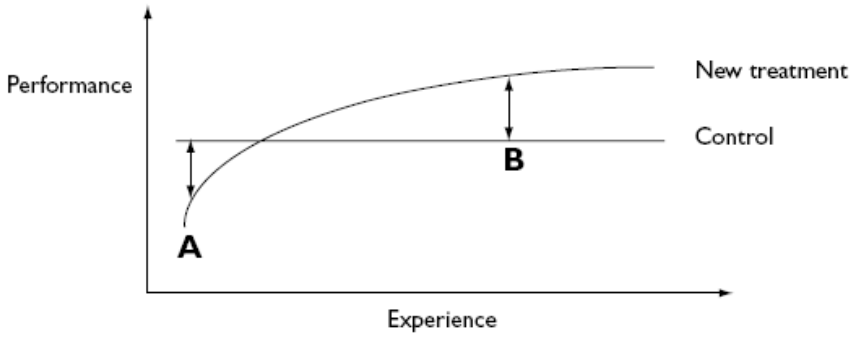
Another issue in the early assessment of emerging technologies is the existence of a learning effect. Emerging technologies are indeed characterized by the fact that they are still evolving when they are introduced into clinical practice, so the users will be both modifying their applications and developing their skills over time. Such improvement over time in the performance of a technology because of the user's increasing experience (i.e. learning effect) could invalidate the rigorous assessment of health technologies.

Early assessment of an emerging technology may indeed give a biased and negative picture of that technology. Early assessment may not reflect all the potential capabilities or real costs of the new technology. This case is illustrated in point A on the graph below. On the other hand, by the time the technology has stabilised (point B on the figure 3), people have probably been convinced of the worth of the technology on the basis of poor quality evidence.

The learning curve effect associated with health technologies is also likely to have an impact on their costs. The cost of a technology may initially be high but decrease in the diffusion phase due to increasing experience of providers. Experience may lead to more efficiency in the application of a technology (equal outcome at lower cost or better outcome at lower cost). In addition, increasing competition between manufacturers may push prices downwards.

Late assessment of a technology would therefore also be of little use to decision-makers. Further, at this stage, people may find it unethical to perform a rigorous evaluation if it involves refusing to give the technology to potential patients.[8] [9] This paradox is clearly illustrated by the Buxton law[10] that "it is always too early (to evaluate a new technology) until, unfortunately it's suddenly too late". Another related phenomenon is the problem that has been called the 'moving target problem'. As technologies mature and more information becomes available, updating analysis and their possible recommendations is important.

Figure 3: Outcome of evaluation at 2 points of the learning curve[9]



[8] Robert G, Stevens A, Gabbay J. 'Early warning systems' for identifying new healthcare technologies. Health Technol Assess. 1999, 3(13).
[9] Ramsay CR, Grant AM, Wallace SA, Garthwaite PH, Monk AF, Russell IT. Statistical assessment of the learning curves of health technologies. Health Technol Assess. 2001;5(12).
[10] Buxton MJ. Problems in the economic appraisal of new health technology: the evaluation of heart transplants in the UK. In Drummond MF, editor. Economic appraisal of health technology in the European Community. Oxford: Oxford Medical Publications. 1987:103–18.

3.7 DIFFERENCE BETWEEN PHARMACEUTICALS AND DEVICES

While assessment of pharmaceuticals is more or less well established in the majority of developed countries, formal health technology assessment (HTA) processes for medical devices are lacking or have been established more recently. There are important differences between technologies that may warrant different application of HTA (table 1). This table only represents general differences between devices and pharmaceuticals and exceptions to the rule can be found easily, such as e.g. PET scanning.

Table 1: Differences between medical devices and pharmaceuticals[11]

	Medical devices	*Pharmaceuticals*
Therapeutic effect	Effective by mechanical and/or electrical action	Effective when absorbed and metabolised by the body
Operator skill	Outcomes often depend on surgical skill	Rarely relevant
Product life cycle	Relatively short (2–4 years)[a]	Longer (10–20 years)
Physical infrastructure	Often necessary for delivery of treatment	Usually not required
Delivery environment	Often delivered in hospitals (public and private)	Usually administered in community settings
HTA processes	Recently established processes	Long-established processes
Evidence base	Good quality scientific data often not available	Good quality scientific data usually available

[a] The Therapeutic Goods Administration observed that there are some devices (such as syringes, bandages, condoms and surgical instruments) which have changed little over the past 10–20 years (DoHA, sub. PR56).

Furthermore, it may be difficult to isolate the effects of non-pharmaceutical technologies from other components of the care delivery system. Devices are often used in conjunction with other interventions (such as surgery, diagnosis or monitoring) and it may be questioned whether it is possible to evaluate the specific effect of devices on health outcomes. Some interventions cannot be 'blinded' either ethically or physically.[12] In these cases, it may be more difficult to run randomized double-blind trials which are designed to eliminate bias. Furthermore, randomized clinical trials to evaluate surgical procedures typically involve greater costs than case series. According to Weil,[13] case series require fewer resources in terms of personnel and funds than do clinical trials. However, their contribution to the generation of reliable unbiased evidence on the clinical effectiveness of the product is limited. Medical devices generally target much smaller populations than do pharmaceuticals. Alternative designs (other than RCTs) and statistical methods could then be used for the evaluation of small samples. Note that such work is currently on the agenda of the European Commission for orphan drugs.

Thus, while useful lessons may be drawn from the experience gained from pharmaceutical assessment, they may not always be directly transferable to the assessment of other technologies such as implants in real life.[14]

[11] Henry, DA., Hill SR. Assessing new health technologies: lessons to be learned from drugs. Medical Journal of Australia. 1999;171(10):554–6.
[12] Weedon D. Health technology assessment in Australia. Medical Journal of Australia. 1999;171(10):551–2.
[13] Weil RJ. The Future of Surgical Research, Public Library of Science Medicines. 2004;1(1)
[14] Productivity Commission. Impacts of Advances in Medical Technology in Australia, Research Report, Melbourne. 2005.

4 PROCEDURES FOR MEDICAL DEVICES: THE EUROPEAN DIRECTIVES

Unlike the pharmaceutical sector, where new pharmaceuticals have to undergo series of regulatory clinical trials during development and for which a comprehensive route for assessment is outlined (cfr. infra), the evaluation of other health technologies such as medical devices, as well as the type of evaluation and their timing is less demarcated. For instance, no pre-market clinical trials are required for obtaining CE marking of medical devices.

On the European level medical devices are mainly regulated by three Directives, dealing with active implantable devices,[15] with medical devices in general[16] and with in vitro diagnostic medical devices.[17] As the directive on medical devices sets the general outline, especially this directive will be focussed on. There is a proposal to amend the medical devices directive and also the directive dealing with active implantable devices in order to align the text of the framework on medical devices (European Parliament decision pending, 1st reading or one reading only).[18] The most important changes will be highlighted in this report.[19] Further the national legislation with regard to medical devices of the European member states will fragmentarily be discussed as they represent a transposition of the European directives. It has to be noted however that the directives designate a large discretionary competence to the member states. Consequently there can be some divergence in the different legislations of the member states. On the European level "medical devices" fall within the competence of the DG enterprise and industry.[20]

Classification

Medical devices can be classified in four classes: class I (low risk), II a (medium risk), II b (elevated risk) and III (high risk) according to the risk linked to the device. The higher the classification, the more elaborate the level of assessment required by the notified bodies will be. Classification rules are set out in Annex IX of the Directive on medical devices.[21] In figure 4, the main constituents of the European Directives according to the different classes are illustrated.

Medical devices have to be distinguished from pharmaceuticals. Sometimes, however, the distinction is not that clear and this may create a grey zone; for instance if a device is used to insert a drug. The directive provides some regulations on these borderline cases (art. 1).

Essential requirements

The Directives define the essential requirements that devices have to meet when they are put on the market or put into service. The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical conditions or the safety and the health of users or, where applicable, other persons, provided that any risk when weighed against the benefits to the patient and are comparable with a high level of protection of health and safety. Requirements regarding design and construction relate to issues such

[15] Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices L 189 20 July 1990
[16] Council Directive of 93/42/EEC of 14 June 1993 concerning medical devices L 169 12 July 1993
[17] Council Directive of 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices L 331 7 December 1998
[18] http://ec.europa.eu/enterprise/medical_devices/consult_docs/Public_Consultation_draft.pdf
[19] For the current state of affairs and the latest documents http://europa.eu.int/eur-lex/lex/Result.do?arg0=medische+hulpmiddelen&arg1=&arg2=&titre=titre&chlang=nl&RechType=RECH_mot&Submit=Zoeken
[20] http://ec.europa.eu/enterprise/
[21] http://europa.eu.int/eur-lex/en/consleg/pdf/1993/en_1993L0042_do_001.pdf

as risk assessment and risk management, chemical, physical and biological properties, infection and microbiological contamination, construction and environmental properties, protection against radiation, etc. Consequently products can only be placed on the market or put into service, if they were subject to a risk assessment, a risk management process and a risk/benefit analysis.

According to the directives, the solutions adopted by the manufacturer for the design and construction of devices must conform to safety principles, taking account of the generally acknowledged state of the art. In selecting the most appropriate solutions, the manufacturer must apply the following principles:

- eliminate or reduce risks as far as possible,
- where appropriate take adequate protection measures including alarms, if necessary, in relation to risks that cannot be eliminated,
- inform users of the residual risks due to any shortcomings of the protection measures adopted.

In order to facilitate compliance with the essential requirements, the Directives foresee recourse to harmonized European standards. [22] Where the references of these standards have been published in the Official Journal of the European Communities, compliance with such standards will provide a presumption of conformity with the relevant essential requirements. Whilst the essential requirements are obligatory, the standards remain voluntary.

Quality system requirements

The international quality system standards for medical devices are issued by the International Organisation for Standardisation (ISO).[23] Regulations for quality systems may cover the methods, facilities and controls used by the manufacturer in the design, manufacture, packaging, labelling, storage, installation, servicing and post-market handling of medical devices. Applicable requirements depend upon the risk class of device and the regulatory system of the country. ISO 13485 and ISO 13488 are specific for medical device manufacturing.

Conformity assessment procedures

The Directives contain a number of conformity assessment procedures, which depend on the type of products and type of risks involved. It concerns a scheme designed to regulate the level of scrutiny required to deem a medical technology or a medical device safe, based on the level of its inherent risk to the patient. Manufacturers of devices of classes II and III, as well as devices of class I with either measuring function or sterility requirements, must submit to the competent authorities a declaration of conformity to the appropriate EC directives and details of the conformity assessment procedure followed. Devices that meet the essential requirements and have undergone the appropriate conformity assessment procedures will be CE marked by the notified body. Devices, other than devices which are custom-made or intended for clinical research, considered to meet the essential requirements must bear the CE marking of conformity when they are placed on the market. The CE mark denotes a formal statement by the manufacturer of compliance with the directives' requirements. Other medical devices of class I are exempt from pre-market submissions, although they must follow the essential principles of safety and performance in their design, construction and labelling requirements.

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[22] http://www.newapproach.org/home.asp

[23] http://www.iso.org/iso/en/CombinedQueryResult.CombinedQueryResult?queryString=devices

Notified bodies[24]

A Notified Body is an organization that has been nominated by a member state and notified by the European Commission. A Notified Body will be nominated based on designated requirements, such as knowledge, experience, independence and resources to conduct the conformity assessments.

Notified bodies are designated to assess the conformity with the essential requirements, and to ensure consistent technical application of these requirements according to the relevant procedures in the directives concerned (cfr. supra).

In the advice of The European Economic and Social Committee[25] on the proposal of the new directive, it believes that the proposal is lacking in terms of the capacity of the notified bodies to carry out the tasks assigned to them. New therapeutic advances and the growing complexity and sophistication of devices require scientific and technical expertise that cannot always be provided at national level.

In Belgium there are two notified bodies who deal with medical devices of specific classes.[26] For most of the devices that will be put on the Belgian market, foreign notified bodies will have to be contacted. Therefore, there should be a European plan or at least coordination to ensure that certain notified bodies are specialised in certain types of particularly complex and sophisticated products.

The notified body shall inform the other notified bodies and the competent authority about all certificates suspended or withdrawn and, on request, about certificates issued or refused. It shall also make available, on request, all additional relevant information.

Clinical evaluation

As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances (referred to in the general requirements Sections 1 1 and 3 of Annex I) under the normal conditions of use of the device and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio (referred to in Section 1 6 of Annex I) must be based on clinical data in particular in the case of implantable devices and devices in class III. In the new proposed version of the directive the specification of the device category is cancelled. Consequently this general rule counts for all classes. The proposal also states that clinical evaluation must follow a defined and methodologically sound procedure based on:

- either a critical evaluation relating to the safety, performance, the design characteristics and the intended purpose of the device, where there is demonstration of equivalence of the device with that to which the data relates and the data adequately demonstrate compliance with the relevant essential requirements;

[24] http://ec.europa.eu/enterprise/newapproach/legislation/guide/document/chap06.pdf#search=%22notified%20bodies%20have%20to%20assess%20the%20essential%20requirements%22

[25] http://europa.eu.int/eur-lex/lex/Notice.do?hwords=medische%20hulpmiddelen~&pgs=10&list=431738:cs,429612:cs,427440:cs,427439:cs,427438:cs,419433:cs,412398:cs,412397:cs,406322:cs,402838:cs,&val=431738:cs&nbl=133&lang=en&visu=&checktexte=checkbox&pos=1&page=1

[26] SGS SYSTEMS & SERVICES CERTIFICATION EESV: They are responsible for the following products: Active medical devices in Class I, IIa or IIb; devices emitting ionising radiation and devices intended to image; In vivo distribution of radiopharmaceuticals; Non-active medical devices. They are responsible for the following procedures: - Full quality assurance system; EC Type-examination; EC verification; Production quality assurance; Product quality Assurance.
APRAGAZ A.S.B.L.: They are responsible for the following products:
Class II a non-invasive devices for gas storage, distribution or Administration with the following procedures: full quality assurance system; EC verification; Production quality assurance; product quality assurance; Class IIb active devices for administering gas and/or extracting medicines/substances with the following procedures: full quality assurance system, EC Type-examination, EC verification, Production quality assurance, Product quality assurance

- critical evaluation of the results of all clinical research made;
- or a critical evaluation of the combined clinical data provided in the above mentioned cases.

The clinical evaluation and its outcome must be documented. This documentation must be included and/or fully referenced in the technical documentation of the device.

Moreover the clinical evaluation and its documentation have to be actively updated. Where Post Market Clinical Follow-up as part of the post market surveillance plan for the device is not deemed necessary, this must be duly justified and documented.

Where demonstration of conformity with essential requirements based on clinical data is not deemed appropriate, adequate justification for any such exclusion has to be given based on risk management output and under consideration of the specifics of the device-body interaction, the clinical performances intended and the claims of the manufacturer. Adequacy of demonstration of conformity with the essential requirements by performance evaluation, bench testing and preclinical evaluation alone has to be duly substantiated, according to the directive.

Particularly for implantable devices and devices in class III, clinical research shall be performed unless it is duly justified to rely on existing clinical data.

The objectives of clinical research are:

- to verify that, under normal conditions of use, the performance of the devices conforms to those intended by the manufacturer.
- to determine any undesirable side-effects, under normal conditions of use, and assess whether they constitute risks when weighed against the intended performance of the device.

Methods for clinical research

In the directives the term "clinical investigation" is used. 'Device intended for clinical investigation' means any device intended for use by a duly qualified medical practitioner when conducting research.

For a good understanding we uniformly used the term "clinical research".

Clinical research must be performed on the basis of an appropriate research plan reflecting the latest scientific and technical knowledge and defined in such a way as to confirm or refute the manufacturer's claims for the device. The research must include an adequate number of observations to guarantee the scientific validity of the conclusions. The procedures used to perform the research must be appropriate to the device under examination. Moreover they must be performed in circumstances similar to the normal conditions of use of the device.

All the appropriate features, including those involving the safety and performances of the device, and its effect on patients must be examined. All serious adverse events, whether device related or not, have to be recorded and immediately notified to the competent authority of the Member State in which the event occurred.

A summary of the adverse events must be provided, on a periodic basis, to all competent authorities of the Member States in which the clinical research is being performed.

Notification of clinical research

In the case of devices intended for clinical research, the manufacturer, or his authorized representative established in the Community, shall notify the competent authorities of the Member States in which the research is to be conducted.

In the case of devices falling within Class III and implantable and long-term invasive devices falling within Class IIa or IIb, the manufacturer may commence the relevant clinical research at the end of a period of 60 days after notification, unless the

competent authorities have notified him within that period of a decision to the contrary based on considerations of public health or public policy. The proposal on the new directive adds that such decisions shall be communicated by the competent authority to the other Member States.

Member States may however authorize manufacturers to commence the relevant clinical research before the expiry of the period of 60 days, in so far as the relevant ethics committee has issued a favourable opinion on the programme of research question.

In the case of devices other than those referred to in the second paragraph, Member States may authorize manufacturers to commence clinical research, immediately after the date of notification, provided that the ethics committee concerned has delivered a favourable opinion with regard to the research plan.

Registration of the responsible person

For class I devices and custom-made devices the Directive also requires the registration of persons responsible for placing devices on the market. The competent authorities of the member state in which the manufacturer has his registered place of business must be informed of the address of the registered place of business and the description of the devices concerned.

For all medical devices of classes II b and III, member states may request to be informed of all data allowing for identification of such devices together with the label and the instructions for use when such devices are put into service within their territory (art .14). It has to be noted that for the medical devices of class II a, there's a gap in the legislation.

The proposal of the new directive adds that member States shall take all necessary measures to ensure that the information referred to in the above two paragraphs, with the exception of information on custom-made devices, is registered immediately in the database EUDAMED.

Confidentiality

In the proposal on the new regulation, article 20 (which previously maintained all information available under the Directive as being confidential) has been relaxed to allow certain information on all devices to be publicly available and to allow a method of making other information non-confidential, such as summary information on the approval of high risk devices.

The following information shall not be treated as confidential:

- information on the registration of persons responsible for placing devices on the market in accordance with article 14,
- competent authority vigilance reports in accordance with article 10,
- data relating to certificates issued, modified, supplemented, suspended, withdrawn or refused.

Moreover the Commission may determine the conditions under which other information may be made publicly available.

European Database[27](EUDAMED)

In order to allow the exchange of regulatory data on devices in the different member states a European data collection system was set up. EUDAMED is a secure web-based portal acting as a central repository for information exchange between national competent Authorities and the Commission. It comprises a database with high quality operational data loaded in accordance with the specifications set out in the medical

[27] http://ec.europa.eu/idabc/en/document/2256/580

devices Directives and an information exchange system that acts as the driver between the relevant bodies in the European Commission Services and Member States. It will contain regulatory data with regard to the registration of manufacturers and devices as mentioned above, data relating to certificates issued, modified, supplemented, suspended, withdrawn or refused and data obtained in accordance with the vigilance procedure (art. 14 a). The focus is placed on ensuring the effective collection and visualisation of all relevant information concerning medical devices. In case of problems with a device, the vigilance module collects vigilance information relative to that device. This gives an overview to every Member State of the incident history of a device present on the market.

EUDAMED could benefit different parties. For citizens, by publishing and immediately distributing vigilance reports to all Member States, EUDAMED could increase the safety of patients across Europe. For public administrations because a common European database would be a great asset for National Competent Authorities, especially when trying to remain vigilant or in conducting Europe-wide investigations or issuing warnings. For medical device manufacturers since launching new products on the market becomes easier avoiding the negative impact of regulation on new innovations. For professionals since a central database will guarantee more control and transparency of the European medical device market.

Where a Member State considers in relation to a given product or group of products, that, in order to ensure protection of health and safety and/or to ensure that public health requirements, the availability of such products should be prohibited, restricted or subjected to particular requirements, such products should be withdrawn from the market, or their placing on the market and putting into service should be prohibited or restricted, it may take any necessary and justified transitional measures.

In that scope, it shall then inform the Commission and all other Member States giving the reasons for its decision. The Commission shall, whenever possible, consult the interested parties and the Member States. Where the national measures are justified, the Commission shall adopt the necessary Community measures. In case the national measures are unjustified, the Commission shall inform all Member States and the consulted interested parties.

The system got a legal basis in the Directive on medical devices but is not transposed to all member states yet. Several experts have expressed their concern on the feasibility and desirability of this database. Several countries seem to have their own data collection system and prefer to maintain their existing way of functioning.

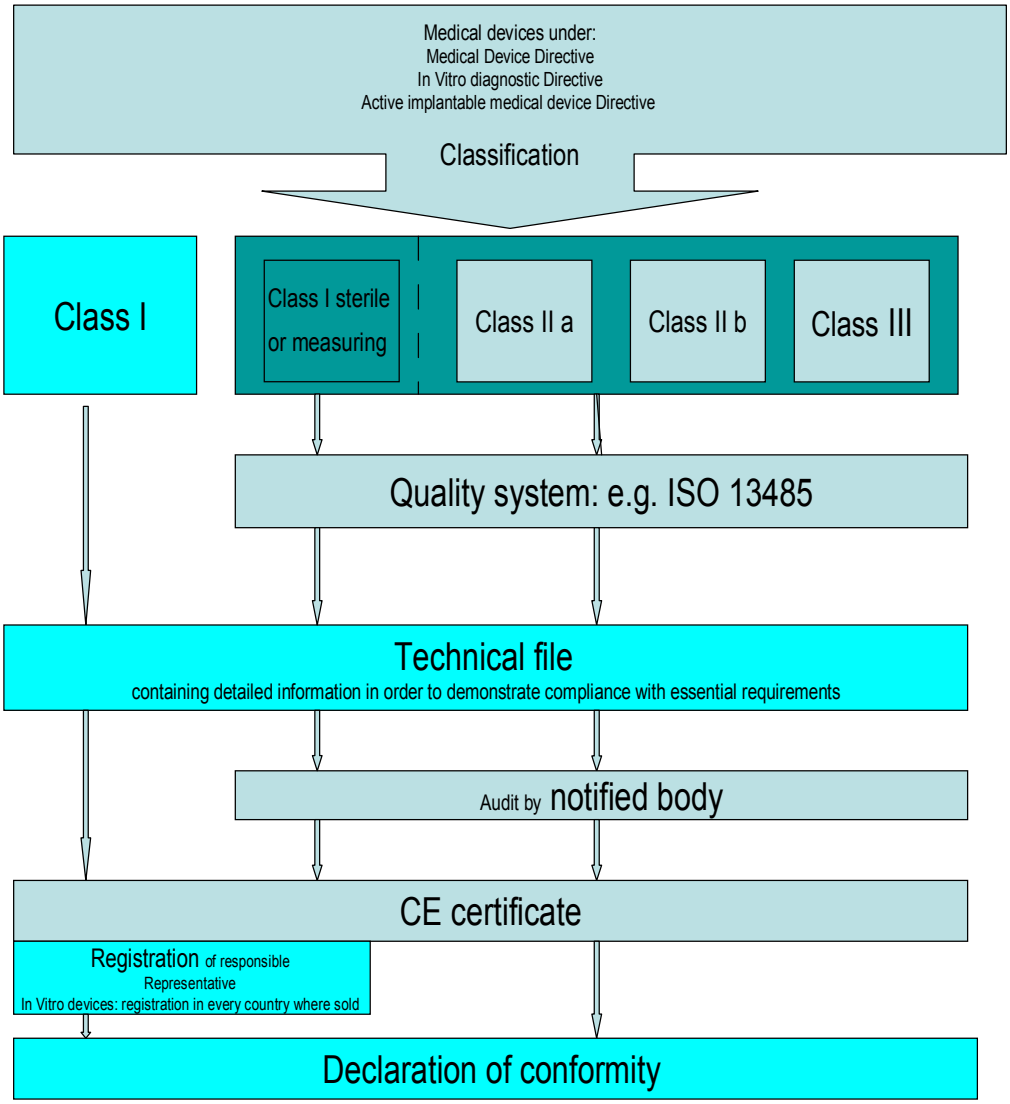
Information on incidents occurring following placement of devices on the market

The necessary steps must be taken by the member states to ensure that any information regarding incidents involving malfunctioning, inadequacy in labelling or instructions leading to the death of the patient or to serious deterioration of health and information regarding technical or medical reasons leading to the systematic recall of devices of the same type, is recorded and evaluated centrally.

Where a Member State requires medical practitioners or the medical institutions to inform the competent authorities of any incidents referred above, it shall take the necessary steps to ensure that the manufacturer of the device concerned, or his authorized representative established in the Community, is also informed of the incident.

After carrying out an assessment, if possible together with the manufacturer, Member States shall immediately inform the Commission and the other Member States of the incidents referred to above for which relevant measures have been taken or are contemplated.

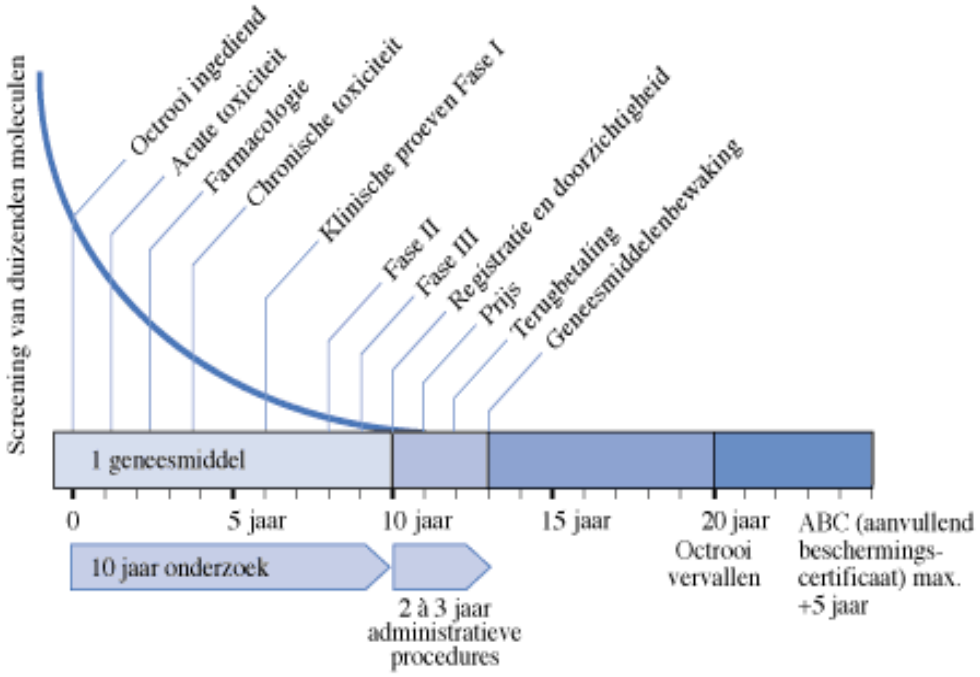
Figure 4: Schematic representation of the main constituents of the European directives



- **In the proposal of the new directive on medical devices there are some attempts to clarify the clinical evaluation of devices in order to obtain the CE mark, in particular for Class III devices and implants. There is, however, no specific procedure for the appraisal of clinical efficacy or (cost-) effectiveness required in the process of approval for marketing. Solely the assessment of safety of the device and the quality of the manufacturing process is required.**
- **Due to therapeutic advances and the growing complexity and sophistication of devices, scientific and technical expertise by the notified bodies cannot always be provided at national level. Therefore cooperation on the European level should be enhanced.**
- **At the European level there are some attempts to help European authorities conduct market surveillance on medical devices through information exchange. In that scope EUDAMED, an information system for exchanging legal information related to the application of European Union Directives on medical devices, has been created and should be supported, despite the reluctance of some member states.**

5 PROCEDURES FOR THE DEVELOPMENT AND REIMBURSEMENT OF PHARMACEUTICALS: THE EXAMPLE OF BELGIUM

Figure 5: Hypothetical research and development curve of "new pharmaceuticals"[28]



Before pharmaceuticals are introduced to the market, their clinical efficacy and safety have to be proven.[29] Therefore, first screening of the biological effectiveness in animals, pharmacological studies in vitro and in animals, toxicological studies in animals and pharmacokinetic studies in animals are performed. Then the method for large scale production of the drug is elaborated.

In the next phase, clinical evaluation is performed by means of clinical trials on patients in three phases. In phase I the safety of the product is tested on healthy volunteers. Dosage is evaluated. Phase II aims at proving the efficacy of the product. Therefore a limited number of patients are selected. For some of these pharmaceuticals placebo-controlled randomised trials are performed. In phase III a larger number of patients are gathered to compare the therapeutic efficacy and toxicity of the new drug with the standard treatment. In figure 5, the development curve of new pharmaceuticals is illustrated.

After the new pharmaceuticals have entered the market there should be a continued surveillance in order to detect adverse effects (pharmacovigilance).

The research and development of pharmaceuticals from the production of new molecules to the introduction to the market takes approximately 11 to 13 years: 10

[28] From www.pharma.be
[29] For the European legal framework on medicinal products see http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev1.htm

years for the research and time for the administrative procedures, previously 2 to 3 years.

The administrative procedures include the registry, the price setting and the procedure of the reimbursement request, where recent changes in legislation shortened the major part of the procedure to 180 days.

If a company wants a drug to be reimbursed in Belgium, a request has to be submitted to the Drug Reimbursement Commission (CTG/CRM, Commissie Tegemoetkoming Geneesmiddelen/Commission de Remboursement des Médicaments). At the same time the pharmaceutical company has to introduce the price request at the ministry of economic affairs. The commission can ask for expert assistance in order to determine the quality and the completeness of the dossier. Sixty days after the submission of the file, the experts of the CTG/CRM have to communicate a definitive assessment report. The firm can react during the 20 following days. Ninety days after the introduction of the dossier the firm has to report the price that has been communicated to them by the Minister of Economic affairs to the CTG/CRM.

Based on this price and the report of the experts, the CTG/CRM will prepare a motivated proposal regarding the class of added value, the conditions of reimbursement, the category of reimbursement, the reimbursed group and the reimbursement price. This file is presented to the minister of social affairs who will ask the Financial Inspection for advice. Moreover the approval of the Minister of Budget has to be obtained. The Minister of Social affairs has to decide within 30 days whether the product will be reimbursed or not. If no decision has been taken, the request of the firm is automatically accepted. The total term within which a decision has to be taken is 180 days.

For class 1 and class 2 pharmaceuticals there is a re-evaluation on the effectiveness after one and a half and after three years.

6 PROCEDURES FOR EMERGING TECHNOLOGIES IN SELECTED COUNTRIES

6.1 THE "IDEAL" PROCEDURE

HTA refers to the processes and mechanisms designed to ensure efficacy, safety, clinical effectiveness and cost-effectiveness in health service delivery. HTA is the systematic process of identifying new medical technologies, evaluating their key dimensions and effects, and monitoring their diffusion into clinical practice.

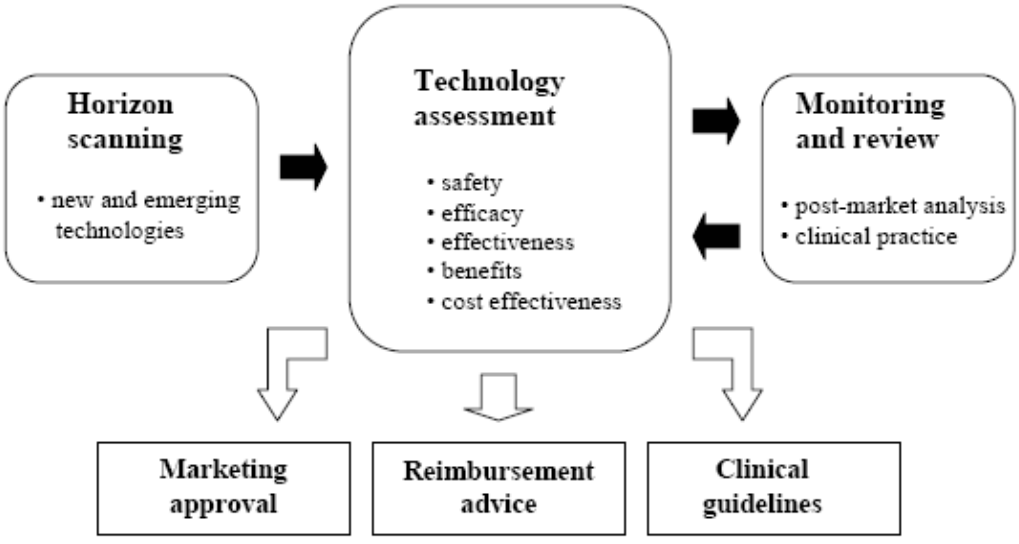
The HTA process generates or assembles information which is used to make policy, funding and clinical decisions. Its primary purpose is to provide objective information to support health care decisions and policy making at the local, regional, national and international level.

Ideally, the HTA process should comprise three main stages (figure 6):

- horizon scanning: an 'early warning' system to identify new and emerging medical technologies and new evidence on deficiencies and safety problems of existing technologies that may have a significant impact on the healthcare system;
- health technology assessment: the in-depth evaluation of the key attributes (safety, efficacy, quality, effectiveness and, if possible, cost-effectiveness) of emerging technologies;
- monitoring and review: periodic re-assessment of a technology's use in practice, such as its rate of diffusion and how it has affected the healthcare system (for example, in terms of costs and health outcomes).

However, as we shall see in the description of the national procedures for the assessment of emerging technologies (see below), not all countries follow this ideal three-step procedure. Further, while some countries have separate procedures for the assessment of pharmaceuticals and non-pharmaceutical technologies, others use a unique assessment procedure for all health technologies.

Figure 6: Schematic representation of the process of HTA[30]



[30] Adapted from Productivity Commission. Impacts of Advances in Medical Technology in Australia. Research Report, Melbourne. 2005 (Figure 8.1, page 179)

6.1.1 Horizon scanning

Early warning, horizon scanning or forecasting systems are the first stage of HTA. Early warning systems are a mechanism for identifying emerging medical technologies (pharmaceuticals, devices and procedures) of importance to a health service, and for disseminating this information. Identification of technologies might occur, for instance, at the point in their development when they are tested on a human being for the very first time.

The aim of early warning systems in the healthcare sector is thus to identify potential healthcare technologies expected to diffuse into that sector in the years to follow. An early assessment of the technology's potential effects and consequences can then be performed if needed.

Early warning systems have been part of the regular approval processes in a few European countries for some years. More recently, systems have developed in many other European countries and are known to be in place (though at different levels of development) in Denmark, England and Wales, France, the Netherlands, Norway, Spain, Sweden and Switzerland. With the recent creation of EUnetHTA, in 2005, a more widespread and systematic use of horizon scanning activities within Europe is expected in the future. One of the specific objectives of EUnetHTA is indeed to effectively monitor emerging health technologies to identify those that will have the greatest impact on health systems and patients.

Countries outside Europe with functioning horizon scanning or early warning programmes include Canada, Israel, and Australia and New Zealand.[31] Various strategies are used to identify new and emerging medical technologies, such as searching the scientific and medical literature, liaising with industry,[8] scanning marketing approvals and trial registers, and direct communication with clinicians.

6.1.2 Health technology assessment

HTA encompasses processes and mechanisms to assess effectiveness and cost-effectiveness in health service delivery. It can be an important instrument for informing and guiding decisions of patients, practitioners, hospitals and other purchasers of technology, as well as informing governments and health insurers about appropriate levels of reimbursement for technological advances.[14]

Medical devices are often significantly improved after first market launch. This may pose the question of whether institutes should offer provisional guidance on the "first generation" products or wait until it can give more definitive guidance on later developments. However, the need for guidance is likely to be most acute immediately after market launch, or in any case at the point at which the new technology first starts to diffuse into routine use to any appreciable extent.[32]

6.1.3 Monitoring and review

Monitoring may indicate when a more detailed review is needed, for instance, a re-assessment may be triggered if utilisation trends in practice diverge greatly from those predicted. Re-assessments consider new evidence that has become available since the initial technology assessment, which may lead to revisions in indications, restrictions, reimbursement and clinical guidelines.[14] Consequently, monitoring can play a role in determining whether a new procedure or device is clinically and cost-effective.

6.2 OVERVIEW OF THE PROCEDURES WORLDWIDE

A survey of different countries that often have a long tradition of HTA and a study of the major constituents of their processes used to assess emerging technologies will be used to inspire a new procedure for Belgium. Noteworthy is the fact that during our

[31] http://www.euroscan.bham.ac.uk/WebEuroScanReport.pdf

[32] Department of Health, National Assembly for Wales. Clinical guidance from the national institute for clinical excellence: timing and selection of topics for appraisal. A discussion paper. 2002.

survey we noticed that in several countries the structure of organisations and of procedures is still evolving. Consequently, our description may omit parts since certainly not all current or planned changes related to the dynamics of the devices domain could be captured.

The main purpose of this survey however, was to catch the aspects in other countries that could serve for our Belgian model. Hereafter, a summary (table 2) and brief description of the nine included countries is given. In appendix a more elaborated description is provided for every individual country.

Table 2: existing procedures in a selection of countries (for abbreviations, see legend)

Country	Horizon scanning	HTA	Early assessment	Registration/ notification	Post-market surveillance	Conditional reimbursement
UK	NHSC is the main institute for horizon scanning in the UK. The institute also hosts Euroscan, a collaborative network of HTA agencies	- NICE (Technology Appraisal Programme) - NCCHTA (NHS HTA Programme) - NHS PASA CEP and others	- NHSC (Technology briefings) - NICE (Interventional Procedures Programme)	MHRA - details of manufacturer and the medical devices they are placing on the market	Adverse events should be reported to the MHRA and the NPSA MHRA: - mandatory for manufacturers. - voluntary system for persons involved in use, maintenance or provision of a device. MHRA issues Medical Device Alerts	Trusts can fund the development and on-going costs of new technology either from surplus income received under Payment by Results, or from the agreed funding of the costs using a 'pass-through payment'.
Australia	- ASERNIP-S - NHSU ASERNIP-S and NHSU are part of ANZHSN	- AHTA - NZHTA	- TGA, advised by MDEC - MSAC, supported by ASERNIP-S - The PDC, supported by CAGs	- TGA licenses Australian manufacturers of therapeutic goods. - Products: ARTG: (a) 'registered': products having a higher level of risk (b) 'listed': products having a lower level of risk DEAL: electronic applications for entry ARTG.	TGA conducts post-market surveillance and investigations of reported problems: - manufacturers are required to report the problem to the TGA. - voluntary reporting provisions for medical device users.	Whereas for pharmaceuticals evaluations are the responsibility of drug manufacturers or suppliers, MSAC may provide funding for a defined period during which further evidence can be gathered for new technologies that show promise of being cost-effective.

US	Organizations with horizon scanning functions in the USA include - ECRI, - UHC, - and Hayes Inc.	OMAR, MTPPI, UBC (formerly MedTap), RAND, Others…	- ECRI, UHC, Hayes Inc. - FDA's CDRH: reviews requests to research or market medical devices. - health insurance organizations (e.g. Blue Cross and Blue Shield's TEC)	FDA's CDRH: - Premarket Notification 510(k) - PMA - investigational device exemption - Establishment registration - Medical Device Listing	FDA - MAUDE: for manufacturers and users - MedWatch: for consumers or health professional FDA may order a manufacturer to conduct post-market surveillance FDA issues warning letters	
		AHRQ's COE oversees the EPCs				
Canada	CADTH ("Emerging Drug List" and "Health Technology Update")	National level: CADTH Regional level: AETMIS, MAS, IHE	- CADTH ("Issues in Emerging Health Technologies") - AETMIS - MAS (assessment of the evidence available collected in a "vignette" on which decision for future action is based)	Therapeutic Product Directorate of Health Canada: Class II to IV (highest risk categories) must obtain a Medical Device License demonstrating the device is safe and effective for its intended application. No such license required for Class I devices.	MedEffects (Health Canada's Marketed Health Products Directorate): programme providing centralized access to health product safety information. The programme is based on health professionals' and consumers' adverse reaction reports.	Upon recommendation from MAS (OHTAC), the Ontario Ministry of Health provides temporary funding for field assessment of new technologies in selected study sites. Data analysis performed by an independent research centre.
The Netherlands	- Health council	- ZonMW - GR - CVZ - CBO - TNO - iMTA - Others…	- ZonMW (early evaluation and medical innovation programme)	VWS - cluster medical technology of the health care inspectorate: Address of the registered place and the device category	Ministry of health, sports and welfare: cluster medical technology of the health care inspectorate: Obligatory for manufacturers	Funding (max. 50%) of selected studies in the scope of the early evaluation and medical innovation programme (ZonMW)
Denmark	- DACEHTA	- DACEHTA	- Mini - HTA	DMA: - Register of Danish manufacturers of Class I, custom made devices and procedure packs	- DMA	/

Finland	No systematic horizon scanning	- FinOHTA	- MUMM project	- NAM: - Register: Name and address of the company, place of business, identification data of the medical device, details of the certificates or rejections by the notified body and other information required for market control	- NAM - Obligatory for the manufacturer	/
France	CEDIT	National level: HAS Regional level: CEDIT	CEDIT (within the general HTA process)	AFSSAPS ensures compliance with laws and regulations concerning market entry and introduction of products	Post-marketing materiovigilance of medical devices managed by the AFSSAPS. The AFSSAPS periodically issues a "Bulletin des vigilances".	National: Programme supporting innovative and expensive technologies to encourage their diffusion (STIC). Financed by the Ministry of Health. Regional: CEDIT may give funds to set up complementary evaluations within AP-HP hospitals.
Belgium	- No systematic horizon scanning	- KCE	- KCE	Section medical devices of the Directorate General pharmaceuticals/DG medicaments: for class I devices and custom made devices: - the name - the address of the registered place - the description of the device - the identity of the notified body	Section medical devices of the Directorate General Pharmaceuticals/DG medicaments: - Obligatory for manufacturers, distributers, notified bodies, physicians, persons responsible for the reception, storage and distribution of the device	- Art. 35 § 3 Category 5 - Conventions

AETMIS: Agence d'Évaluation des Technologies et des Modes d'Intervention en Santé (Quebec), AFSSAPS: Agence Française de Sécurité Sanitaire des Produits de Santé, AHRQ: Agency for Healthcare Research and Quality, AHTA: Adelaide Health Technology Assessment, ANZHSN: Australian and New Zealand Horizon Scanning Network, AP-HP: Assistance Publique des Hopitaux de Paris, ARTG: Australian Register of Therapeutic Goods, ASERNIP-S: the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical, CADTH: Canadian Agency for Drugs and Technologies in Health, CAGs: Clinical Advisory Groups, CBO: National Organization for Quality Assurance in Hospitals, CDRH: Center for Devices and Radiological Health, COE: Center for Outcomes and Evidence, CVZ: Health care insurance, DACEHTA: Danish Centre for Evaluation and Health Technology Assessment, DEAL: Device Electronic Application Lodgement system, DMA : Danish medicines agency, EPCs: Evidence-based Practice Centers, FinOHTA : Finnish Office for Health Technology Assessment, GR: Health council, HAS: Haute Autorité de Santé; IHE: Institute for Health Economics (Alberta), that recently integrated the Alberta Heritage Foundation for Medical Research (AHFMR), iMTA: The institute for medical technology assessment, KCE: Federaal Kenniscentrum voor Gezondheidszorg/Centre d'expertise pour les soins de santé, MAS: Medical Advisory Secretariat (MAS) of the Ontario Ministry of Health and Long-Term Care , MAUDE: Manufacturer and User Facility Device Experience Database, MDEC: Medical Device Evaluation Committee, MHRA: Medicines and Healthcare products Regulatory Agency, MSAC: Medical Services Advisory Committee, MTPPI: Medical Technology & Practice Patterns Institute, MUMM : Managed uptake of medical methods, NAM: National agency for medicines, NHSC: National Horizon Scanning Centre, NHSU: National Horizon Scanning Unit, NPSA: National Patient Safety Agency, NZHTA: New Zealand Health Technology Assessment, ODBT: Office of Devices, Blood and Tissues, OMAR: Office of Medical Applications of Research, PDC: Prostheses and Devices Committee, PMA: Premarket Approval, STIC: Soutien aux Techniques Innovantes Coûteuses, TEC: Technology Evaluation Center, TGA: Therapeutic Goods Administration, TNO: Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek, UBC: United Biosource Corporation, UHC: University HealthSystem Consortium, VWS: Ministry of health, sports and welfare, ZonMW: Dutch organisation for health care research and innovation of care.

From our international comparison of available procedures for emerging technologies, the Australian and UK systems can be considered as the most complete ones. Both systems show a lot of similarities.

First of all, an active system of horizon scanning is available, i.e. NHSC in the UK which hosts the collaborative network of HTA agencies 'Euroscan', and NHSU and ASERNIP-S in Australia which are part of ANZHSN.

Secondly, both countries perform early assessments of new and emerging technologies. In Australia, ASERNIP-S assesses new surgical procedures and provides advice to MSAC. For prostheses and devices, clinical advisory groups provide advice to the PDC. In the UK, NICE's Interventional Procedures Programme (replacing SERNIP) supports people in the NHS in the process of introducing new procedures. The Interventional Procedures Advisory Committee (IPAC) makes recommendations to NICE about the safety and efficacy of interventional procedures and other aspects such as the conditions under which the procedures should be used. Furthermore, IPAC may also select procedures for referral to the Review Body for further investigation. This body organises data collection and informs NICE as a matter of urgency of any procedure that appears to be associated with an unduly high rate of adverse events. Finally, NICE issues guidance to the NHS in England, Wales and Scotland.

In both countries, details of manufacturers and devices have to be registered, respectively to MHRA and TGA in UK and Australia. Particularly for Australia, a difference is made between products with a high and low level of risk to become respectively 'registered' or 'listed' on the ARTG. The high risk products do not only have to be evaluated for quality and safety but also for efficacy. Another unique characteristic of the Australian system is the electronic applications system 'DEAL'. Concerning post-market surveillance, both countries have a mandatory reporting system for manufacturers and a voluntary system for users. Finally, with respect to reimbursement, both countries also have a possibility of conditional or interim funding. In the UK trusts can fund the development and on-going costs of new technologies either from surplus income received under Payment by Results, or from the agreed funding of the costs using a 'pass-through payment'. In the latter, trusts and hospitals may negotiate about the additional funding of new innovative technologies not yet covered by their tariff.

Next to the UK and Australia, the US also has a well elaborated procedure in comparison to several EU countries. Horizon scanning is performed by several institutes that also provide early assessments. (Early) HTA is performed by both governmental, private and health insurance companies. The most remarkable difference with EU countries are the requirements for placing devices on the market. Medical devices are classified into three classes depending on the intended use of the device, indications for use, and risk. Regulatory control increases from Class I to Class III. Most Class I devices are exempt from Premarket Notification 510(k); most Class II devices require Premarket Notification 510(k); and most Class III devices require Premarket Approval (PMA). An investigational device exemption (IDE) can be provided to allow the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a PMA application or a Premarket Notification (510(k)) submission to FDA. The 510(k) is a premarketing submission made to FDA to demonstrate that the device to be marketed is as safe and effective to a legally marketed device that is not subject to PMA. In contrast with the EU system FDA's PMA requires the demonstration of a medical device's clinical effectiveness as a precondition for marketing. This is not the case with CE marking.

Comparable to the UK and Australia, FDA registration consists of both establishment registration and medical device listing. With regard to the post-market surveillance system, a system for manufacturers and users (MAUDE) and for consumers or health professionals (MedWatch) exists. The FDA may also order a manufacturer to conduct post-market surveillance. This is described as the active, systematic, scientifically valid collection, analysis, and interpretation of data or other information about a marketed device. Finally, safety alerts issued by FDA are publicly accessible and everybody can receive these alerts by e-mail.

In Canada, the Canadian Agency for Drugs and Technologies in Health (CADTH) started his Horizon Scanning Service in 1997. CADTH provides horizon scanning reports for drug (Emerging Drug List) and non-drug (Health Technology Update) health technologies. There does not seem to be any formal horizon scanning activities at the provincial level. Health technology assessments are performed both at the national (CADTH) and provincial level (AETMIS in Quebec, MAS in Ontario and IHE in Alberta). Assessment of emerging technologies is performed within the general HTA process in CADTH and AETMIS since, depending on the maturity of the technology (diffusion stage, evidence available) and on the timelines, a brief or a thorough assessment of the technology is performed. MAS (Ontario) only has a system of conditional reimbursement of emerging technologies. Funds are provided by the Ontario Ministry of Health to specified academic health centres for a new technology to be used in a specific target group and under specified conditions, as part of a field evaluation. Based on the results of the evaluation, a recommandation about the introduction of the technology as an insured health service is made. Though conditional reimbursement of emerging technologies is not formally put in place at the national level, it is a component of the Pan-Canada Health Technology Strategy that is currently being developed in Canada.

In Denmark, the Danish Centre for evaluation and health technology assessment (DACEHTA) operates an early warning system which aims to inform relevant decision makers of new health technologies and the expected consequences in health care. Moreover DACEHTA is also the key body in Health Technology Assessment. Currently, there have been some attempts to elaborate a process of managed uptake of new technologies. In this scope DACEHTA prepared in 2000 a form and a guide on the acquisition of medical devices for hospitals aimed at inspiring to a systematic assessment before new investments are made, the so called 'mini HTA'. Later the use of HTA forms has been enlarged to the introduction of new treatments and technologies.

The Danish Centre for Health services (DSI) research has a collaboration agreement with DACETHA regarding the provision of expert advice in relation to HTA projects. Typically, DSI will carry out the economic evaluation, but they also carry out analyses of the patient perspective and organisational elements in health technology assessments.

In Finland there's no structured process of early warning, although the Finnish Office for Health Technology Assessment (FinOHTA) tries to keep up to date. FinOHTA tends to produce, support and co-ordinate HTA in Finland. In the scope of the early evaluation of new and emerging technologies, the MUMM project has been launched. The aim of the project is to develop collectively national rules for the uptake of new medical technologies. For the uptake of new technologies, some kind of horizon scanning will be built in. Moreover, the mini-HTA procedure developed in Denmark will be translated and disseminated for use.

In the Netherlands horizon scanning is primarily performed by the Health Council in order to allow a proactive policy for different stakeholders, such as for instance the ministry of health, sports and welfare. The ministry of health, welfare and sports can commission parties, such as ZonMw, to execute research programmes. Particularly in the scope of assessment of new and emerging technologies a new innovation sub-programme has been created by ZonMw. The programme allows targeted fostering (up to 50%) of developments that could enhance the efficiency of health care. It focuses on new technologies in their second or third stage of development, where their safety has been established, there is some indication as to their efficacy, but there is insufficient information to underpin a cost-effectiveness study. In order to be admitted to the innovation programme there are some requirements with regard to the research design.

A structured follow-up trajectory after the research performed in the scope of the innovation programme similar to the procedure in Australia or UK however does not exist. Moreover there is no formal link between assessment of new technologies and reimbursement policy.

In France, the Committee for the Evaluation and Diffusion of Innovative Technologies (CEDIT) is a member of Euroscan. Although it is one of its missions, the CEDIT has no

formal horizon scanning activity. The Haute Autorité de Santé (HAS) plans to join Euroscan in 2007. HTAs are performed partly at the national level (HAS) but mainly at the regional level (CEDIT). Assessment of emerging technologies is performed within the general HTA processes of CEDIT. Specific funds for field assessment of technologies for which information is insufficient to make a recommendation of diffusion may be allocated by the CEDIT and by the Ministry of Health (Programme de Soutien aux Techniques Innovantes Coûteuses - STIC).

In Belgium finally, no systematic horizon scanning is organised to date. Assessments of emerging technologies were and are being done by individual members and experts of the 'Technische Raden' of the RIZIV/INAMI. Since 2003, the Belgian Health Care Knowledge Centre (KCE), has performed several HTA's to support this decision making process. Recently, the KCE also started with rapid assessments on specific requests of the Minister of Health and Social Affairs or of the RIZIV/INAMI. Conditional reimbursement of new implants as emerging technology is possible in the health insurance law (so-called category 5), and has been used for the controlled uptake of several implants. Part of them was accompanied by some type of research design often through a mandatory registration of data on included patients. Only one topic from category 5, i.e. EVAR (Endovascular Repair of Abdominal Aortic Aneurysms)[3933] has led to a full HTA by KCE in collaboration with the Intermutualistic Agency IMA/AIM so far.

- **Ideally, the HTA process should comprise three stages: horizon scanning, health technology assessment, and monitoring and re-assessment.**
- **Horizon scanning is not present in all countries. Several institutes have joined forces through Euroscan, a collaborative network of HTA agencies.**
- **Registration/notification procedures exist in all studied countries.**
- **All countries in our review have HTA institutes. Separate procedures for rapid assessments of emerging technologies are not always clearly present.**
- **In theory, post-market surveillance systems exist. Next to mandatory systems for manufacturers, voluntary systems for users are often available.**
- **Some countries have possibilities to provide interim funding or conditional reimbursement.**

[33] Bonneux L, Cleemput I, Vrijens F, Vanoverloop J, Galloo P, Ramaekers D. HTA Le traitement électif endovasculaire de l'anévrysme de l'aorte abdominale (AAA). Bruxelles : Centre Fédéral d'Expertise des Soins de Santé (KCE) ; 2005. KCE Reports vol. 23B. Ref. D/2005/10.273/33

7 PROPOSITION OF A FUTURE PROCEDURE FOR THE ASSESSMENT OF EMERGING TECHNOLOGIES IN BELGIUM

7.1 CURRENT SITUATION OF CONDITIONAL REIMBURSEMENT OF NEW IMPLANTS IN BELGIUM

According to the Belgian legislation, the conditional reimbursement of new implants already has a regulatory base (within category 5). In the Belgian health insurance law, implants are defined as:

"*Every instrument, machine, tool, every substance or other item used alone or in combination, the accessories and the software for the well functioning of it included and addressed by the producer to be used solely in patients and primarily for the following purposes:*

- Diagnosis, prevention, surveillance, treatment or alleviation of a disease, wound or handicap
- Examination, replacement or change of the anatomy or of a physiological process

The primary aimed effect on the human body cannot be obtained by pharmacological, chemical or immunological means or by the metabolism, but can be supported by means similar to those described above.

The implant is implanted entirely or partly in the human body or in a natural gap or replaces a part of the epithelium tissue; the implant is meant to stay for at least 30 days after the intervention. The implant can only be removed by a surgical or a medical intervention."

Following this definition, the implants are part of the medical devices. Article 35 of the medical nomenclature distinguishes 5 categories of implants: category 1 being the active implants, category 2 being the high risk implants, category 3 being the medium or low risk implants, category 4, the custom made implants. Category 5 concerns implants for limited clinical use or new implants for which the Technical Council for implants (TRI/CTI) decides that an evaluation is necessary. This means each implant which is meant to be at the disposal of physician-specialists, in order to be used in an appropriate clinical human environment during a specific period of evaluation and/or to be used for a specific indication. It encompasses

- A new or a slightly modified version of an implant of category 1 or 2 figuring on the limitative lists for an accepted indication, or an implant figuring on the limitative list but used for a new indication; or
- An entirely new implant for which the "Technical Council for Implants" (TRI/CTI) considers that a period for evaluation of the reimbursement is necessary. Table 3 gives an overview of implants that were or are being financed via category 5.

According to the category of the implant, there are different conditions for reimbursement and surcharges for the patient. For category 5, requests for reimbursement are introduced to the TRI/CTI (figure 7). The TRI/CTI proposes the modalities of the evaluation, the criteria for reimbursement and the amount of reimbursement by social security. It transmits this proposition to the "Commission for Conventions between the hospitals and sickness funds" (OI/CCI). The OI/CCI advises on the proposition and transfers its advice for approval to the "Insurance Committee".

The proposition contains a proposition of a convention with scientific societies, physicians or hospitals. It determines the conditions for reimbursement:

- the target group and the criteria of inclusion of the patients are defined
- an evaluation period is scheduled

- norms aimed for the implantation centres/physicians are set
- the number of implants or patients is (can be) limited
- the feedback between the physicians and the system is compulsory in order to be reimbursed
- the reimbursement and the evaluation are specified
- the evaluation method is described
- the reimbursement procedure is clearly defined. Mostly, the "College of physician-directors" (CGD/CMD) is charged with the examination of the individuals file.

Before the end of the agreed period of evaluation, the peer review group competent in the domain at stake should present a report based on the collected data and the scientific literature on behalf of the TRI/CTI and the CGD/CMD. The report also contains a proposition for a permanent reimbursement regulation. This proposition is then transmitted with the advice of the CGD/CMD to the TRI/CTI, who works out, in case of a favourable evaluation, the proposition into a full reimbursement regulation. It transmits its proposition to the OI/CCI. The OI/CCI advises on the proposition and submits its advice to the "Insurance Committee" for approval.

Figure 7: current procedure for reimbursement of implants (Art. 35, §3, cat. 5 medical nomenclature):

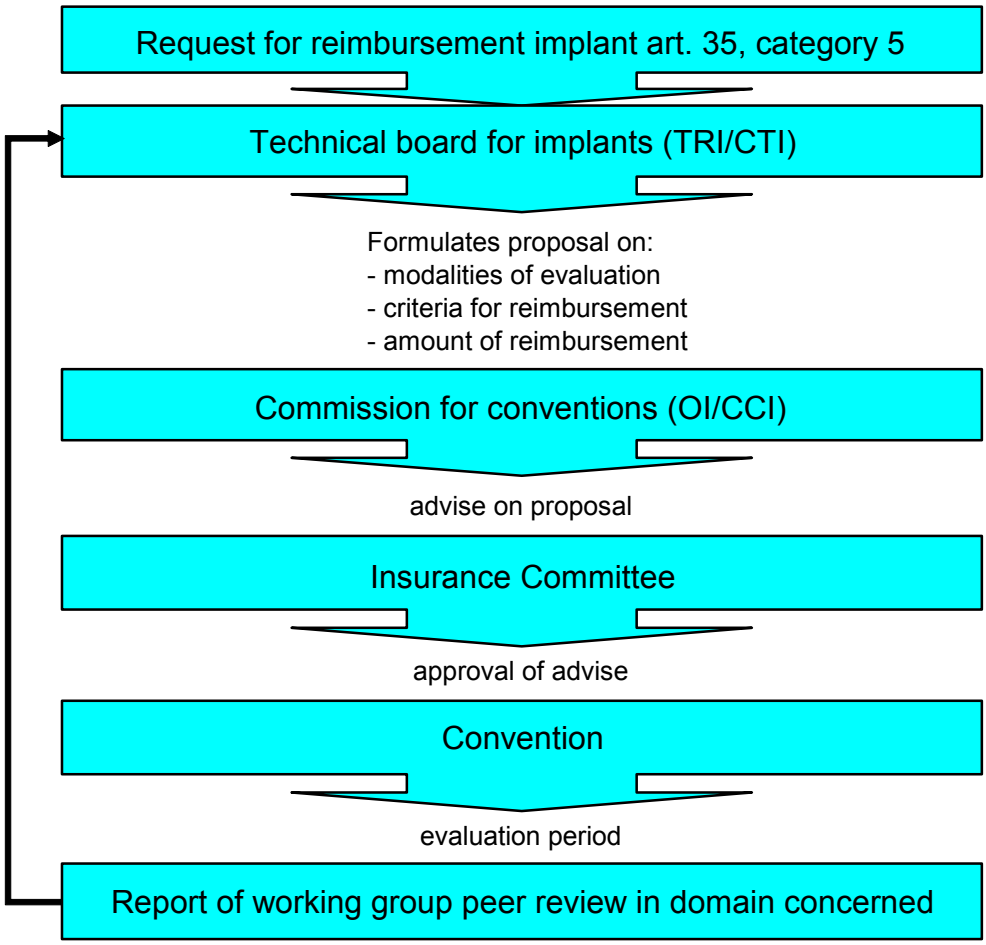


Table 3 : Overview of the implants or invasive devices reimbursed via Art. 35, §3, cat 5 medical nomenclature

Implant/invasive device	Outcome	Population/indication Subject of evaluation/purpose	Research design and setting	Intermediary Monitoring evaluation and follow-up
Vagal nerve stimulation (for refractory epilepsy)	expires 31/12/2007	- Formulating indications and contra-indications for the reimbursement of vagal nerve stimulation in a specific target population.	- Centres of reference in the domain of epileptics - Collaboration with such a centre if the rehabilitation after the implantation takes place outside the centre of reference	/
Deep brain stimulation	Expected in 2008	- Specified target population - formulating indications and contra-indications for the reimbursement of DBS in an evidence based way for specific target population - Setting procedures for reimbursement for the different interventions (stimulation d'essay – definitive implant- revision) - evaluation of the short and long term results of DBS - evaluation evolution of the direct and indirect costs	- Team «Abnormal movements» (EMA): Collaboration of Neurosurgeon with experience in DBS with other neurosurgeon to guarantee continuity Neurologist with experience in DBS with other neurologist to guarantee continuity Psychologists with experience in neuropsychology Personnel needed to provide the material and give instructions to the patient Video installation Composition and names of the team members has to be declares to INAMI	-Intermediary evaluation of the results at Meeting of "societé belge de neurochirurgie», the teams "mouvements anormaux" in 2005 and 2007 - The "service Soins de santé" can ask the EMA at the any moment for additional information concerning the research
Neurostimulation for inoperable chronic ischemia of the lower limb	- Expired 1/04/2004 - convention will be modified and prolonged	- Specific target population – Restriction to max. 50 patients per year - -Formulating indications and contra-indications for the reimbursement of neurostimulator after evaluation of three years - setting the conditions and the specific modalities of the intervention	- Specialist working in a centre with a daily experience of obstructive vascular disorders and who are able to perform a "atériograhie doppler" - The preoperative measure of the diffusion of oxygen en transcutane may be realised in an other specialized centre	- Intermediary report in the third year by the "groupe de travail Neurostimulation de l'association belge de chirurgie vasculaire" + Proposition of definitive regulation - Information on the follow up of the patient 6 months and 1 year after the implantation has to be sent to the peer review committee At any moment a meeting can be organised
Artificial heart for «bridge-	- Prolonged till	- Specified target population	- Hospital with a continued activity of	- /

to-transplant»	30 june 2007	restriction to 20 patient/ year	heart transplantation in the three years preceding 1/1/1999 (date of the start of the convention)	
Endoprostheses for abdominal and thoracic aortic aneurysm	- HTA by the KCE - discussion on reimbursement - expires 31/12/2006 but new convention is being prepared: approved by the TRI	- Provision of endoprothesis to specified target group of patients with abdominal or thoracic aneurysm during an evaluation period of 5 years	- Specialists working in a centre with a daily experience of endovascular procedures and surgical treatment - Personnel: at least 2 specialists in vascular surgery and radiology + educated in interventional radiology + 50% of their activity is related to vascular surgery. Implanting specialist is trained in the technique endoprothesis + performed at least 10 implants - Accessibility of the service 24/24 - Availability of Minimum of radiological material - Availability of Urgency and intensive care - Limited to centres with agreement for the programme B 3 "Cardiac pathology" for thoracic endoprosthesis	- Registration of the results of EVAR (EUROSTAT) enabling the evaluation of clinical effectiveness and the costs - HTA by the KCE that demonstrated that EVAR is not cost-effective
Contralateral cochlear implant	Period of evaluation if 42 patients have undergone an implantation	- Specific target population children< 12 years old - Period of evaluation ends , if 42 patients have undergone an implantation	- Physician ORL – no further specifications - Every centre can maximally implant 15 patients	An agreement council (conseil d'accord) is created, in which members of the participating centres are seated: - Production of an annual report of the results - Final conclusion 1 year after the last implant - Yearly evaluation of the patient that got an implant during 5 years
Drug eluting stents for diabetic patients		- Evaluation during 2 years of the provision of drug eluting stents to specific target population - Setting conditions and specific	- An institute with an agreement for the partial B2 and B3 of the programme "cardiac pathologie"	- Intermediary report (after one year) on the results (number of implantations, number of patients, mean number of implants per

		modalities for reimbursement		procedure, % implantation de DES compared to classic stents and PTCA), demographic data of the patient, re-interventions CABG, PTCA) by the Belgian working group on invasive cardiology and the working group "Cardio" of the TRI + Proposition of definitive regulation At any moment a meeting can be organised
Neurostimulation for inferior urinary tract dysfunction	- discussion to include in nomenclature	- Evaluation during 5 years of neurostimulators for specified target group - Restriction to 80 patients/year	- Urologists working in a centre with a daily experience in Urodynamics + specified material - Expertise in neurophysiological examinations du nervus pudendus and reflexes du plancher pelvien - Adequate education for the personnel	

7.2 PROPOSITION FOR A FUTURE PROCEDURE

For a good understanding of the following procedure it has to be noted that the current Belgian legislation ('category 5') only focuses on the conditional reimbursement of new implants. In order to continue this line of thought the procedure described underneath and in figure 8 primarily focuses on new and emerging implants. However, the application of the procedure can easily be extended to other health technologies (excluding pharmaceuticals where at least non-inferiority clinical trials proving clinical efficacy are mandatory for medicines evaluation) and interventional procedures.

This report provides a preliminary procedure that will need to be evaluated and adapted progressively. However, the proposed procedure can be applied within the current legal framework. Currently, the legislation for the reimbursement of implants and invasive devices is being modified.[34] However, with regard to the reimbursement of new and emerging technologies for which no or insufficient evidence is available nothing has been changed. As the primary scope of this report is to propose a new procedure for emerging technologies, solely the basics of the new legislation will be treated. The primary purpose of the new legislation is to protect patients from high financial co-payments (so called 'supplements') that are nowadays often linked to implants and to clarify the conditions for reimbursement of implants and invasive devices in general.

Ideally, such a procedure for emerging technologies is preceded and fed by a system of organised horizon scanning. Since this topic falls largely outside the scope of this procedure in the current local context, it will not be discussed in this proposition. However, there are several rational arguments to implement pro-active horizon scanning that will be elaborated on in the discussion chapter.

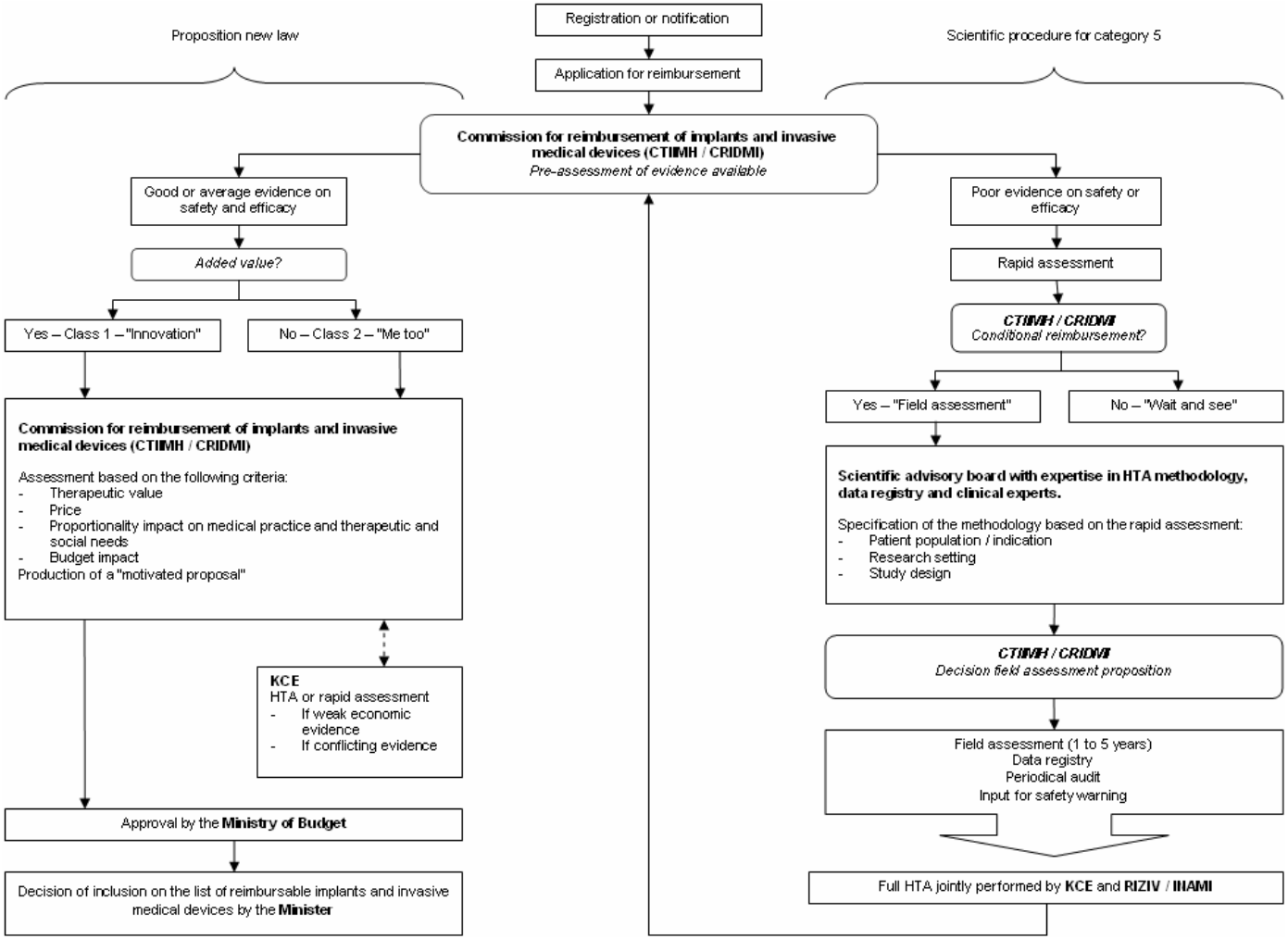
7.2.1 Step 1: Registration and notification

One of the principles of the draft of the new legislation is the 'notification' of implants with a CE mark to the "Dienst voor geneeskundige verzorging" of the RIZIV/INAMI (apart from some exceptions e.g. implants and invasive devices for clinical research, custom made devices, etc.). The purpose is to provide a list of the existing implants on the market. Only implants that have complied with the obligation of notification can be the subject of a reimbursement according to the legislation. The CE mark nor the notification to the RIZIV/INAMI in itself assesses the clinical effectiveness or the quality of the devices or the implants at stake.

For devices with a minor impact, notification following the attribution of a CE mark can be sufficient. For new and emerging technologies with a major impact such as invasive class III devices more than a proof of the technical device safety is needed. From a societal and patients perspective, it can certainly be defended that before such devices are placed on the market, clinical studies on the patient safety and clinical effectiveness should first be available and they should be registered, as is the case in the FDA of the US. Such a register should then be centralized nationally and publicly accessible in order to guarantee transparency and public accountability. Pragmatically and taken into consideration the current national and European liberal legislation and available resources, an up-to-date and easily accessible notification list providing details of all implants marketed on Belgian sole is an important first step.

[34] http://www.dekamer.be/kvvcr/showpage.cfm?section=flwb&language=nl&rightmenu=right&cfm=/site/wwwcfm/flwb/flwbn.cfm?lang=N&legislat=51&dossierID=2594

Figure 8: future procedure for new emerging technologies (right side of the graph).



7.2.2 Step 2: Availability of evidence

In order to categorize an emerging health technology a pre-assessment on the available evidence for both efficacy and safety of the technology has to be performed. Based on a critical appraisal of the available evidence on a new implant, it is possible to rate the evidence (including the absence of any clinical evidence and only a CE label). Practically, the Technical Council for Implants or in the future the Commission for Reimbursement of Implants and Invasive Medical Devices (CTIIMH/CRIDMI) will then be able to judge whether a new implant enters in class 1 or class 2 (see next point) or whether category 5 for an emerging experimental implant should be considered as an option.

Different levels of evidence can be designated from the pre-assessment (table 4). The KCE generally uses the internationally developed GRADE system[35] for grading the quality of evidence for guidelines. This type of classification can be applied to other domains and disciplines as well. Its major advantage is its simplicity and ease of use.

Table 4: Quality of evidence and definitions[36]

Quality	Definition
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

In one of the first applications of the GRADE system, the 'low' and 'very low' category were merged, leading to three possible gradings of the quality of evidence: 'High', 'Moderate' and 'Low'.[37]

Specifically for the domain of medical implants and interventional procedures, the definitions of the GRADE system are still too vague and should be refined to specific research designs that can be applied to the invasive intervention related to the implantation of these devices. For this purpose, several more detailed definitions have been developed. One is the most renown and for this project probably most practical classification system of the Australian Safety & Efficacy Register of New Interventional Procedures (ASERNIP) of the Royal Australian College of Surgeons. The evidence is again classified in 3 levels, ranging from good to poor. In their definition (table 5), not surprisingly, high quality RCTs are regarded as the best kind of evidence for interventions, with the lowest risk of bias. It may however be unpractical or unethical to undertake an RCT for some procedures, which means that these will never be classified in the highest level.

[35] http://bmj.bmjjournals.com/cgi/content/full/328/7454/1490

[36] Guyatt G, Vist G, Falck-Ytter Y, Kunz R, Magrini N, Schunemann H. An emerging consensus on grading recommendations? ACP J Club. 2006;144(1).

[37] Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an american college of chest physicians task force. Chest. 2006;129(1):174-81.

Table 5: Rating of the quality of evidence according to ASERNIP.

Evidence rating	Definition
Good	Most of the evidence is from a high-quality systematic review of all relevant randomised trials or from at least one high-quality randomised controlled trial of sufficient power. The component studies should show consistent results, the differences between the interventions being compared should be large enough to be important, and the results should be precise with minimal uncertainty.
Average	Most of the evidence is from high-quality quasi-randomised controlled trials, or from non-randomised comparative studies without significant flaws, such as large losses to follow-up and obvious baseline differences between the comparison groups. There is a greater risk of bias, confounding and chance relationships compared to high-quality randomised controlled trials, but there is still a moderate probability that the relationships are causal. An inconclusive systematic review based on small randomised controlled trials that lack the power to detect a difference between interventions and randomised controlled trials of moderate or uncertain quality may attract a rating of average.
Poor	Most of the evidence is from case series, or studies of the above designs with significant flaws or a high risk of bias. A poor rating may also be given if there is insufficient evidence.

7.2.2.1 Good or at least average evidence of efficacy as well as safety – class 1 and class 2 devices within the new legislation

In cases where at least average evidence exists for both safety and efficacy of a new device, the importance of the outcome that the new health technology changes and the magnitude and relevance of these changes needs to be assessed. Therefore, the question has to be raised whether the new device or technology has a potential added value. Added value can in theory be defined as either the added therapeutic value of a new technology compared to existing therapeutic alternatives (clinical benefit) or increased cost-effectiveness (the same clinical effect for a lower cost or a better clinical effect for the same cost). It has to be noted that the concept of added value in the draft text of the new legislation on the reimbursement of implants and invasive devices solely focusses on added "therapeutic" value.

In order to guarantee more legal certainty about the timing of the evaluation of the request for reimbursement, a new procedure with time limits has been set up by the draft legislation. Moreover a new commission, "Commission for Reimbursement of Implants and Invasive Medical Devices (CTIIMH/CRIDMI)", has been created. Different university representatives, representatives of the insurers, of the professional organisations of physicians and hospital pharmacists, representatives of producers, importers and distributors of implants and invasive medical devices, representatives of the hospital managers, representatives of the minister of social affairs, of the minister of health affairs and the minister of budgetary affairs and of the "Dienst voor geneeskundige evaluatie en controle" are seated in the commission. A limitative list of reimbursable implants or invasive devices defined in art. 34, 4 bis of the health insurance law will be created. If a company applies for reimbursement of an implant, the commission decides within 45 days on the admissibility of the request. If the information needed for the evaluation of the request is insufficient the applicant will have to provide additional information. A new period of 45 days will start after the reception of the additional information. Then the commission has to formulate a motivated proposition within 180 days after the date of declaration of admissibility. If it appears that additional information is needed the term can be suspended. The motivated proposal of the "Commission" needs to be approved by the Minister of Budget. If the Minister of Budget fails to respond within 30 days after the request for approval, the proposal is presumed to be approved. The final decision on the adoption of the implant at stake on

the list of reimbursable implants has to be taken by the minister within 60 days after the term of 180 days. If within this term there is no decision of the minister, the decision is presumed to follow the commissions' proposal. In case of absence of a proposal by the commission within the term of 180 days and consequently absence of a decision of the minister within the postulated term, the request is presumed to be refused. This latter procedure is however currently discussed in the senate. The same procedure is followed for applications for reimbursement of an invasive medical device. However, the periods of 45 days, 180 days and 60 days are not applicable. If the demand for reimbursement of an implant is not made by a company (distribution or fabrication) those periods are not applicable either.

One of the criteria for reimbursement of the implants or the invasive medical device is the therapeutic value. In order to evaluate the therapeutic value, 2 classes have been distinguished in the new procedure. Class II implants or invasive devices have no established added therapeutic value compared to existing alternatives (so called 'me too' devices). Class I implants or invasive devices have an established added therapeutic value compared to other already existing therapeutic alternatives and refers to the implants or invasive devices that are new or have a new indication. Apart from the added value, there are other criteria for the evaluation of the request for reimbursement such as the price, the budgetary impact on health insurance, the relation between the costs for health insurance and the therapeutic value, and the interest of the implant or the invasive medical device in medical practice related to the therapeutic and social needs. This implies that offering a qualitatively equal implant or invasive device as an existing alternative at a more beneficial price can be a profound reason to allow reimbursement. In case there are doubts on the cost-effectiveness or the proportionality of medical practice and the therapeutic or social needs it might be necessary to perform a rapid assessment or a full HTA, although this is not mandatory in the current legislation. Since 2003, the national health insurance institution can ask the KCE to perform rapid assessments (such as e.g. for total disc replacement) or full HTA's (such as e.g. EVAR[38]).

7.2.2.2 Poor evidence for efficacy or safety – a scientific procedure to evaluate category 5 implants as emerging technology

If there is no or poor clinical evidence available, a process of managed uptake of the technology or the device can be considered. Following an industry push or a user pull the question for reimbursement of new and emerging technologies will most often be raised quite rapidly. A rapid assessment can support the strategy for managed uptake to be followed.

Rapid assessment

Internationally, faced by demands of decision makers under pressure, an increasing number of HTA agencies are more and more encountering in rapid assessments of new technologies. The differences between a rapid assessment and a full HTA are as yet not clear. In table 6, an attempt is made to describe these differences, based on the experiences so far in Canada, UK and Denmark and our own short experience with rapid or urgent assessments. One major difference is the time frame of the assessment, where a rapid assessment is done in about half the time of a full HTA. This requires more experienced researchers and clinicians with research experience. Good project management is essential in such a short timeframe. Input of industry is demanded in both cases. The systematic review of the literature on clinical effectiveness is done as rigorously by the same methodology in general. The economic evaluation part is restricted to a synthesis of the economic literature, without the often time consuming economic analysis or economic modelling on primary local data. The scope of a rapid assessment will in general be more limited, requiring an even more intensive delineation

[38] Bonneux L, Cleemput I, Vrijens F, Vanoverloop J, Galloo P, Ramaekers D. HTA Le traitement électif endovasculaire de l'anévrysme de l'aorte abdominale (AAA). Bruxelles : Centre Fédéral d'Expertise des Soins de Santé (KCE) ; 2005. KCE Reports vol. 23B. Ref. D/2005/10.273/33

of the topic at the beginning of the project. The shorter time frame will also influence the final editing process.

Table 6: Similarities and differences between rapid assessment and full assessment

	Rapid assessment	Full HTA
Time frame	3-6 months	6-15 months
Scope	Specific topic, technology oriented	Can be much broader, even disease oriented
Input from industry	Yes	Yes
Clinical effectiveness	Systematic review literature	Systematic review literature
Meta-analysis	Often not possible	If data allow pooling
Cost-effectiveness	Literature synthesis	Literature synthesis
Primary data collection	No (or limited)	Often to describe local real life situations
Modelling	No (or simple model)	Possible
Estimation budget impact	If possible, but with larger uncertainty	Yes
Organisational and patient (ethical) issues	Not or limited	Yes
Involvement of clinical experts	Yes	Yes
External review (validation)	Variable	Variable

Depending on the outcome of a rapid assessment the competent RIZIV/INAMI bodies can opt for the strategy to "wait and see" if e.g. major safety concerns exist and if there are ongoing clinical trials about to provide evidence on efficacy and safety, or a strategy of conditional and temporary reimbursement. In both cases safeguards for safety and budgetary impact will have to be taken. A "wait and see" strategy risks leading to an uncontrolled dissemination of a possibly inferior or harmful technology being paid by the patient or by health insurance through the assimilation of other health insurance billing codes. Previous HTA reports already forwarded examples of this phenomenon (e.g. in the case of carotid stenting[39] and bariatric surgery[40]).

[39] Bonneux L, Cleemput I, Vrijens F, Vanoverloop J, Galloo P, Ramaekers D. HTA Le traitement électif endovasculaire de l'anévrysme de l'aorte abdominale (AAA). Bruxelles : Centre Fédéral d'Expertise des Soins de Santé (KCE) ; 2005. KCE Reports vol. 23B. Ref. D/2005/10.273/33

[40] Lambert M-L, Kohn L, Vinck I, Cleemput I, Vlayen J, Leys M, et al. Traitement pharmacologique et chirurgical de l'obésité. Prise en charge résidentielle des enfants sévèrement obèses en Belgique. Health Technology Assessment (HTA). Bruxelles: Centre fédéral d'expertise des soins de santé (KCE); 2006. KCE reports 36B (D/2006/10.273/29)

The rapid assessment can lead to the following results:

1. For the *efficacy* of the device:

- At least as efficacious compared to comparator procedure(s) or efficacy is not yet sufficiently determined since it is an emerging technology
- Less efficacious compared to comparator procedure(s)

2. For the *safety* of the device:

- At least as safe compared to comparator procedure(s) or
- safety was not yet determined sufficiently or it is less safe compared to comparator procedure(s)

In the rapid assessment, an overview of all the ongoing clinical trials should be provided, including as much as possible all planned trials.

If the rapid assessment concludes that the emerging procedure is less efficacious or that there are still substantial safety concerns, this technology can not be regarded as an emerging technology (yet) and a wait and see policy will be the logical conclusion. In the other cases the assessment will provide arguments for a promising emerging health technology (possibly as efficacious and at least as safe) and if budgetary possibilities exist, conditional reimbursement can be allowed. Conditional reimbursement should serve two objectives: Firstly, the controlled diffusion of a possibly innovative technology preventing uncontrolled experimenting and possible patient harms and avoiding budgetary spillage. Secondly, during the period of conditional reimbursement scientific - clinical and health economic - evidence should be produced.

7.2.3 Step 3: Conditional reimbursement and scientific evaluation by field assessment (hospital HTA)

In this step a clear timeline can be distinguished: a preparatory phase in which the research design and formalities of the implementation are discussed. Next, over a period extending in general from 1 to 5 years the evaluation phase including data registry, intermediary analysis and possibly auditing. And finally a full HTA concluding on the clinical effectiveness and cost-effectiveness of the new technology.

Research design

The controlled diffusion of an emerging technology is accompanied by a research design to objectively prove the hypothesized added value of the technology. In order to specify the research design behind the conditional reimbursement an advisory expert group with, next to clinical experts, methodological experts in clinical research, HTA and data registry is pivotal. At this stage the presence of patient groups is not advisable since patient issues will be assessed during the HTA later on (cfr. infra). The members of such a group should be selected for their scientific merits and not merely for their representation. It should also be made clear which contribution the manufacturer or distributor will make, since health insurance is financing part of its research and development.

In order to strengthen the evidence base of the emerging technology, either a controlled clinical trial, ideally with random allocation to the emerging technology and an established treatment, or an observational trial with longitudinal data registry and possible audit are the two main research designs. In some cases an RCT will not be possible, based on practical issues such as feasibility or problems with patient recruitment. Rarely, ethical issues will prevail. Although, from a scientific and societal point of view, for the majority of certainly invasive emerging technologies this will not be the case. To the contrary, uncontrolled dissemination of experimental implants without evidence that more benefit than harm is invoked to patients can be coined as unethical behaviour.

For the conditional reimbursement the use of the new technology will often be restricted to a specific population and for specific indications. Moreover the research setting has to be specified. In that scope it is necessary to establish criteria determining which hospitals or which research settings can be eligible for the research at stake. Clinical experiments can only be performed if they are guided by scientific interest. In order to guarantee the independency and transparency of the research team eventual conflicts of interest must be declared.

Data registry and audit

Depending on different criteria such as the amount of patients involved, the nature of the technology of the device at stake, and the potential budgetary impact on health insurance, the evaluation period should be specified and in general will cover one to five years. During this period, data gathered in the collaborating hospitals should be registered and possibly audited. This task can be assigned to the RIZIV/INAMI in collaboration with KCE and other useful partners. In order to allow a timely intervention of the RIZIV/INAMI in case of lapses in the research (e.g. extreme mortality rates in one centre), data should be exploitable for intermediary analysis and the research team should present a brief yearly progress report. At the end of the evaluation period there should be an evaluation of the clinical effectiveness and cost-effectiveness by a full HTA. In that scope the results of the HTA can offer an independent guiding tool for decisions of the competent bodies of the RIZIV/INAMI.

7.2.4 Step 4: Vigilance for medical devices

Apart from a registration procedure, the vigilance system should be publicly accessible in order to guarantee the continuity of safety and quality of the device. Nowadays, the Belgian legislation on medical devices states that the producer, the authorized representative, the distributors, the notified bodies, the physicians and the persons responsible for the reception and the distribution of devices have to inform the directorate general Pharmaceuticals (www.health.fgov.be and click on 'medicines') immediately on incidents with devices.[41] Depending on the nature of the device the incident is reported to the competent body and the Evaluation commission, in which physicians, engineers and pharmacists are seated. The commission can also ask for the opinion of external experts. Following the advice of the competent body and the eventual remarks of the producer or his authorized representative, the evaluation commission proposes the appropriate measures. The competent governmental body informs immediately the producer or the authorized representative and the person that declared the incident, the European commission and the other member states. There are also regulations in case a device, although CE marked, is not conform to the general requirements. Since the purpose of the report is not to give an exhaustive overview of all possible procedures, this procedure will not be described.

Today, information on incidents and failures of devices is not publicly accessible. Needs for more transparency have also been translated in the proposal of the new directive on medical devices. In that scope the regulation on the confidentiality has been relaxed (cfr. supra). Vigilance reports for example are no longer considered to be confidential information. According to the European economic and social committee a reasonable amount of non-confidential information, in a concise form, should be made available to the stakeholders directly concerned. Information on product safety and quality and on post-marketing surveillance should also be made available to health operator associations, to enable them to use the medical devices more knowledgeably and safely[42]. The FDA is a good example in this case: every professional and every patient or citizen has public access to constantly updated news on new devices and ongoing

[41] https://portal.health.fgov.be/portal/page?_pageid=56,513103&_dad=portal&_schema=PORTAL

[42] http://europa.eu.int/eur-lex/lex/Notice.do?hwords=medische%20hulpmiddelen~&pgs=10&list=431738:cs,429612:cs,427440:cs,427439:cs,427438:cs,419433:cs,412398:cs,412397:cs,406322:cs,402838:cs,&val=431738:cs&nbl=133&lang=en&visu=&checktexte=checkbox&pos=1&page=1

procedures[43] including information on medical devices recalls and safety information[44]. In addition, the FDA Safety Information and Adverse Event Reporting Program called MedWatch provides an e-mail notification service[45] and even RSS feed of timely safety information, that can be joined freely. In some other countries, similar systems albeit less developed, exist (AFSSAPS's Bulletin des vigilances [46]). Some scientific or professional associations have developed their own private system for distribution of safety information.

It is clear that an individual notification of a medical device failure should be treated with caution since the problem will often have a clear explanation related to the operator and not necessarily a technical failure of the implant. However, when several similar failures accumulate and experts, industry and other international sources agree that a serious safety issue is a problem, then a publicly accessible information system with safety warnings is to be recommended in addition to already existing circuits from industry and government. Currently, the manufacturer or distributor of the implant contacts the physicians concerned and possibly a 'dear doctor' letter is disseminated. From personal communications with several experts we learned that this system performs quite well and that there were indeed some serious safety problems for particular implants in the past (e.g. certain pacemaker leads, certain breast implants and lens implants) as in other countries. We were unable to publicly access that type of safety warnings.

[43] http://www.fda.gov/cdrh/index.html
[44] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/index.cfm
[45] http://www.fda.gov/medwatch/
[46] http://agmed.sante.gouv.fr/htm/10/mv/indmv.htm

8 CONCLUSION

Dealing with emerging and promising possibly innovative technologies where the evidence on (cost-) effectiveness is often still lacking is a major challenge. Specifically for implants and invasive medical devices the procedure of conditional reimbursement described in art. 35 category 5 of the medical nomenclature can be used. From an international perspective this legal framework is quite unique and offers clear opportunities for the managed uptake of possibly innovative emerging implants. However, no clear scientific procedure allowing the controlled introduction of an emerging technology and a health technology assessment with public reporting at the end of the experiment was developed in Belgium so far.

In this report, we proposed the framework for a future procedure for the assessment of new and emerging technologies in Belgium, in particular for new implants and invasive devices, within the current existing legal possibilities of the health insurance law. In the first place, the availability of procedures in other countries was investigated. The international overview of the available procedures demonstrates that the managed uptake of new and emerging technologies is in a relatively initial stage, with UK and Australia providing the relatively most advanced procedures. If procedures are available they differ according to and following the existing health care system. Furthermore, there are also enormous differences in the utilisation rate of devices in these different countries.

Our non-exhaustive descriptive overview has several limitations. In several countries health care systems are being reformed leading to changes in their procedures so that some of the information we gathered is probably already outdated. From the written information as well as from the several personal contacts we had, it remains unclear to what extent assessment procedures are actually used within each country. Another source of bias in our overview is caused by the fact that the majority of HTA agencies we contacted are publicly funded institutions most often working for government or social security. We did not retrieve information on how private insurers, managing a substantial part of the health care market in some countries next to the public system, deal with emerging technologies.

However, our overviews' main purpose was to serve as a source of inspiration for a framework for the rational and subsidized managed uptake of implants as emerging technology. From the international comparison we could indeed discover the major building blocks that should be taken into consideration in the framework we developed.

Managed uptake of emerging technologies should support innovation

Belgium is apparently one of the European countries where emerging technologies are quite rapidly introduced and adopted. Certain past practices such as the premature and free distribution of certain still experimental implants by the manufacturer to multiple hospitals and use on patients outside a proper research design were clearly inappropriate. However, manufacturers of devices will keep seeking for ways to have their emerging technology on the market. The 'category 5' conventions of the Belgian health insurance have already been used for the managed uptake of several implants successfully. However, a research design was often lacking, hampering a health technology assessment on the clinical effectiveness, cost-effectiveness and patient as well as organisational issues at the end of the convention.

The framework developed in this report and the existing possibilities for category 5 within the medical nomenclature offers an innovative approach for the Belgian health care system: the combination of a managed uptake that limits budgetary risks with the production of solid impartial evidence on the clinical effectiveness and cost-effectiveness of the emerging technology. We did not find a similar well elaborated procedure in other countries. By this, Belgian health insurance can play a leading role in the support and assessment of some promising innovative technologies in Europe. For the manufacturers that produce innovative devices with a so-called 'added value' the framework can offer several advantages: the managed uptake procedure allows the gradual and controllable introduction of an emerging device on the market preventing

wrong use and operator problems; a (partially or full) government supported clinical trial - either randomized or observational - and a health technology assessment forwarding impartial conclusions on the effectiveness, costs and possibly cost-effectiveness and in addition organisational and patient issues. The use of a scientific procedure for category 5 implants in itself is not expected to slow down the decision making process. To the contrary, once the competent bodies of the RIZIV/INAMI are considering a conditional reimbursement via category 5, the relatively short time frame of a rapid assessment is set. Next, the rapid assessment should be able to facilitate well-informed decisions. It should be clear that the use of such a framework should be well evaluated, both on the level of output and time frames, and undoubtedly adapted and optimized after a few years.

Those implants where no reimbursement is asked or obtained and for which there is yet no evidence on clinical effectiveness and safety will remain in no man's land. Either the implant is being used in a good clinical trial with informed consent by the patient and financed by the manufacturer – in this case the clinical trial should have the approval of an ethical committee and registration – or the experimental implant is being paid by the patient outside a research setting with at most some type of registry from the manufacturer.

Do we need Horizon Scanning and Vigilance for medical devices?

Although somewhat outside the scope of this project, we also encountered that in the process of HTA, the actual dissemination of an emerging technology is ideally preceded by horizon scanning and followed by a system of vigilance. Currently, there is no structured horizon scanning for new and emerging technologies in Belgium such as instituted in several other countries (The Netherlands, UK, Denmark, Sweden, Canada, Australia, New Zealand) in the last 10-15 years. Often, horizon scanning is closely linked to the HTA activities in a country. Formalised and publicly available health technology assessment was only started in Belgium in 2003. The establishment of a list of all the implants voluntarily notified by the industry will shed some light on new implants coming on the Belgian market. This list however, can not be regarded as a full horizon scanning including proactive searching in different sources (medical literature, early warning systems, professionals, industry) and an early assessment of all emerging technologies, not only implants, that are retrieved. In the Netherlands, the Health Council developed an elaborate procedure for horizon scanning and early warning in a recent advice (2005/08) to the Dutch health minister. Resources at the KCE and INAMI/RIZIV are insufficient to develop a Belgian systematic and unbiased horizon scanning system.

Separate horizon scanning in every single European country is not efficient however and should be questioned in the particular case of Belgium. The devices market is clearly an international market and several member states of the EU will be dealing with the same technologies simultaneously. The EUNetHTA-project (2006-2008) that aims at developing an organisational framework for a sustainable European network for HTA and that is being co-financed by the European Commission (DG Sanco) includes Euroscan as a collaborating partner and contains a specific working package on emerging and new technology development and prioritization. For Belgium, KCE is an associate partner in the network. Another option for the future is a more close collaboration in the Benelux context.

There is clearly a need for more regulation in the field of implants and devices in general. In Finland, the devices market was only recently coined as 'the Wild West', meaning an unexplored territory compared to other sectors of health care such as e.g. pharmaceuticals. It can be argued that the pharmaceuticals and devices market differ substantially, which is true, but the major argument above all unrelated to the technology applied is the protection of patients from harms. Currently, health insurance law is being adapted offering a distinction between class I and class 2 but also a more rapid procedure, enabling a reliable and impartial evaluation for the reimbursement decision. At the end, a new procedure for medical devices may and should result in a faster and wider diffusion of innovative cost-effective technologies on the market.

Since it's beginning, the KCE has performed several HTA's for the RIZIV/INAMI. In the annual programme of the KCE, part of the HTA activity is specifically reserved for questions of the RIZIV/INAMI. More and more, as in other countries, there is a need for more rapid assessments in which safety, efficacy and economic implications should be considered. Such rapid assessments are particularly useful for new technologies before they become widely distributed. Several of the reports clearly forwarded evidence for the fact that the technical CE label does by no means provide evidence for the clinical effectiveness nor the real life safety and long term adverse events in the patient populations concerned. A scientific rapid assessment is not performed (at least we were not able to find any trace that part of the evaluation could be considered as some type of brief health technology assessment using established methods for the critical appraisal of clinical trial data). For health insurance, the efficacy (does this device work?) in itself is not that relevant. In reimbursement issues, the clinical effectiveness of the new technology especially in relation to a relevant comparator (does this device work better than a well established effective procedure with a better benefit/risk ratio?) and the cost-effectiveness are of more paramount importance for the decision process.

A legal device regulation should in addition not only deal with reimbursement issues, but ideally also with safety and quality issues. Currently, there is primarily information on technical safety (CE mark) of reimbursed implants and invasive devices. For class III implants clinical data on conformity with the 'essential requirements' (i.e. characteristics and performance of the device) or the justification why clinical data are not necessary, is required. This requirement is part of the assessment of the technical file by the notified bodies and it is unclear by which methodology these clinical data are critically appraised. Several implants and invasive devices easily obtained their CE label in the past, while there were at most ongoing clinical trials. For some devices, only several years later the first trials were published, possibly not showing clear clinical benefits. This highly questions the extent and the rigour of the CE labelling process. It can be regarded as a necessary first step to guarantee technical safety and good manufacturing of a device, but it's value in health technology assessment for health insurance is limited.

So, there is to our knowledge and as current practice confirms no requirement in Belgium as in several other European countries for high quality clinical trials proving clinical effectiveness for relevant and sufficiently long-term patient outcomes. Manufacturers can thus distribute their products to hospitals without many restraints. In case medical devices are not reimbursed by social security however, the budgetary impact for the patient can be a financial restraint to distribution of new medical devices, as far as they are not freely distributed.

The voluntary participation of manufacturers to a listing at the level of RIZIV/INAMI is one step forward. Such a list can not be considered as a sufficient guarantee for patient benefits and clinical safety specifically for invasive devices such as implants. To reply to this problem a registration system including evidence from clinical trials with relevant patient outcomes will be needed. It is regrettable that apparently not all European member states are willing to participate in a European database such as EUDAMED.

Information on systematic device failures and thus safety problems are primarily disseminated by the manufacturer to the physicians. Individual failures can be related to the operator and the public reporting of all these problems would probably lead to unnecessary patient anxiety and useless additional health care interventions. However, from patients' and societal perspective, a system of publicly accessible safety warnings with e-mail notification to physicians, hospital pharmacist and interested citizens is a service to be provided within the competence of government in the future. Moreover post market surveillance should be organised at the European level to ensure a rapid identification of potential problems. Despite the reluctance of some member states, the existence of an information exchanging system, such as EUDAMED, should be supported.

9 APPENDIX: PROCEDURES IN SEVERAL COUNTRIES

9.1 UK

9.1.1 Health care system

All legal residents of the United Kingdom are entitled to cover under the UK National Health Service (NHS). The NHS was created under the National Health Service Act 1946. It is predominantly funded through national taxation and is run by the Department of Health.

Health services are divided into "primary" and "secondary" and are provided by local NHS organisations called "trusts". Primary care covers everyday health services such as general practitioner's surgeries, dentists and opticians and these are delivered by "primary care trusts" (PCTs). There are about 300 PCTs in England. They are a crucial part of the NHS. The burden of prioritising service provision falls to PCTs. They decide what health services their area needs and have responsibility for making sure these are delivered efficiently. These organisations receive about 75% of the NHS budget and are subject to an obligation to keep within their financial allocation.[47]

Secondary care refers to specialised services such as hospitals, ambulances and mental health provision and these are delivered by a range of other NHS trusts. NHS trusts run most hospitals and are responsible for specialised patient care and services, such as mental health care. The trusts' role is to make sure that hospitals provide high quality health care and spend their money efficiently.[48]

Regulation and policy play an important role in determining which services are available within the NHS. Important components of the regulation include National service Frameworks; the work of NICE, and guidance from the Department of Health.[49]

- National Service Frameworks (NSFs), introduced in the 1997 White Paper, embodied new approach to rationing. They set national standards, identify key interventions for a defined service or care group that should be available, establish strategies to support implementation and outline ways to ensure progress within an agreed time scale (Department of Health, 1997).[50] By specifying national standards, they encourage the selection and adoption of some treatments and approaches, whilst rejecting others.[51]
- The National Institute for Clinical Excellence (NICE) publishes guidelines and advice for the public and for healthcare professionals in England and Wales (see further).
- The Department of Health is responsible for the overall planning, regulation and inspection of the health service. It develops policies and decides the general direction of healthcare.

9.1.2 Horizon scanning

The National Horizon Scanning Centre (NHSC) is the main institute for horizon scanning in the UK. The institute also hosts Euroscan, a collaborative network of health technology assessment agencies to exchange information and evaluate emerging technologies.

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[47] http://www.bbc.co.uk/dna/actionnetwork/A2454978
[48] http://www.bbc.co.uk/dna/actionnetwork/A2454978
[49] http://www.ehma.org/_fileupload/File/Projects/Benefit_Report_United_Kingdom.pdf
[50] Department of Health (1997) "The New NHS: Modern, Dependable." HMSO, London. (http://www.archive.official-documents.co.uk/document/doh/newnhs/newnhs.htm)
[51] Montgomery, J. Health Care Law. Oxford University Press, Oxford. 2003.

9.1.2.1 National Horizon Scanning Centre[52]

The National Horizon Scanning Centre (NHSC) is funded under contract by the Department of Health's R&D Directorate. This centre aims to provide advance notice to the Department of Health in England and Wales of selected key new and emerging health technologies (including changing applications and uses of existing technologies) that might require urgent evaluation, consideration of clinical and cost impact or modification of clinical guidance.

The scope of the horizon scanning activity includes health technologies in the broadest sense and includes pharmaceuticals, devices, diagnostic tests and procedures, surgical and other interventions, rehabilitation, and therapy, public health and health promotion activities.

Identification

A balance of sources is used to identify advances up to 5 years before launch in the National Health Service and includes: (i) focused routine scanning and (ii) a specialty-based work programme.

i) Focused routine scanning

These scanning processes are designed to identify urgent significant advances regardless of clinical specialty. Regular scanning of primary, secondary and tertiary information sources is undertaken by networking with research units and commercial developers, by extensive searching of specialist and general medical and pharmaceutical literature, news and financial reports, licensing agencies, and selected internet sites and databases. Individual health professionals and researchers can also propose technologies that may need attention.

ii) Specialty based work programme

A specialty review programme has been developed to ensure that all clinical specialties and technology types are allocated time for an in-depth investigation of new developments. The programme involves liaison with the Royal Colleges and other professional organisations in a specialty to (i) identify any gaps in NHSC's identification phase and (ii) help NHSC with the prioritisation of technologies in that specialty.

Filtration and prioritisation

Once technologies have been identified there is a multi-stage filtration and prioritisation process. This initially discards trivial developments and groups related technologies together. A search for additional information, including contacting commercial developers and clinical or technological experts in the field, is then undertaken to enable an assessment of potential significance. The criteria for selection to the National Horizon Scanning Centre's final list are that the technology is:

- emerging and likely to be available to the NHS in the next 3 years time, or
- new, or
- represents a significant change in indication or use of an existing technology, or
- is part of a group of developing technologies that, as a whole, may make a significant impact.

In addition it is thought that there may be:

- significant health benefit if the technology is widely adopted, or
- a major cost impact if the technology is widely diffused because of moderate to high unit costs and/or patient numbers and/or service re-organisation or training requirements, or

[52] http://pcpoh.bham.ac.uk/publichealth/horizon/index.htm

- indications that the speed of diffusion of the technology may be inappropriate given the available evidence (either too slow or too fast), or
- significant ethical, social, political or legal issues, or other issues and concerns related to the use of the technology, or
- current guidelines and clinical guidance will be significantly affected if the technology is adopted.

9.1.2.2 Euroscan[53]

The European Information Network on New and Changing Health Technologies (EuroScan) is a collaboration of researchers and policy makers interested in the early identification and assessment of new and changing health technologies. EuroScan's primary aim is to share and evaluate information on selected emerging health technologies or new applications of existing ones in order to address their effects and the anticipated short and long term consequences of their use for health care and society.

The EuroScan member agencies are the following:

- Agencia de Evaluacion de Tecnologias Sanitarias (AETS), Madrid, Spain
- Agencia de Evaluación de Technologías Sanitarias de Andalucía (AETSA), Seville, Spain
- Assistance Publique-Hôpitaux de Paris, Committee for Evaluation and Diffusion of Innovative Technologies, France (CEDIT)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Basque Office for Health Technology Assessment (Osteba), Spain
- Canadian Agency for Drugs and Technologies in Health (CADTH)
- Danish Centre for Evaluation and Health Technology Assessment (DACEHTA)
- Division of Medical Technology Policy (DMTP), Ministry of Health, Israel
- Health Council of the Netherlands (GR)
- Norwegian Knowledge Centre for the Health Services (NOKC)
- National Horizon Scanning Centre (NHSC), England and Wales (hosts the Secretariat)
- Swedish Council on Technology Assessment in Health Care (SBU)
- Swiss Federal Office of Public Health (SFOPH)

The long-term aim of EuroScan is to establish a permanent network among agencies and organisations in the field of HTA to:

- evaluate and exchange information on new and changing technologies,
- develop the sources of information used,
- share applied methods for early assessment, and
- disseminate information on early identification and assessment activities.

[53] http://www.euroscan.bham.ac.uk/position.htm, http://www.euroscan.bham.ac.uk/WebEuroScanReport.pdf

Other intentions of the EuroScan collaboration for the future are:

- To evaluate the exchange of early assessments and the use of the early warning database with the ultimate aim that the use of the database will be consolidated and become entirely routine for EuroScan members.
- To continue to support both member and non-member agencies who are establishing an early warning system.
- To develop a research programme partly to evaluate EuroScan activities and partly to inform a deeper understanding of the determinants of diffusion and impact in member countries.
- To consider wider access to the EuroScan database or limited fields within the database and to work towards becoming part of a European clearinghouse function.
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9.1.2.3 The National Innovation Centre[54]

The National Innovation Centre (NIC) will be launched in September as part of the Technology and Product Innovation directorate. This centre will work to speed up the development and adoption of technological innovations that deliver the best results for the patient. The NIC will provide a single point of entry to innovators of healthcare technology, whether an NHS employee or an external organisation. Through a web based assessment process, the NIC will consider ideas and products at every stage of development and will signpost them to the most suitable parties for further development. By identifying promising technologies and providing investment to the best innovative ideas coming from healthcare, the NIC plays an important role in bringing good ideas into frontline practice where they can have the greatest impact on patient care.[55] However, we may remarks that this institute's role is not primarily horizon scanning with the purpose of assessment but with the aim of supporting development.

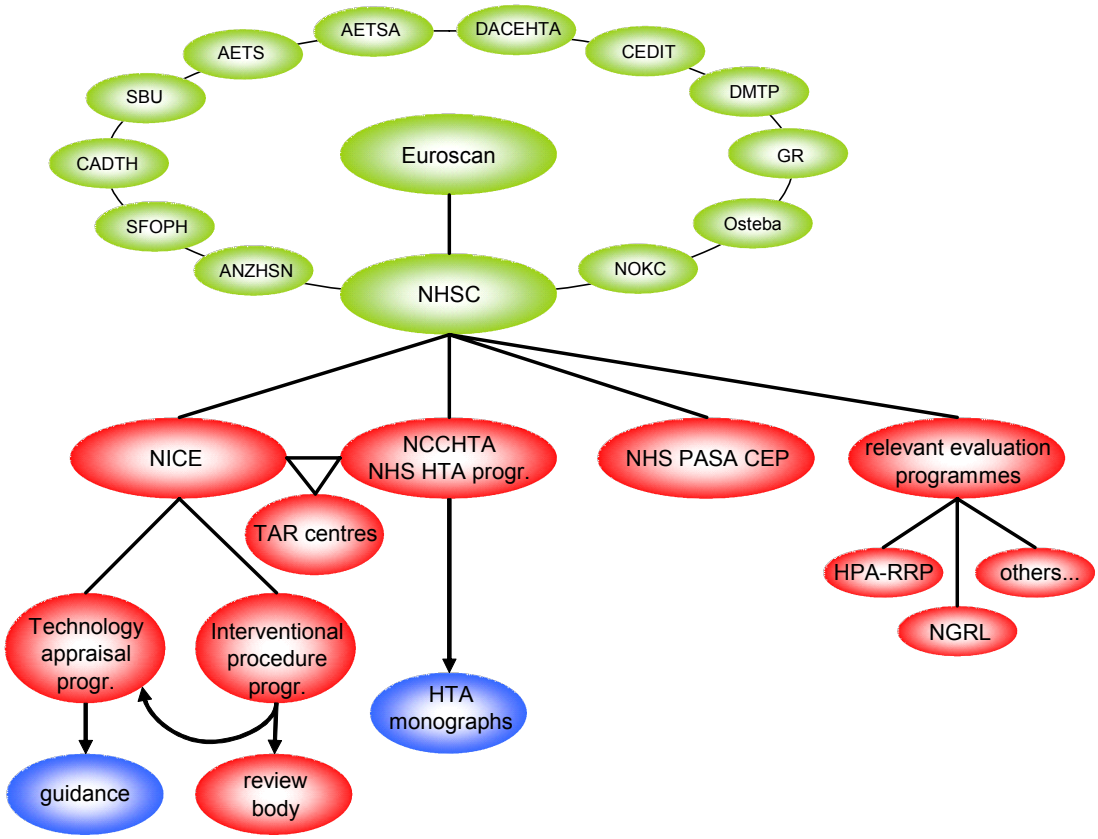
9.1.3 Medical technology assessment

The National Horizon Scanning Centre provides a first short assessment of new technologies which may be included in the National Institute of Health and Clinical Excellence's (NICE) work programme. The National Coordinating Centre for Health Technology Assessment (NCCHTA) supports and develops the NHS HTA programme and administers contracts for NICE Technology Assessment Reviews. The Centre for Evidence-based Purchasing and some smaller agencies such as the Rapid Review Panel of the Health Protection Agency are also involved in the assessment of new or emerging technologies. We have to remark that this structure is changing but a clear view on how this will look like is lacking for the moment. Figure 9 gives an overview of the current structure of horizon scanning and HTA in the UK.

[54] http://www.institute.nhs.uk/TechnologyAndProductInnovation/NationalInnovationCentre/Introduction.htm

[55] http://www.institute.nhs.uk/NR/rdonlyres/24B2D962-F96D-473D-8CE5-0B0A561B6283/0/Strategicplanoverview_20067FINAL.pdf

Figure 9: Horizon scanning and HTA in the UK[56]



9.1.3.1 National Horizon Scanning Centre's short assessments[57]

Information is provided to the Department of Health in the form of *technology briefings*. The briefings (approximately 4 pages long) include:

- a description of the technology,
- a description of the patient group (with estimated patient numbers),
- the current diagnostic or treatment alternatives,
- an estimated unit cost of the technology (if available),
- the current research evidence of clinical and cost effectiveness,
- details of any ongoing or related research activities, and
- an overall horizon scanning impact assessment in terms of estimated clinical, service and financial impact.

Until recently, the technology briefings are considered by a cross-directorate body within the Department of Health - The Advisory Committee on Topic Selection (ACTS) previously the Technology Advisory Group (TAG) for consideration of inclusion in the National Institute of Health and Clinical Excellence's (NICE) work programme. Other national customers are the NCCHTA (National Coordinating Centre for Health Technology Assessment) and The Interventional Procedures Programme at NICE.

[56] In all following figures, green and red respectively indicate horizon scanning and technology assessment.

[57] http://pcpoh.bham.ac.uk/publichealth/horizon/customers.htm

9.1.3.2 NICE and the Interventional Procedure Programme[58]

The National Institute for Health and Clinical Excellence (NICE) was established as a Special Health Authority in April 1999 to promote clinical excellence and the effective use of resources within the NHS. It is responsible, through technology appraisals, for providing national guidance on new and existing medicines and treatment within England and Wales. Topics for appraisal by NICE are suggested by a wide range of sources, including the National Horizon Scanning Centre, healthcare professionals, patient groups, and Department of Health policy teams.

NICE only appraises technologies that have been identified through a topic selection process and approved by ministers of health. In order to select a topic for assessment, two main criteria are applied. First of all, the guidance on the topic should promote the best possible improvement in patient care given the available resources. Factors include:[59]

- how the guidance relates to NHS clinical priority areas or government health-related policies
- the achievement of significant health benefits
- whether or not the conditions are associated with significant disability, morbidity or mortality
- the impact on NHS or societal resources (financial or other)
- the opportunity for disinvestment without detriment to patient care

Second, guidance on the topic must add value. There should be a sufficient evidence base for consideration. In addition, there must be existing or potential inappropriate practice (or variation in clinical practice) or variation in terms of access to treatment.

Once the Department of Health and the Secretary of State for Health have identified the technologies they wish NICE to appraise, the HTA programme commissions review groups from one of seven independent academic centres to produce Technology Assessment Reports (TARs). Within NICE, the Centre for Health Technology Evaluation develops technology appraisals and interventional procedures guidance.

Technology appraisal procedure

NICE is asked to look at particular pharmaceuticals and devices when the availability of the drug or device varies across the country. This may be because of different local prescribing or funding policies, or because there is confusion or uncertainty over its value. The aim is to end the uncertainty and help to standardise access to healthcare across the country.

Technology appraisals are recommendations on the use of new and existing medicines and treatments within the NHS, such as:

- medicines
- medical devices (for example, hearing aids or inhalers)
- diagnostic techniques (tests used to identify diseases)
- surgical procedures (such as repairing hernias)
- health promotion activities (for example, ways of helping people with diabetes manage their condition)

Recommendations are based on a review of clinical and economic evidence, i.e. how well the medicine or treatment works in relation to how much it costs the NHS (does it represent value for money?). The NHS is legally obliged to fund and resource

[58] http://www.nice.org.uk/

[59] Garner S. How decisions on the use of medicines and medical devices are made. The Pharmaceutical Journal. 2005;275:254-256.

medicines and treatments recommended by NICE's technology appraisals.[60] Funding must be made available within three months unless, in exceptional circumstances, this requirement is waived by the Secretary of State in England. Health professionals are expected to take the guidance fully into account when exercising clinical judgement.[59]

Interventional Procedures Programme[61]

The interventional procedures programme was added to the NICE repertory in February 2002, replacing the safety and efficacy register of new interventional procedures (SERNIP), which reviewed novel surgical techniques.[59] The aim is to protect patients' safety and support people in the NHS in the process of introducing new procedures. Many of the procedures that NICE investigates are new, but they also look at more established procedures if there is uncertainty about their safety or how well they work. By providing guidance on how safe procedures are and how well they work, NICE makes it possible for new treatments and tests to be introduced into the NHS in a responsible way.[62]

NICE issues guidance on interventional procedures to ensure that:[63]

- patients and carers are reassured that new interventional procedures are being monitored and reviewed to protect patient safety, and that they have access to information about procedures
- clinicians, healthcare organisations and the NHS as a whole will be supported in the process of introducing new procedures
- NICE can foster innovation by facilitating data collection and analysis, arranging systematic reviews, recommending training and providing advice on the safety and efficacy of new procedures.

An interventional procedure is a procedure used for diagnosis or for treatment that involves:[64]

- making a cut or a hole to gain access to the inside of a patient's body - for example, when carrying out an operation or inserting a tube into a blood vessel, or
- gaining access to a body cavity (such as the digestive system, lungs, womb or bladder) without cutting into the body - for example, examining or carrying out treatment on the inside of the stomach using an instrument inserted via the mouth, or
- using electromagnetic radiation (which includes X-rays, lasers, gamma-rays and ultraviolet light) - for example, using a laser to treat eye problems.

Anyone may make a notification of a new interventional procedure. The main source of notifications is clinicians. The list of interventional procedures is available on the NICE website. The inclusion of a procedure on the list does not imply that it has been or will be selected for investigation, nor does it imply anything about the procedure's safety and efficacy. It simply means that NICE has been notified of the procedure.

Once a procedure has been notified, NICE assesses whether it falls within the scope of the Programme. To fall within the Programme's scope, a notified procedure must:

- involve an incision or a puncture or entry into a body cavity, or the use of ionising, electromagnetic or acoustic energy, and

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[60] http://www.nice.org.uk/

[61] *http://www.nice.org.uk/page.aspx?o=202671 and* NHS, National Institute for Clinical Excellence. The Interventional Procedures Programme: Programme Manual. 2004.

[62] *http://www.nice.org.uk/page.aspx?o=202671*

[63] NHS, National Institute for Clinical Excellence. The Interventional Procedures Programme: Programme Manual. 2004.

[64] *http://www.nice.org.uk/page.aspx?o=202671*

- be available within the NHS or about to be used for the first time in the NHS, outside formal research, and
- either not yet be generally considered standard clinical practice, or
- be a standard clinical procedure, the safety or efficacy of which has been called into question by new information.

A list of notified procedures not included in the Programme is provided on the website. NICE prepares an overview for each notified procedure that falls within the Programme's scope. In contrast to the NICE Technology Appraisals and Clinical Guideline Programmes, these overviews are not systematic reviews. The overview summarises the:

- nature and purpose of the procedure
- results of the most valid studies found in a rapid review of the literature
- key safety and efficacy issues that arise from review of the literature
- opinions of the Specialist Advisors

The Interventional Procedures Advisory Committee (IPAC, or 'the Advisory Committee') makes recommendations to NICE about the safety and efficacy of interventional procedures and the other content of guidance, such as conditions under which the procedures should be used.[63]

Some interventional procedures may be referred to NICE by the Advisory Committee on Topic Selection to be included in the Technology Appraisals Programme. It is usually appropriate for consideration of safety and efficacy to occur before the Technology Appraisals Programme addresses clinical and cost effectiveness.

The Review Body[63]

After considering the overview and the Specialist Advisors' opinions, the Advisory Committee also decides whether or not the procedure should be selected for referral to the Review Body for further investigation. NICE commissions the Review Body to produce a systematic review and/or to organise the collection and analysis of data. The Review Body presents its review to the Advisory Committee, who may then be able to make further recommendations. If the systematic review is not conclusive, or is judged unlikely to be conclusive when it is begun, NICE commissions the Review Body to collect data on the outcomes of the procedure. The Review Body organises the data collection in collaboration, where possible, with the relevant specialist societies, Royal Colleges or other professional organisations. The Review Body informs NICE, as a matter of urgency, of any procedure that appears to be associated with an unduly high rate of adverse events, either generally or in an individual hospital. When sufficient data have been collected to draw conclusions, the Review Body reports to the Advisory Committee.

The recommendations of the Review Body are published as an Interventional Procedures Consultation Document, issued by NICE on its website for 4 weeks. During consultation, anyone may submit comments. Patient organisations, medical device manufacturers, professional groups, the notifier, persons who are named in the overview, etc. are informed about the procedure so they have the opportunity to respond. The Advisory Committee reviews the consultation document in the light of the comments received during the consultation period and produces draft Interventional Procedures Guidance. The NICE Guidance Executive receives and considers the draft guidance on the Board's behalf. NICE then issues the guidance to the NHS in England, Wales and Scotland.

9.1.3.3 HTA NCCHTA[65]

The National Coordinating Centre for Health Technology Assessment (NCCHTA) manages, supports and develops the NHS HTA programme under contract from the Department of Health's Research and Development Division. The results of the research are published as reports in the HTA monograph series. The HTA programme also provides support for the work of NICE. The development of NICE's Technology Appraisal Guidance involves independent assessment of the evidence. This assessment is undertaken by individual TAR Teams (also known as Assessment Groups) in Academic Centres (also known as TAR Centres) hosted in Universities across the United Kingdom. The TAR Centres prepare, under contract to the Department of Health, Technology Assessment Reports (TARs) for consideration by the NICE Appraisal Committees and for inclusion in the HTA monograph series, *Health Technology Assessment*.

The NCCHTA manages the TAR contracts on behalf of the Department of Health. So, whilst the Department of Health retains responsibility for the contracts, its responsibilities are largely delegated to the Director of the HTA Programme and discharged through the NCCHTA.

9.1.3.4 NHS – pasa Centre for Evidence-based Purchasing (CEP)

(The former) Device Evaluation Service (DES)

The Device Evaluation Service (DES) aims to provide independent and objective evaluations of medical devices available on the UK market. Specialist centres, mainly in NHS Trusts, do the evaluations under long term contract to, and in accordance with protocols approved by, the Medicines and Healthcare products Regulatory Agency (MHRA).[66] The service offers guidance on best choice to the NHS and Social Service organisations. DES evaluates medical devices used for pathology, diagnostic imaging, and general medical and assistive technology. The evaluations are carried out by device evaluation centres (DECs) funded by the Department of Health and located in NHS Trusts and University medical schools across England and Wales.[67]

The Healthcare Industries Task Force (HITF) recommended moving DES to the NHS Purchasing and Supply Agency (PASA) and creating a new and enhanced evaluation service to encourage and support the uptake of useful, safe and innovative products by health and social care services.[67]

NHS PASA Centre for Evidence-based Purchasing (CEP)[68]

As a result of a recommendation made by the HITF to forge closer links between product evaluation and purchasing, the NHS PASA Centre for Evidence-based Purchasing was created on 1 September 2005 when the Device Evaluation Service transferred from the Medicines and Healthcare products Regulatory Agency (MHRA).

The Centre for Evidence-based Purchasing underpins purchasing decisions by providing objective evidence to support the uptake of useful, safe, innovative products and related procedures in health and social care.

The service will expand to:

- cover more products, not just medical devices
- provide the NHS and Social Services with cost benefit analysis where appropriate
- develop nationally agreed evaluation protocols

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[65] http://www.hta.nhsweb.nhs.uk/

[66] http://www.noharm.org/details.cfm?type=document&ID=1166

[67] Crawford DC. Medical device evaluation in the United Kingdom: past, present and future. Journal of Medical Engineering & Technology. 2005;29(3):108-111.

[68] http://www.pasa.doh.gov.uk/

- gather evidence globally to support the use of new technologies

The Centre for Evidence-based Purchasing is being re-designed to ensure it meets the requirements of the Healthcare Industries Task Force and the needs of purchasers throughout health and social care. Operationally the main changes to the service will be:

- separation of business planning and work prioritisation from commissioning and delivery of projects
- greater focus on health benefits and cost benefits
- new skills, including medical writers and a health economist
- clear governance measures, including input from industry
- to allow anyone to suggest a project for the Centre for Evidence-based Purchasing

The restructuring should be completed in 2006.

9.1.3.5 Others programmes or agencies

New and Emerging Applications of Technology (NEAT)[69]

The New and Emerging Applications of Technology (NEAT) programme has been commissioning research since 1999. The NEAT programme covers all areas of health and social care and funds initiatives in both the life and physical sciences. The programme promotes and supports applied research into the use of new or emerging technologies to develop health care products and interventions that improve the quality, efficiency and effectiveness of health and social care.

The main purpose of this programme is to overcome a development barrier. By fulfilling this purpose NEAT also fills a perceived "funding gap" among current funding streams. The institute looks for outputs that could:

- study the way that NHS services are provided and used
- evaluate whether interventions are effective and provide value for money
- examine whether alternative means for providing healthcare would be more effective in terms of cost and effectiveness
- formally assess innovations and developments in healthcare
- pilot or consider the feasibility of projects requiring major grant applications to other funders

Health Protection Agency – Rapid Review Panel (HPA RRP)[70]

The Health Protection Agency (HPA) is an independent body that protects the health and well-being of the population. The Agency plays a critical role in protecting people from infectious diseases and in preventing harm when hazards involving chemicals, poisons or radiation occur. The Rapid Review Panel (RRP) has been convened by the HPA at the request of The Department of Health. The panel provides a prompt assessment of new and novel equipment, materials, and other products or protocols that may be of value to the NHS in improving hospital infection control and reducing hospital acquired infections. The panel does not conduct evaluations of products but reviews information and evidence provided and make recommendations to the Department of Health.

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[69] http://www.nihr-ccf.org.uk/site/programmes/neat/ *and* http://www.dh.gov.uk/PolicyAndGuidance/ResearchAndDevelopment/ResearchAndDevelopmentAZ/NEATProgramme/fs/en?CONTENT_ID=4016454&chk=/1/HSD

[70] http://www.hpa.org.uk/

National Genetics Reference Laboratories[71]

In 2002, National Genetics Reference Laboratories in Manchester & Wessex were established as an initiative by the Department of Health to support the UK genetic laboratory services. The specific remit of the laboratories includes:

- Horizon Scanning and Technology Assessment
- Developing new Quality Assessment Systems
- Developing reference and control reagents
- Developing information systems for genetics
- Providing advice to government and other bodies

9.1.4 Regulation of medical devices

For medical devices, licensing approval may only require demonstration of performance (i.e. the device does what it claims to) and not clinical effectiveness (use of the device will actually improve clinical outcomes).[32] In practice this means products that are on the market should only have a CE mark. Studies involving non-CE marked medical devices carried out in the UK may be regulated as clinical investigations under the Medical Devices Regulations 2002 and require approval from the UK Competent Authority.

9.1.4.1 Medicines and Healthcare products Regulatory Agency (MHRA)[72]

The MHRA was set up in April 2003 from a merger of the Medicines Control Agency and the Medical Devices Agency. It is an executive agency of the Department of Health. This government agency is responsible for ensuring that medicines and medical devices work, and are acceptably safe. They enable greater access to products, and the timely introduction of innovative treatments and technologies that benefit patients and the public. They keep watch over medicines and devices, and take any necessary action to protect the public promptly if there is a problem.

Their key objectives are to:

- maintain rigorous authorisation and inspection programmes;
- maintain and develop pro-active surveillance and enforcement programmes;
- communicate authoritative and reliable information and advice to improve public and professional awareness;
- engage with and influence other Government bodies and European and worldwide regulators concerned with medicines or medical devices;
- support innovation and product development, offering constructive and impartial advice to scientific communities and health services;
- minimise the cost of regulation so far as is compatible with our public health role; and
- run a successful business with a skilled and equipped workforce dedicated to the Agency's aims

Their main activities are:

- assessing the safety, quality and efficacy of medicines, and authorising their sale or supply in the UK for human use;

[71] *http://www.ngrl.org.uk/Pages/index.htm*
[72] http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=20

- overseeing the UK Notified Bodies that audit medical device manufacturers;
- operating post-marketing surveillance and other systems for reporting, investigating and monitoring adverse reactions to medicines and adverse incidents involving medical devices and taking any necessary action to safeguard public health, for example through safety warnings, removing or restricting the availability of products or improving designs;
- operating a proactive compliance programme for medical devices;
- operating a quality surveillance system to sample and test medicines and to address quality defects, monitoring the safety and quality of imported unlicensed medicines and investigating Internet sales and potential counterfeiting of medicines;
- regulating clinical trials of medicines and medical devices;
- monitoring and ensuring compliance with statutory obligations relating to medicines and medical devices through inspection, taking enforcement action where necessary;
- promoting good practice in the safe use of medicines and medical devices;
- managing the General Practice Research Database (GPRD) and the British Pharmacopoeia (BP) and contributing to the development of performance standards for medical devices;
- offering scientific, technical and regulatory advice on medicines and medical devices; and
- providing the public and professions with authoritative information to enable informed dialogue on treatment choices

Regulation

The MHRA regulates a wide range of materials from medicines and medical devices to blood and therapeutic products/services that are derived from tissue engineering. There are currently two sets of Medical Device Regulations implementing all of the Medical Devices Directives and amendments to date; Statutory Instruments 2002 No. 618 (Consolidated legislation) and 2003 No. 1697 (Amendments to cover the re-classification of breast implants and additional requirements covering devices utilising materials from TSE susceptible animal species). They have been issued under the Consumer Protection Act. The Regulations implement the EC Medical Devices Directives into UK law. They place obligations on manufacturers to ensure that their devices are safe and fit for their intended purpose before they are CE marked and placed on the market in any EC member state.

Registration[73]

The Regulations require manufacturers and authorised representatives based in the UK to register with the MHRA details of themselves and the medical devices they are placing on the market. They must register with one Competent Authority in a Member State in which they have their registered place of business if they:[74]

- manufacture class I or custom made devices and place them on the market under their own name, or trading name(s);
- fully refurbish class I devices, or label one or more ready made devices, with a view to placing them on the market under their own name;

[73] http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=196

[74] MHRA. EC Medical Devices Directives: guidance notes for the registration of persons responsible for placing devices on the market. Updated January 2006.

- place devices bearing the CE marking on the market, under their own name in a system or a procedure pack within their intended purposes and within the limits of uses specified by their original manufacturers;
- sterilise, for the purpose of placing on the market under their own name, systems or procedure packs or other CE marked medical devices designed by the manufacturer to be sterilised before use;
- are the authorised representative of a manufacturer who does not have a registered place of business in the Community, or if they import and place on the Community market for a manufacturer who has no authorised representative in the Community, devices within the above listed categories.

9.1.5 Vigilance

In the UK both a mandatory vigilance system for manufacturers and a voluntary system for users exists. The MHRA has a duty to enforce the legislation relating to medical devices.

9.1.5.1 Reporting system for manufacturers and users[75]

If the adverse event arose from problems with a medical device, its instructions for use, labelling or device/user interface issues, the event should be reported to the MHRA and the National Patient Safety Agency (NPSA). The NPSA is responsible for monitoring patient safety incidents (adverse events) in the NHS in England and Wales. If the NPSA receives reports that give rise to serious concerns about the safety of a procedure, an assessment of the procedure may be prompted; this applies whether or not the procedure has already been the subject of guidance.

In parallel with the manufacturers vigilance reporting system, MHRA currently operates a voluntary system under which the person involved in the use, maintenance or provision of a device reports any problems to the Adverse Incident Centre (AIC) for investigation by the Agency's staff. The system covers categories of medical devices and equipment used within the UK healthcare system. All incidents involving these should be reported in accordance with Medical Device Alert MDA/2003/001.

9.1.5.2 MHRA Enforcement Responsibilities[76]

The Secretary of State for health is responsible for administering legislation relating to medical devices and for ensuring the safety and quality of devices. The relevant legislation is the Medical Devices Regulations 2002 (SI 2002 No 618) and Medical Devices (Amendment) Regulations 2003 (SI 2003 No 1697) and General Product Safety Regulations 2005 (SI 2005 No 1803). MHRA has a duty to enforce this legislation on behalf of the Secretary of State and has delegated responsibility for England, Wales, Scotland and Northern Ireland. This involves establishing that the Medical Devices Regulations and General Product Safety Regulations have been complied with, and ensuring that the appropriate action is taken wherever necessary to prohibit or restrict unsafe products being placed on the market. This obligation is met by MHRA in 5 basic ways:

- Any complaints about CE marked products or products which are not CE marked that are drawn to our attention, will be investigated.
- Selection for inspection of a sample of manufacturers who place their products on the UK market. Inclusion in this proactive exercise does not mean that there has been a breach of the Regulations.

[75] MHRA. The vigilance system. Bulletin No. 3. Amended November 2005.
[76] http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=204

- Regular monitoring of the activity of Notified Bodies designated by MHRA to assess the compliance of manufacturers of, in the main, higher risk devices.
- Investigations undertaken as a result of vigilance reports.
- Investigations as to complaints concerning unsafe products supplied/distributed to consumers under the General Product Safety Regulations 2005.

The MHRA issues safety warnings (Medical Device Alerts) to health and social care providers and other users of medical devices. These warn of particular problems and risks and recommend appropriate action to minimise them. These notices are distributed to NHS trusts and social services for direct action and for onward transmission to relevant healthcare professionals including, where the device is used in primary care, to general practitioners.

9.1.6 Reimbursement

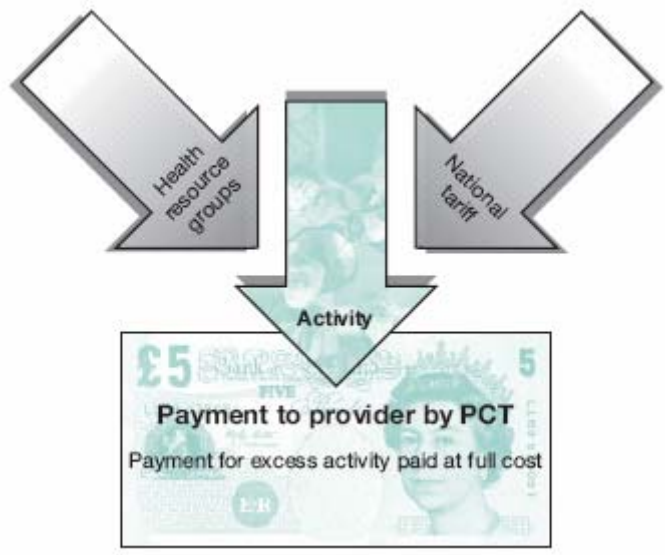
A new 'payment by results' system is being set up in the UK. For new technologies, not being covered yet, a pass-through system exists.

9.1.6.1 Payment by results

In October 2002, the Department of Health (DH) published *Reforming NHS Financial Flows*, outlining plans to introduce payment by results – a new funding system for work done by the NHS in England (figure 10).[77] Payment by results aims to support NHS modernisation by paying hospitals for the work they do, rewarding efficiency and quality. It does this by paying a nationally set price or tariff for each procedure, classified by Healthcare Resource Group (HRG), based on an average of all hospital costs for that procedure (reference costs). The base data for setting the tariff will always be two years in arrears (for example the 2004/05 tariff is based on 2002/03 reference costs data). All contracts between PCTs and trusts will be 'cost and volume' with payment linked directly to the actual work done. Trusts will be compensated through national funding for unavoidable regional cost variations. [78] This system should ensure a fair and consistent basis for hospital funding rather than being reliant principally on historic budgets and the negotiating skills of individual managers.[79] The implementation of this system is ongoing and the transitional phase should be completed in 2008/2009.[78]

[77] Department of Health, Reforming NHS Financial Flows. 2002.
[78] Audit Commission. Introducing payment by results: getting the balance right for the NHS and taxpayers. 2004.
[79] http://www.dh.gov.uk/PolicyAndGuidance/OrganisationPolicy/FinanceAndPlanning/NHSFinancialReforms/fs/en

Figure 10: Key elements of the payment by results system.[78]



9.1.6.2 Pass-through funding

A pass-through system following representations from industry enables trusts to get funding for new innovative technology not yet covered by the tariff.[80] For new technology that was not anticipated by NICE recommendations, trusts will be able to use additional 'pass-through' funding. This interim measure will run for two years from 1 April 2005. The funding is to be primarily used for new devices, pharmaceuticals, treatments or technologies, or for new applications of existing technology. At the end of the two years, the costs will be built into the relevant tariffs.[81] As such, trusts can fund the development and on-going costs of new technology either from surplus income received under Payment by Results, or from the agreed funding of the costs using this pass-through payment. Pass-through payments are made on top of the national tariff. They are specifically designed to allow the commissioner to cover the development and adoption costs of new technologies.[82]

[80] Innovation report. Procuring for healthcare 2006: investing in innovation. 2006.
[81] http://www.hesmagazine.com/story.asp?storyCode=2026554
[82] Government response to the Health Committee's report on the use of new medical technologies within the NHS. 2005.

- **In the UK, there is a horizon scanning activity performed by the National Horizon Scanning Centre. This centre cooperates worldwide with other horizon scanning institutes through Euroscan.**
- **Regulations require manufacturers and authorised representatives based in the UK to register with the Medicines and Healthcare products Regulatory Agency (MHRA) details of themselves and the medical devices they are placing on the market.**
- **NICE's interventional procedures programme (IPP) protects patients' safety and support people in the NHS in the process of introducing new procedures.**
- **A special Review Body may provide further follow-up.**
- **MHRA also operates post-marketing surveillance. Next to an obligatory system for manufacturers there is also a voluntary system for users. MHRA issues safety warnings (Medical Device Alerts).**
- **Trusts can fund the development and on-going costs of new technology either from surplus income received under Payment by Results, or from the agreed funding of the costs using a "pass-through funding".**

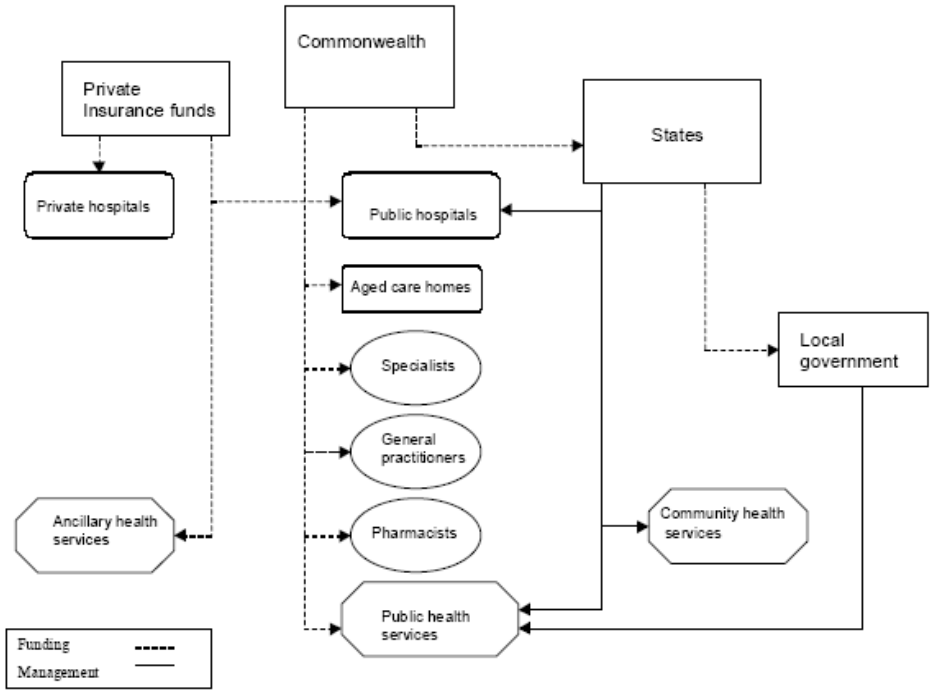
9.2 AUSTRALIA

9.2.1 Health care system[83] [84]

Australia has a three-tier political system. The first tier is the national government or Commonwealth, the next tier is the six state and two territory governments, and the third is local government (see figure 11). The Commonwealth funds rather than provides health services. The six state and two territory governments, with Commonwealth financial assistance, primarily are responsible for funding and administering public hospitals, mental health services, and community health services, as well as for regulating health workers. The states are essentially autonomous in administering health services. Local governments are responsible for some public health services and for public health surveillance, but not for clinical medical services.

[83] Commonwealth Department of Health and Aged Care. The Australian health care system: an outline. 2000. (http://www.health.gov.au/)
[84] Hilless M, Healy J. Health Care Systems in Transition: Australia. European Observatory on Health Care Systems. 2001. (http://www.who.dk/)

Figure 11: Organizational chart of health care system[85]



The major part of the national health care system is called 'Medicare'. Medicare provides high quality health care which is both affordable and accessible to all Australians, often provided free of charge at the point of care. Revenue for the health care system comes mainly from taxation (general taxation and compulsory tax-based health insurance). Health services are funded through two national subsidy schemes, Medicare Benefits Schedule (payments to practitioners) and the Pharmaceutical Benefits Schedule (subsidized drug purchases). Public hospitals and public health are funded partly through joint Commonwealth and State funding agreements.

There is a large and vigorous private sector in health services. The Commonwealth Government considers that strong private sector involvement in health services provision and financing is essential to the viability of the Australian health system.[86] The private sector plays a major role in providing and to a lesser extent in funding health services. Primary medical care is provided mostly by private practitioners, hospital care by both public and private hospitals, and most long-term care by the private and voluntary sectors. Individuals eligible for Medicare can elect to have free accommodation and medical, nursing and other care as public patients in State-funded hospitals. Outpatient treatment is free of charge in public hospitals. Alternatively, they may choose treatment as private patients in public or private hospitals, with some assistance from Medicare.

[85] http://www.who.dk/document/E74466.pdf

[86] Some measures are designed to encourage people to take out private health insurance and decrease the pressure on the public system. For example, the Commonwealth Government introduced a 30% rebate on private health insurance in January 1999.
Private insurance funds' activities are tightly controlled. For example, insurers must accept all applicants and must not discriminate in setting premiums and paying benefits (known as community rating).

9.2.2 Horizon scanning[87]

There are two publicly-funded horizon scanning centres in Australia:

- the Australian Safety and Efficacy Register of New Interventional Procedures — Surgical (ASERNIP-S); and
- the National Horizon Scanning Unit (NHSU).

ASERNIP-S and NHSU are part of the Australian and New Zealand Horizon Scanning Network (ANZHSN) which was established in 2003 by the Department of Health and Ageing (DoHA), the Australian Health Ministers Advisory Council (AHMAC) and the Medical Services Advisory Committee (MSAC). The horizon scanning programme was established under MSAC to provide advance notice of significant new and emerging technologies to health departments in Australia and New Zealand, and to exchange information and evaluate the potential impact of emerging technologies on their respective health systems.

On occasion, it may be unclear whether horizon scanning for a particular procedure should be performed by ASERNIP-S or the NHSU. The general rule is that ASERNIP-S will undertake the horizon scan if the procedure involves an incision. There appears to be considerable cooperation and communication between the two centres which would help to clarify responsibilities in ambiguous cases.

The activities are overseen by the Health Policy Advisory Committee on Technology (HealthPACT). HealthPACT is a sub-committee of MSAC and comprises representatives from State and Territory government health departments, MSAC, ASERNIP-S, DoHA and the New Zealand Ministry of Health. HealthPACT's work is supported by the National Horizon Scanning Unit (NHSU). The role of HealthPACT is to assist the introduction of new and emerging medical technologies into the public sector, with consideration to the private sector, in Australia and New Zealand through horizon scanning, including reporting on safety, effectiveness and cost implications.

9.2.2.1 The National Horizon Scanning Unit (NHSU)

A team from Adelaide Health Technology Assessment (AHTA) Unit, Department of Public Health at the University of Adelaide has been funded to establish the National Horizon Scanning Unit and to undertake horizon scanning on behalf of HealthPACT which reports to the Australian Health Ministers' Advisory Council, and the Medical Services Advisory Committee. It alerts the health departments of the Australian Government, the States and Territories, and New Zealand to new and emerging technologies that may impact on their public healthcare systems within a three year time horizon.

New and emerging technologies identified by the NHSU are prioritised according to predefined criteria. Those that meet a pre-determined 'priority threshold' undergo a preliminary assessment and a prioritising summary is prepared. These summaries are forwarded to HealthPACT on a quarterly basis. Prioritising summaries and horizon scanning reports address clinical need, safety, effectiveness and the cost impact aspects of the identified technology. Horizon scanning reports also seek to establish the availability of cost-effectiveness evidence, but usually there is a paucity of such evidence in the early stages of diffusion or pre-diffusion of a new technology. The documents also look at ethical, religious or cultural dimensions where relevant.

[87] http://www.horizonscanning.gov.au/

9.2.2.2 ASERNIP-S & NET-S

In 1998, the Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S[88]) was funded by the Australian Government. It is administered by the Royal Australasian College of Surgeons (RACS). The ASERNIP-S mission is to provide quality and timely assessments of new and emerging surgical technologies and techniques. Services provided include:

- systematic and accelerated systematic reviews of the peer-reviewed literature
- the establishment and facilitation of clinical and research audits or trials
- the identification and assessment of new and emerging techniques and technologies by horizon scanning, and
- the production of clinical practice guidelines

In 1999, ASERNIP-S, together with the Royal Australasian College of Surgeons' New Technology Committee, established an Australian based horizon scanning project: NET-S (New and Emerging Techniques - Surgical) to provide an early warning system for identifying new and emerging surgical techniques and technologies into Australian healthcare. In late 2003, NET-S became a member of the Australian and New Zealand Horizon Scanning Network (ANZHSN), which seeks to provide policy and planning advice to Australian State and Territory Governments and the New Zealand Ministry of Health on the potential impact of emerging health technologies on their respective health systems.

The activities of NET-S aim to parallel those of other centres recently established throughout the world. Additionally the aim is to derive unique methodologies to improve the specificity and efficacy of the process:

- NET-S focuses its scanning activities on surgical techniques and technologies, thereby intensifying searching capabilities in the area of surgery.
- NET-S has developed an approach that eliminates those methods that have shown to be less than effective in identifying new technologies.
- By communicating directly with Fellows of the Royal Australasian College of Surgeons, NET-S has an enormous advantage over searching processes that focus primarily on published literature.

NET-S directs some of its outputs to the ASERNIP-S programme, thereby enhancing its activities through having access to an innovative and effective early warning system.

NET-S has developed unique methodologies to improve the horizon scanning process, particularly in the area of surgery. This is occurring through the following strategies:

- direct communication with Fellows of the Royal Australasian College of Surgeons
- close surveillance of abstracts presented at relevant specialty meetings
- ongoing searching of the literature describing new techniques and technologies
- establishing links with key players and targeting other appropriate groups, such as medical device manufacturers
- soliciting input from surgeons, consumers and other relevant groups via this website

[88] http://www.surgeons.org/Content/NavigationMenu/Research/ASERNIPS/

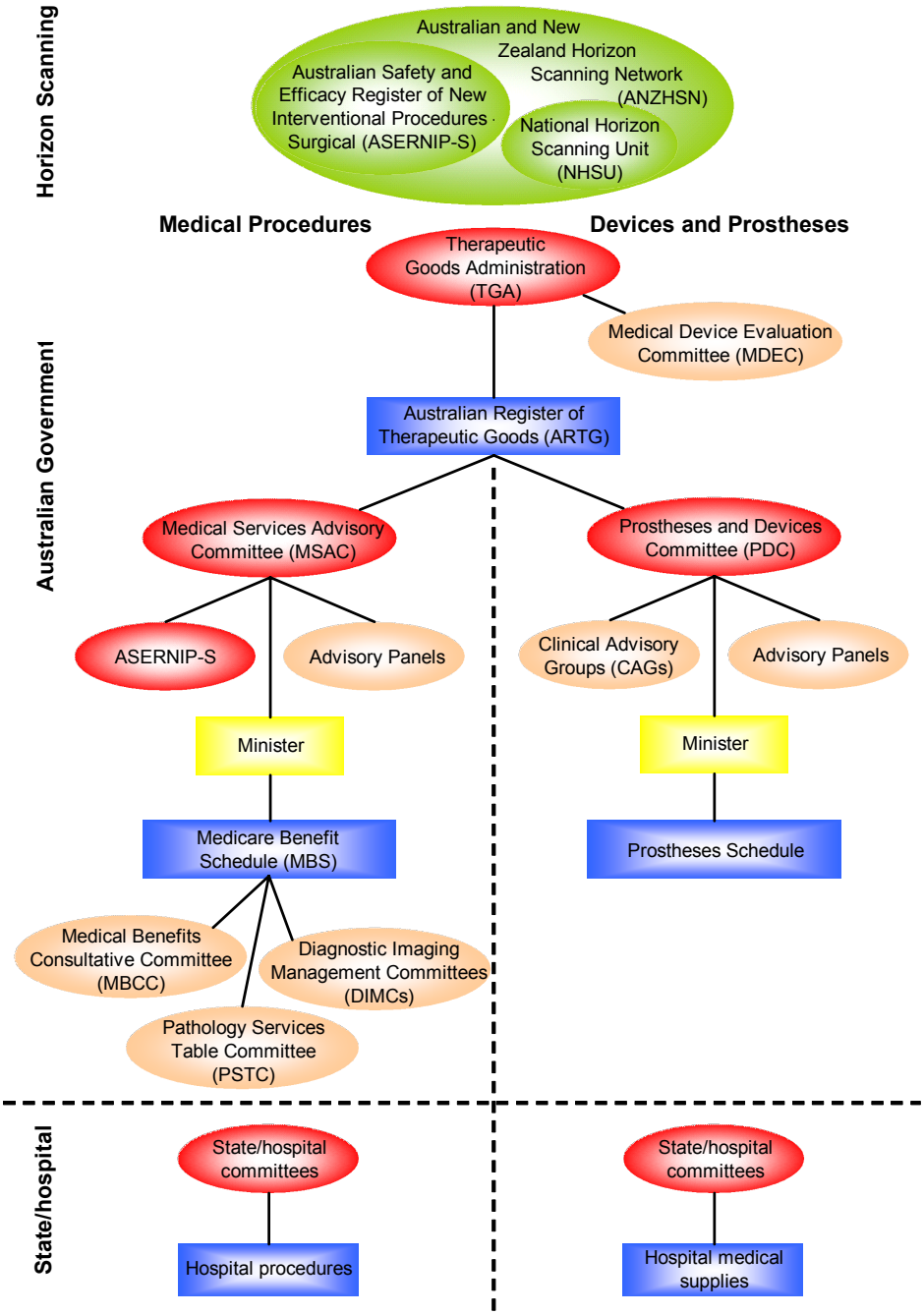
9.2.3 Medical technology assessment

Next to the well-known HTA institutes, i.e. Adelaide Health Technology Assessment (AHTA) and New Zealand Health Technology Assessment (NZHTA) which also undertakes technology assessment for the Australian Medical Services Advisory Committee (MSAC), other institutes, which are discussed hereafter, also perform (pre-market) assessments of new or emerging medical devices.

Existing HTA processes are quite sophisticated compared with international counterparts, but they are complex (figure 12). In part, this complexity reflects overlapping responsibilities of different levels of government and, in part, different assessment processes and skill requirements for different categories of technology.[14] The key agencies involved in the assessment of procedures, prostheses and devices at the national level are the Therapeutic Goods Administration (TGA); MSAC; ASERNIP-S; and Prostheses and Devices Committee (PDC) The TGA is responsible for assessment of product safety and clinical efficacy. The MSAC, supported by ASERNIP-S, advises the Health Minister on the safety and clinical and cost effectiveness of new and existing technologies. The PDC advises and makes recommendations to the Health Minister on the listing of new prostheses and setting of reimbursement levels for new and existing prostheses that private health insurers need to cover their members.[89] Table 7 lists the technologies assessed by these HTA agencies, as well as their key assessment criteria. These agencies are discussed hereafter.

[89] Australian Government, Department of Industry, Tourism and Resources. Medical Devices Industry Action Agenda. Discussion paper, 2005.

Figure 12: horizon scanning and HTA in Australia[90]



[90] Adapted from Productivity Commission. Impacts of Advances in Medical Technology in Australia. Research Report, Melbourne. 2005 (Figure 8.2, page 184)

Table 7: Key assessment criteria of TGA, MSAC, ASERNIP-S and PDC.[91]

Agency or committee	Technologies assessed	Safety	Clinical efficacy	Clinical effectiveness	Cost effectiveness
TGA	Medicines and Devices	X	X		
MSAC	Procedures, devices and equipment	X		X	X
ASERNIP-S	Surgical Procedures	X	X		
PDC	Devices and prostheses		X		

9.2.3.1 Therapeutic Goods Administration (TGA)[14]

The TGA is responsible for assessing the safety and efficacy of new therapeutic goods, whether the suppliers are seeking reimbursement from government or other sources. The TGA is required to assess pharmaceuticals, medical devices, blood, tissues and cellular therapies. It regulates the overall supply of therapeutic goods through three main processes:

- Pre-market evaluation: Before a product can be released to the market, the TGA must undertake an assessment. Products assessed as having a higher level of risk are evaluated for quality, safety and efficacy. If approved by the TGA, these products are included on the Australian Register of Therapeutic Goods (ARTG) as 'registered' products. Products assessed by the TGA as lower risk are evaluated for quality and safety only. If approved by the TGA, they are included on the ARTG as 'listed' products.
- Licensing of manufacturers: The TGA also licenses Australian manufacturers of therapeutic goods to ensure that their manufacturing processes comply with principles of good manufacturing practice.
- Post-market surveillance: Once technologies are approved, the TGA conducts post-market surveillance and testing of products to ensure compliance with legislation. It also conducts investigations of reported problems. (cfr. infra)

In making its decisions, the TGA is advised by a range of other committees. For medical devices, this is the Medical Device Evaluation Committee (MDEC).

Medical Device Evaluation Committee (MDEC)[14 92]

The Medical Device Evaluation Committee (MDEC) is established under Regulation 35 of the *Therapeutic Goods Regulations 1990*. With the commencement of Australia's new regulatory framework for medical devices on 4 October 2002, MDEC replaces the previous statutory expert committee, the Therapeutic Device Evaluation Committee (TDEC).

MDEC members are appointed by the Minister for Health and Ageing to provide independent medical and scientific advice to the Minister and the Therapeutic Goods Administration (TGA) on the safety, quality and performance of medical devices supplied in Australia including issues relating to premarket conformity assessment and post market monitoring. The Committee is supported by the Office of Devices, Blood and Tissues (ODBT) within the TGA which is responsible for regulating medical devices.

[91] Adapted from Productivity Commission. Impacts of Advances in Medical Technology in Australia. Research Report, Melbourne. 2005 (Figure 8.3, page 185)
[92] http://www.tga.gov.au/devices/devices.htm

9.2.3.2 Medical Services Advisory Committee (MSAC)[14]

Established in 1998, MSAC advises the Minister on the safety, clinical effectiveness and cost effectiveness of new and existing medical technologies in response to submissions from the medical industry or references from government. MSAC examines procedures, diagnostic tests and devices but not pharmaceuticals. MSAC makes recommendations to the Minister on whether a new procedure should receive public funding, including listing on the Medicare Benefits Schedule (MBS).

Unlike pharmaceuticals, there is no mandatory requirement for economic evaluation of all medical services submitted for MSAC assessment. MSAC determines the need for a full economic evaluation on a case-by-case basis. Whereas for pharmaceuticals evaluations are the responsibility of drug manufacturers or suppliers, MSAC may provide funding for a defined period during which further evidence can be gathered for new technologies that show promise of being cost-effective.

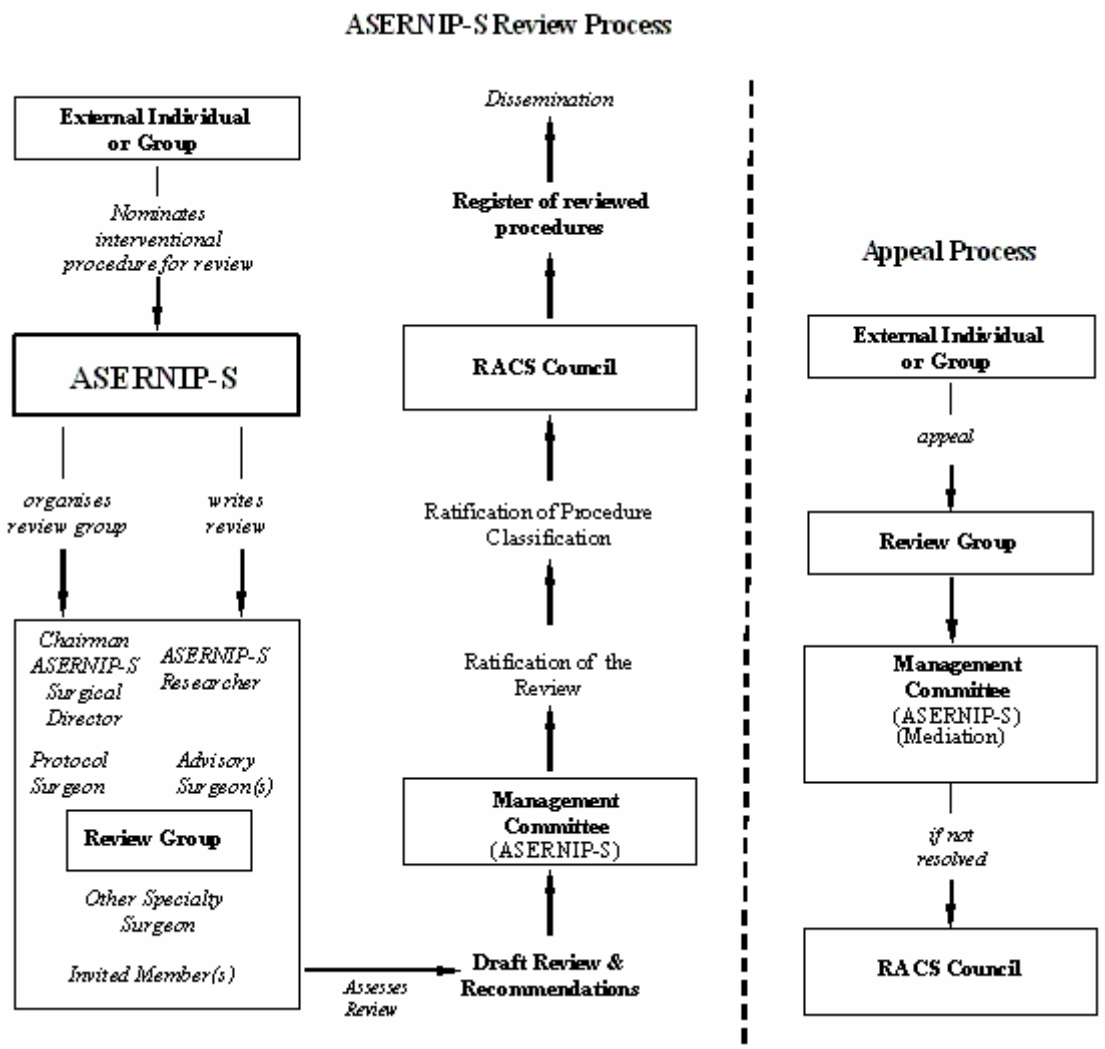
Contracted evaluators undertake the majority of the assessment, overseen by an advisory panel comprising experts in the technology under examination. The experts are selected from nominations provided by relevant medical colleges and/or specialty groups. A consumer representative and a person with knowledge of health finance and/or epidemiology may be included on an advisory panel. The panel is chaired by a member of MSAC.

9.2.3.3 ASERNIP-S[93]

The flow chart below (figure 13) illustrates the process adopted by ASERNIP-S to assess new surgical procedures. The process commences with nomination of procedures from a variety of sources including the Divisions/Sections of the Royal Australasian College of Surgeons (RACS), specialist societies, hospitals, Consumer Complaints Commissions, Consumers Health Forum and from individuals. The ASERNIP-S Management Committee endorses the nominations and assessment of the procedure commences when time is available. The output of the process is a draft review, recommendations and a safety and efficacy classification, which is submitted to the ASERNIP-S Management Committee for ratification. Once the review is endorsed by the RACS Council the final document is then disseminated to relevant groups of the RACS, hospital credentials committees, consumer groups and any other interested parties.

[93] http://www.surgeons.org/Content/NavigationMenu/Research/ASERNIPS/ASERNIPsReviewProcess/Procedure_Assessment.htm

Figure 13: ASERNIP-S appeal and review process[94]



The web site of ASERNIP-S[95] has the full text of their health technology assessments on new surgical procedures. An identification and tracking database, New and Emerging Techniques Surgical (NET-S) that provides information on the stage of development of new surgical procedures is also available at this Web site.[96] NET-S produces reports on new and emerging technologies. These reports are assigned one of the following classifications:[97]

- Horizon Scanning Technology Prioritising Summary: Short (approximately two to three pages) reports that provide a summary of new and emerging surgical technologies or techniques which can be used as a basis for deciding if a procedure should be further assessed, monitored in a further 12 months or archived. If further assessment is required on a procedure which is yet to emerge or is emerging into

[94] http://www.surgeons.org/Content/NavigationMenu/Research/ASERNIPS/ASERNIPsReviewProcess/Procedure_Assessment.htm
[95] http://www.surgeons.org/open/asernip-s.htm
[96] http://www.surgeons.org/asernip-s/net-s/index.htm
[97] http://www.surgeons.org/Content/NavigationMenu/Research/ASERNIPS/ASERNIPSNETS/default.htm

Australian healthcare following a prioritising summary, then it would be recommended for a Horizon Scanning Report.

- Horizon Scanning Report: Reports that assess surgical technologies or techniques that are new or emerging into Australian healthcare.
- Accelerated Systematic Review: Accelerated systematic reviews assess surgical procedures that have more widespread use in Australia, and generally have more peer-reviewed information available, than a Horizon Scanning Report. Accelerated systematic reviews are produced in response to a need for a systematic summary and appraisal of available literature for a new or emerging surgical procedure. This need may arise if the uptake of the new technique or technology appears to be inappropriate given the evidence available at the time (it may be diffusing too quickly or too slowly). Alternatively, there may be uncertainty or controversy regarding the clinical or cost-effectiveness of the new procedure, or there may be significant concerns regarding its safety or indications for use in particular populations. Accelerated systematic reviews use the same methodology as full systematic reviews, but may restrict the types of studies considered (for example, by only including comparative studies and not case series) in order to produce the review in a shorter time period than a full systematic review.

A number of strategies are used to disseminate the information held on the NET-S database. These include:

- The development of an information dissemination and exchange facility with targeted groups
- Providing regular updates of activities in surgical newsletters and conference presentations
- Providing advance notice to the Department of Health and Aged Care, Sections and Divisions of the College and other interested agencies about new and emerging surgical techniques and technologies that might require evaluation, consideration of clinical and cost impact or modification of clinical guidance

9.2.3.4 Prostheses and Devices Committee (PDC)[14]

Once a prosthesis or device has been listed on the ARTG, manufacturers or suppliers may apply to list the item on the Prostheses Schedule. The PDC (which was established in 2004 and replaced the Private Health Industry Medical Devices Expert Committee) advises, and makes recommendations to, the Minister on the listing of new prostheses and the setting of reimbursement levels that private health insurers need to cover for their members for new and existing prostheses. Clinical Advisory Groups (CAGs) — comprising mainly clinical specialists — provide advice to the PDC primarily on the relative clinical efficacy of prostheses and devices. Where practicable, CAGs also may provide information to the PDC on cost-effectiveness.

The relative clinical efficacy information will be used by the PDC to establish price ranges and by the Benefit Negotiation Group (BNG) to establish best prices for different categories of items grouped by clinical efficacy. The BNG advises the PDC on the appropriate level of reimbursement for products. It will negotiate prices for prostheses and devices with manufacturers, suppliers and distributors, taking account of the available evidence on efficacy, efficiency, alternative devices and other factors. The reimbursement negotiated will not be greater than the threshold recommended by the PDC. DoHA argued that the centralised reimbursement negotiation aims to introduce competitive tension into the market.

The new assessment process for prostheses is an improvement on previous arrangements whereby items were listed for reimbursement with little or no evaluation. While the current focus is on relative clinical efficacy rather than cost-effectiveness, the

application of cost-effectiveness assessment is hampered by the lack of comparative clinical and price information. However, the new arrangements establish a base from which cost-effectiveness assessment can be applied in the future.

9.2.3.5 At a regional level

Some State Governments have established advisory committees and working groups to assess requests to use new medicines or other medical technologies in hospital settings. For example, the Victorian Policy Advisory Committee on Technology (VPACT) was created in 2004 to promote a systematic approach to the introduction and use of new and existing health technologies in Victoria. VPACT has a range of roles, from horizon scanning to assessment and monitoring.[14]

Similar mechanisms, however with an emphasis on drug evaluation, exist in Queensland (Queensland Hospitals Drug Advisory Committee (QHDAC)), Western Australia (Western Australian Drug Evaluation Panel (WADEP)) and South Australia (Sub-Committee for New Technologies).

9.2.3.6 Remarks[14]

Some remarks were made by the Productivity Commission (2005) on the existing processes. With respect to the assessment of new or emerging technologies the following remarks were identified:

- in the future, the existing 'silo' approach to assessment may inhibit efficient assessment of emerging converging technologies, including targeted therapies that combine screening, diagnosis and treatment, and pharmaceuticals and device combinations.
- Cost-effectiveness assessment of medical devices and prostheses is not as well developed as for pharmaceuticals and medical procedures.
- There is no systematic, prioritised process for reviewing efficacy and cost effectiveness of new technologies once they are in use. Post-release monitoring and reviews can allow conditional introduction of new technologies and may be particularly suited to assessment of new medical procedures and devices as well as new biological pharmaceuticals.

Other interesting findings were formulated by the Productivity Commission (2005). Those with respect to the assessments of new or emerging technologies are reproduced.

- Some new medical technologies deemed to fit under existing MBS codes may not have been assessed or have been assessed only after significant diffusion has occurred.
- The use of formal economic evaluation, such as cost-effectiveness analysis, is hampered by the generally weaker clinical evidence base that exists for medical procedures and devices, compared with that for pharmaceuticals. MSAC may commission further work in order to assess new technologies more fully.
- Prior to the introduction of the Prostheses Act, medical devices and prostheses were subject to little, if any, assessment or re-assessment of their clinical or cost effectiveness. Unlike PBAC and MSAC, a major focus of the new Prostheses and Devices Committee will be relative clinical efficacy rather than cost-effectiveness. There appears to be greater scope for prostheses and devices to be assessed for cost-effectiveness, bearing in mind that evaluation methods may need to differ from those applying to pharmaceuticals and medical procedures.

9.2.4 Regulation of medical devices[98]

A new regulatory system for medical devices in Australia has commenced on 4 October 2002. The new system has been established by the '*Therapeutic Goods Act 1989*' as amended by the '*Therapeutic Goods Amendment (Medical Devices) Bill 2002*' and the '*Therapeutic Goods (Medical Devices) Regulations 2002*'. The Australian Register of Therapeutic Goods forms the central point of control for the legal supply of medical devices in Australia.

9.2.4.1 'Therapeutic Goods Act 1989' as amended by the 'Therapeutic Goods Amendment (Medical Devices) Act 2002'[99]

The Therapeutic Goods Administration (TGA) is a unit of the Australian Government Department of Health and Ageing and is responsible for administering the provisions of the legislation. The TGA carries out a range of assessment and monitoring activities to ensure therapeutic goods available in Australia are of an acceptable standard. At the same time the TGA aims to ensure that the Australian community has access, within a reasonable time, to therapeutic advances.

The Office of Devices, Blood and Tissues (ODBT) is the department within the TGA responsible for regulating medical devices. Three statutory committees have been established to provide advice on the regulation of therapeutic goods, i.e.: the Medical Devices Evaluation Committee (MDEC), the Therapeutic Goods Committee (TGC), and the National Coordinating Committee on Therapeutic Goods (NCCTG).

The new regulatory system has the following features:

- a device classification scheme based on different levels of risk for each class of device;
- essential principles for the quality, safety and performance of the medical device that must be complied with before the product can be supplied;
- options as to how compliance with the essential principles can be satisfied and assessed
- manufacturer quality systems, type testing, and design evaluation;
- the use of recognised standards to satisfy the requirements of the essential principles;
- a comprehensive post market surveillance and adverse incident reporting programme;
- appropriate regulatory controls for the manufacturing processes of medical devices; and
- the continued use of the Australian Register of Therapeutic Goods as the central point of control for the legal supply of medical devices in Australia

Most medical devices will be classified into one of five classes (I, IIa, IIb, III and Active Implantable Medical Devices - AIMDs). All classes will comply with a minimum requirement for safety and performance and be included in the ARTG. Class IIa, IIb, III and AIMD devices will require quality systems. Class III devices and AIMDs are subject to the most extensive premarket assessment in the new regulatory system in Australia. The following schedule (figure 14) gives an overview of the TGA medical device regulatory process.

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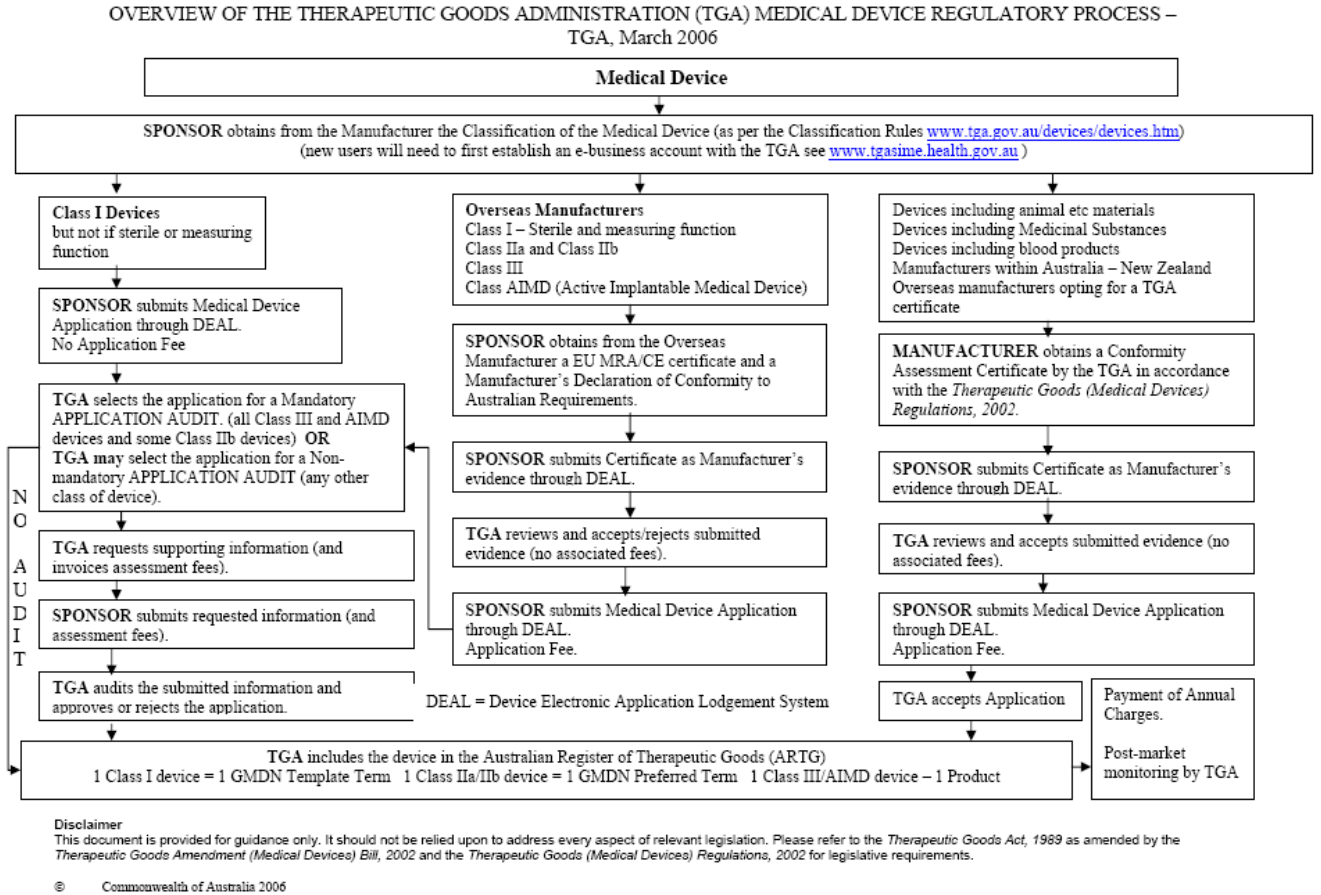
[98] http://www.tga.gov.au/devices/devices.htm and http://www.comlaw.gov.au/ComLaw/Legislation/

[99] TGA. Australian medical devices guidelines: an overview of the new medical devices regulatory system. Guidance document number 1. 2003.

Figure 14: the TGA medical device regulatory process[100]



[100] http://www.tga.gov.au/devices/process.pdf

9.2.4.2 Australian Register of Therapeutic Goods (ARTG)[99 101]

The Australian Register of Therapeutic Goods (ARTG) was established under the *Therapeutic Goods Act 1989*. The ARTG is a computer database of therapeutic goods. Therapeutic goods are divided broadly into two classes - medicines and medical devices. Unless exempt, therapeutic goods must be entered as either 'registered' goods or 'listed' goods before they may be supplied in, or exported from Australia. Registered goods are products assessed as having a higher level of risk and evaluated for quality, safety and efficacy. Listed goods are products assessed by the TGA as lower risk and evaluated for quality and safety only. Therapeutic goods for human use on the ARTG may be imported, supplied in, or exported from Australia. Following the amendments to the Therapeutic Goods Act 1989, an additional part has been created in the ARTG for medical devices.

Applications for entry on the Australian Register of Therapeutic Goods can be lodged electronically using the Device Electronic Application Lodgement system (DEAL). The new DEAL system handles online electronic applications for the inclusion of all classes of medical devices onto the ARTG. This new system is the world's first web based electronic application lodgement system. Additionally, the recently developed international standardised device nomenclature system known as the Global Medical Device Nomenclature System (GMDNS) is used to categorise devices on the ARTG.

There is a 5 year transition period. Sponsors of medical devices that were on the ARTG as registered or listed devices as at 4 October 2002 have until 4 October 2007 to demonstrate their products meet the new regulatory requirements. The transitional arrangements for the implementation of the new regulatory system included a two year transition period for devices that met the definition of a medical device but were exempt from entry on the ARTG or were excluded under the Therapeutic Goods (Excluded Goods) Order of 1998. Devices not transitioned by October 2007 will be cancelled from the ARTG and cancelled devices may no longer be supplied.

The revised Therapeutic Goods Act 1989 as amended by the Therapeutic Goods Amendment (Medical Devices) Bill 2002 and the Therapeutic Goods (Medical Devices) Regulations 2002 provide access to medical devices not entered on the ARTG under the following special access and supply arrangements:

- clinical trials (either the clinical trial exemption (CTX) scheme or the clinical trial notification (CTN) scheme, where both schemes require human research ethics committee approval;
- the Special Access Scheme (Categories A and B);
- authorised prescribers; and
- importation for personal use

The Special Access Scheme (SAS) refers to the arrangements that allow access to unapproved products by individual patients, other than by personal importation. The arrangements are dependent on whether the patients are classified as Category A, as defined in the Regulations. The use of a medical device for a Category A patient only requires notification while Category B patients require approval by a TGA delegate. A detailed document, "Access to Unapproved Therapeutic Goods in Australia" is available from the TGA website, "www.tga.gov.au/devices/devices.htm".

9.2.5 Post-market surveillance

9.2.5.1 Monitoring

Although DoHA has primary responsibility for managing the MBS, the Health Insurance Commission (HIC) monitors and analyses MBS items to identify trends in specific item

[101] http://www.tga.gov.au/docs/html/artg.htm

usage, broad types of service, costs and future audit topics.[102] As part of its reporting functions, the HIC examines the number, average cost and expenditure of medical services including general practitioner attendances, specialist attendances, obstetrics, anaesthetics, pathology tests, diagnostic imaging and optometry. The HIC regularly transmits this information to DoHA, which uses it to develop and review health policy relating to Medicare.

The Private Health Insurance Administration Council (PHIAC) monitors and publishes aggregate data on medical benefits paid by health funds for medical services provided in hospital. It also monitors trends in the use and costs of medical services including prostheses services. [103] Individual health funds conduct their own monitoring, for example, the Hospitals Contribution Fund publishes statistics on various hospital admissions and the associated costs by type of admission.[104]

Furthermore, several registries have been established for diseases, medical procedures and prostheses. For instance, the National Coronary Angioplasty Register collects data from cardiac catheterisation units around Australia on coronary angioplasty procedures, indications, associated complications, lesion location, success rates and adjunctive techniques such as stenting.[105] Another example is the National Joint Replacement Registry which monitors the performance of prosthetic items. It collects data on patient details, the implants in their joints, the procedures adopted and the survival of the prostheses.

9.2.5.2 Review

While MSAC examines new medical procedures, a range of committees reviews existing MBS items. The Medical Benefits Consultative Committee is an informal advisory committee which reviews particular services or groups of services on the General Medical Services Table of the MBS and considers appropriate fee levels. The Pathology Services Table Committee's primary role is to advise the Minister on the need for changes to the structure and content of the Pathology Services Table of the MBS, including the level of fees.[106] Similar roles are undertaken by the four diagnostic imaging Memoranda of Understanding (MoU) Management Committees. These include the Radiology Management Committee, Cardiac Imaging Management Committee, Nuclear Imaging Consultative and Economics Committee, and Obstetric and Gynaecological Ultrasound Management Committee.

DoHA indicated that such reviews can result in amendments to service descriptions in the MBS or deletion of items if procedures are no longer applicable or have been superseded by new technologies. Nevertheless, an important remark reported by ACT Health was that Australia has strong gate-keeping processes for new technologies, but there are insufficient processes for the regular review of approved technologies.

9.2.5.3 Vigilance system[99]

The new legislation includes a mandatory reporting system for adverse events involving all medical devices. The system is known as the Vigilance System and is based on the recommendations of the Global Harmonisation Task Force (GHTF) Study Group 2: Vigilance and Surveillance.

Sponsors are required to report any problem to the manufacturer of the device. Manufacturers are required to report the problem to the TGA. In accordance with postmarket requirements, sponsors must advise the TGA of serious public health

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[102] HIC (Health Insurance Commission) 2003, Annual Report 2002-03, Canberra.
[103] PHIAC (Private Health Insurance Administration Council) 2005, Statistical Trends in Membership and Benefits, Canberra.
104 HCF (Hospitals Contribution Fund of Australia). Annual Report 2002-03, Sydney. 2004.
[105] ABS (Australian Bureau of Statistics). Australian Historical Population Statistics. Cat. no. 3105.0.65.001, ABS, Canberra. 2004.
[106] DoHA (Department of Health and Ageing). Medicare Benefits Schedule Book, Canberra. 2004.

threats or concerns within 48 hours, incidents involving serious injury or death within 10 days and non serious incidents within 30 days.

The Vigilance System comprises:

- penalties and time frames
- recall and seizure provisions
- voluntary reporting provisions for medical device users
- international information exchange between conformity assessment bodies
- information exchange between inter governmental agencies within Australia

9.2.5.4 Remarks

Remarks formulated by the Productivity Commission (2005) on post-assessment processes are the following:[14]

- Once listed on the MBS (Medicare Benefits Scheme), medical procedures are not subject to systematic reassessment of their clinical or cost-effectiveness. While MSAC can undertake such re-assessments, its ability to do so is limited by its resources and by the types of reference it receives.
- Appropriate monitoring and review processes could help to improve the overall cost-effectiveness of medical technologies on the MBS and Prostheses Schedule. Such processes could facilitate the conditional introduction of new procedures and devices where evidence of cost-effectiveness only becomes available over time.

9.2.6 Reimbursement

Medical devices can be reimbursed through the private or the public health system. Only devices approved by the TGA as being safe and efficacious can be reimbursed. The public health system determines whether or not the devices are worth having. This purchasing decision happens at a state level and may differ across states. In the private sector, medical insurance funds determine whether a device will be reimbursed which happens through negotiations with individual funds.

MSAC may provide funding for a defined period during which further evidence can be gathered for new technologies that show promise of being cost-effective. Once the assessment has been completed over a period of time, the device may then become available unconditionally, i.e. without data collection being associated with it. However, this happened rather rarely in Australia in recent years and has, unfortunately, not become a mainstream approach yet.[107]

[107] Personal communication with Prof. Dr. G. Maddern [August 2006].

- **There are two publicly-funded horizon scanning centres in Australia, i.e. the Australian Safety and Efficacy Register of New Interventional Procedures — Surgical (ASERNIP-S) and the National Horizon Scanning Unit (NHSU), forming the Australian and New Zealand Horizon Scanning Network (ANZHSN)**
- **The Therapeutic Goods Administration (TGA) is responsible for assessing the safety and efficacy of new therapeutic goods.**
- **The Medical Device Evaluation Committee (MDEC) provides independent medical and scientific advice to the Minister and the TGA on the safety, quality and performance of medical devices.**
- **The Office of Devices, Blood and Tissues (ODBT) within the TGA is responsible for regulating medical devices.**
- **The Australian Register of Therapeutic Goods (ARTG) is a computer database of therapeutic goods. Applications for entry on the ARTG can be lodged electronically using the Device Electronic Application Lodgement system (DEAL).**
- **ASERNIP-S assesses new surgical procedures. For prostheses and devices, Clinical Advisory Groups provide advice to the PDC on the relative clinical efficacy and where practicable on cost-effectiveness.**
- **The TGA conducts post-market surveillance and testing of products to ensure compliance with legislation. It also conducts investigations of reported problems.**
- **Whereas for pharmaceuticals evaluations are the responsibility of drug manufacturers or suppliers, MSAC may provide funding for a defined period during which further evidence can be gathered for new technologies that show promise of being cost effective.**

9.3 THE USA

9.3.1 Health care system

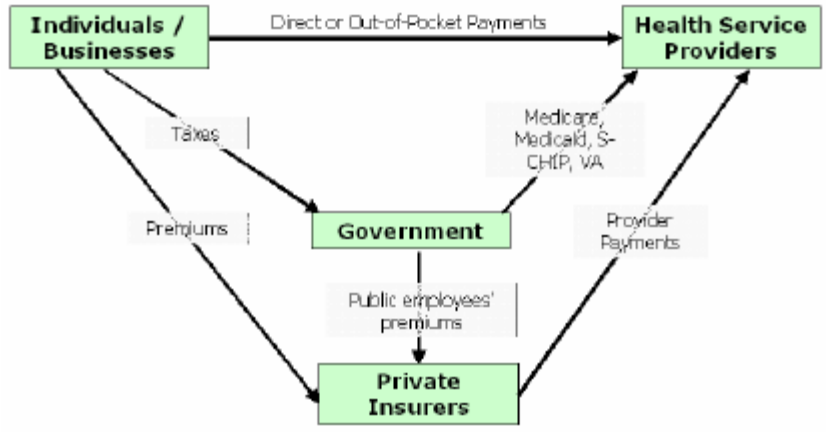
There are both private and public insurers in the U.S. health care system. But, there is a dominance of the private element over the public element. The federal government does not guarantee universal health care to all its citizens, but certain publicly-funded health care programmes help to provide for the elderly, disabled, and the poor.[108][109] Furthermore, the federal law ensures public access to emergency services regardless of ability to pay.[110] The Centres for Medicare and Medicaid Services (CMS), a component of the Department of Health and Human Services, administers the public health insurance. The first one is Medicare which is a federal programme that covers individuals aged 65 or older, younger people with disabilities, and people with End Stage Renal Disease. The Social Security Administration is responsible for determining Medicare eligibility and processing premium payments for the Medicare programme. There are many gaps in Medicare coverage, including incomplete coverage for skilled nursing facilities, incomplete preventive care coverage, and no coverage for dental, hearing, or vision care. Because of this, the vast majority of enrolees obtain supplemental insurance. Secondly, Medicaid is a programme designed for the low-income and disabled. By federal law, states must cover very poor pregnant women, children, elderly, disabled, and parents. Childless adults are not covered, and many poor individuals make too much to qualify for Medicaid. Medicaid offers a fairly

[108] http://www.cms.hhs.gov/home/medicare.asp
[109] http://www.cms.hhs.gov/home/medicaid.asp
[110] http://www.cms.hhs.gov/EMTALA/

comprehensive set of benefits, including prescription pharmaceuticals. Despite this, many enrolees have difficulty finding providers that accept Medicaid due to its low reimbursement rate. Furthermore, there are other public health insurances such as the State Children's Health Insurance Program (S-CHIP) which was designed in 1997 to cover children whose families make too much money to qualify for Medicaid but make too little to purchase private health insurance.[111]

People without health Medicare or Medicaid coverage are expected to have a private health insurance. The private health Insurance consists in the first place in an employer-sponsored insurance. This represents the main way in which Americans receive health insurance. Employers provide health insurance as part of the benefits package for employees. Insurance plans are administered by private companies, both for-profit (e.g. Aetna, Cigna) and non-for-profit (e.g. Blue Cross/Blue Shield). A special case is represented by companies that are "self-insured" (e.g. General Motors). Next to employer-sponsored insurance, private non-group (individual market) insurance exists. The individual market covers part of the population that is self-employed or retired. In addition, it covers some people who are unable to obtain insurance through their employer. The individual market allows health insurance companies to deny people coverage based on pre-existing conditions. Figure 15 provides a simplified representation of the financing of the US health care system.[112]

Figure 15: financing of the US health care system[113]



For institutional care such as hospital and nursing home care, Medicare uses prospective payment systems in which the health care institution receives a set amount of money for each episode of care provided to a patient, regardless of the actual amount of care used. The actual allotment of funds is based on a list of diagnosis-related groups (DRGs). The actual amount depends on the kind of diagnosis made at the hospital. There are some issues surrounding Medicare's use of DRGs because if the patient uses less care, the hospital gets to keep the remainder. This, in theory, should balance the costs for the hospital. However, if the patient uses more care, then the hospital has to cover its own losses. This results in the issue of "upcoding," when a physician makes a more severe diagnosis to hedge against accidental costs.[114]

9.3.2 Horizon scanning[115]

Organizations with horizon scanning functions in the USA include ECRI, the University HealthSystem Consortium (UHC), and Hayes Inc.

[111] http://www.amsa.org/uhc/HealthCareSystemOverview.pdf#search=%22united%20
[112] http://www.amsa.org/uhc/HealthCareSystemOverview.pdf#search=%22united%20
[113] http://www.amsa.org/uhc/HealthCareSystemOverview.pdf#search=%22united%20
[114] http://en.wikipedia.org/wiki/Medicare_(United_States)
[115] http://www.nlm.nih.gov/nichsr/ehta/chapter15.html

9.3.2.1 ECRI[116]

ECRI (formerly the Emergency Care Research Institute) is a nonprofit health services research agency and a Collaborating Center of the World Health Organization (WHO). It is designated as an Evidence-based Practice Center (EPC) by the U.S. Agency for Healthcare Research and Quality (AHRQ). ECRI publishes several series that cover new and emerging health technologies. Series related to horizon scanning of emerging medical technologies are:

- Health Technology Forecast: a new online horizon-scanning tool for healthcare executives. It is a continually updated online resource which identifies developing healthcare technologies and those soon to emerge from the research pipeline into the marketplace.
- Health Technology Trends: a monthly newsletter with information on the latest developments and topics in healthcare technology. Each issue includes fast-reading news and feature articles on emerging medical technologies, primarily focusing on new devices and procedures in cardiology, radiology, oncology, orthopedics and neurosciences.

9.3.2.2 University HealthSystem Consortium [117]

The University HealthSystem Consortium (UHC), formed in 1984, is an alliance of academic health centres situated mainly in the United States. UHC identifies numerous new and emerging technologies, including devices, that may have the greatest potential impact on member organizations. The Clinical Technology @dvisory is a monthly newsletter that tracks technology developments. It focuses both on technologies that are in the early stages of adoption and on those that present an opportunity for academic medical centres to participate in research involving new technologies.

9.3.2.3 Hayes Inc.[118]

Hayes Inc. is an independent U.S. consulting health technology assessment company. This company offers several products that cover new and emerging health technologies.

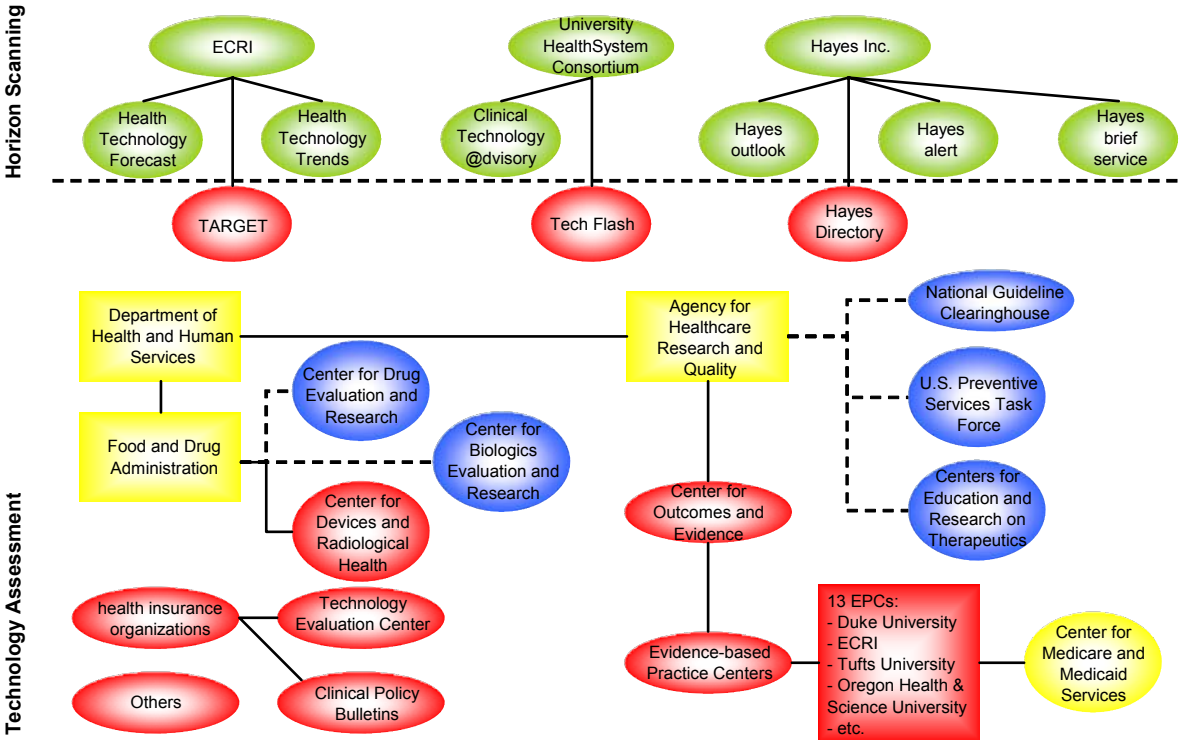
- Hayes outlook: a horizon scanning service which identifies and monitors emerging medical technologies that have not yet been approved by the FDA or adopted by health care providers outside the research setting. The tracked technologies are expected to have a significant impact on health care utilization or costs when they become commercially available.
- Hayes alert: a monthly newsletter that contains summaries of clinical research studies that reflect major advances in clinical knowledge of medical technologies. It covers, among other things, the latest healthcare news and new FDA approvals.
- Hayes brief service: Hayes Health Technology Brief Service is designed for health care decision makers who need to make rapid decisions about the acquisition of a new health technology. The Brief Service includes first of all the Hayes Search and Summary which summarizes all the available information about applicable regulatory approvals and abstracts of studies identified in a literature search. Secondly, the Health Technology Brief is a report that provides information on new health technologies for which there are at least 3 clinical studies of sufficient quality to allow evaluation of safety and efficacy, but for which there is not enough published evidence to warrant a full length Directory report.

[116] http://www.ecri.org
[117] http://www.uhc.edu/
[118] http://www.hayesinc.com/

9.3.3 Assessment

There are several institutes in the US involved in (emerging) health technology assessment. On the Federal level, FDA's Center for Devices and Radiological Health and the Agency for Healthcare Research and Quality (especially with its Evidence-based Practice Centers), are involved in this activity. Next, the previous mentioned horizon scanning institutes, i.e. ECRI, University HealthSystem Consortium (UHC) and Hayes Inc. also provide first assessments. Furthermore, some U.S. health insurance organizations are also sources of emerging technology assessments. An overview of the discussed institutes is provided in figure 16. Other companies such as The Office of Medical Applications of Research (OMAR), the Medical Technology & Practice Patterns Institute (MTPPI), United Biosource Corporation (formerly MedTap), RAND, are mentioned very briefly.

Figure 16: Horizon scanning and HTA in the US.



9.3.3.1 Food and Drug Administration [119]

The U.S. Food and Drug Administration (FDA) reviews the results of laboratory, animal and human clinical testing done by companies to determine if the product they want to market is safe and effective. The FDA does not develop or test products itself. The Agency conducts these reviews for new human pharmaceuticals, biologics (such as vaccines, blood products, biotechnology products and gene therapy), and complex medical devices, as well as for food and colour additives, infant formulas and veterinary pharmaceuticals. To facilitate the review of such a wide diversity of products, the FDA is comprised of multiple Centers responsible for overseeing specific groups of products:

- Center for Drug Evaluation and Research
- Center for Biologics Evaluation and Research
- Center for Devices and Radiological Health

[119] http://www.nlm.nih.gov/nichsr/ehta/chapter8.html

The Center for Devices and Radiological Health (CDRH) reviews requests to research or market medical devices.

9.3.3.2 The Agency for Healthcare Research and Quality [120] [121]

The Agency for Healthcare Research and Quality (AHRQ) is the lead U.S. federal agency charged with supporting research designed to improve the quality, safety, efficiency, and effectiveness of health care. AHRQ's Center for Outcomes and Evidence (COE) (formerly Center for Outcomes and Effectiveness Research and the Center for Practice and Technology Assessment) conducts and supports research and assessment of health care practices, technologies, processes, and systems. The technology assessment programme within COE serves as a point of contact for organizations and individuals searching for comprehensive evidence reviews on health conditions, treatments, and technologies in the United States.

AHRQ supports a variety of investigator-initiated and targeted projects focused on quality measurement and improvement, evidence-based medicine and implementation of research. Those that are most relevant to health technology assessment researchers are the following:

- National Guideline Clearinghouse™ (NGC)
- Evidence-based Practice Centers (EPCs)
- U.S. Preventive Services Task Force (USPSTF)
- Centers for Education and Research on Therapeutics™ (CERTs)

National Guideline Clearinghouse™ [122]

AHRQ supports the National Guideline Clearinghouse™ (NGC), which is a comprehensive database of evidence-based clinical practice guidelines and related documents, including those with a major focus on technology assessment.

Evidence-based Practice Centers[123]

Under the Evidence-based Practice Centers (EPC) Program of the Agency for Healthcare Research and Quality, 5-year contracts are awarded to institutions in the United States and Canada to serve as EPCs. Currently, AHRQ supports 13 EPCs. AHRQ's COE oversees the Evidence-based Practice Centers Program. The EPCs develop evidence reports and technology assessments on clinical topics that are common, expensive, and/or significant for the Medicare and Medicaid populations. Topic nominations are solicited from both public and private groups. EPCs collaborate with other medical and research organizations to include a broad range of experts. Three of the EPCs specialize in conduction technology assessments for the Center for Medicare and Medicaid Services (CMS): Duke University, ECRI and Tufts University–New England Medical Center.

U.S. Preventive Services Task Force[124]

The U.S. Preventive Services Task Force (USPSTF) is an independent panel of experts in primary care and prevention that systematically reviews the evidence of effectiveness and develops recommendations for clinical preventive services. The USPSTF evaluates the accuracy and reliability of screening tests and the effectiveness of early detection. The USPSTF is supported by an EPC, i.e. Oregon Health & Science University.

Centers for Education and Research on Therapeutics™ [125]

[120] http://www.ahrq.gov
[121] http://www.nlm.nih.gov/nichsr/ehta/chapter7.html
[122] http://www.guidelines.gov
[123] http://www.ahrq.gov/clinic/epcix/htm
[124] http://www.ahrq.gov/clinic/uspstfix.htm
[125] http://www.ahrq.gov/path/certs.htm

The Centers for Education and Research on Therapeutics™ (CERTs) programme is a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research. Seven Centers are currently funded, each focusing on therapies used in a particular patient population or therapeutic area. Research conducted by these Centers is, among other things, designed to increase awareness of new uses of medical products, ways to improve effective use, and risks of new uses and combinations. AHRQ's COE oversees the CERTs programme and provides technical assistance and research support.

9.3.3.3 ECRI[126]

ECRI has a web-based Technology Assessment Resource Guide for Emerging Technologies™ (TARGET). Each TARGET record on a specific technology details the technology's associated costs, Medicare and regulatory status, impact on other technologies, and phase of diffusion, as well as ECRI's specific and knowledgeable recommendations.

9.3.3.4 University HealthSystem Consortium[127]

To reduce the financial risks inherent in the process of testing and adopting new clinical technologies, UHC provides strategic counsel, analytic services, and peer networking opportunities. To guide organizations in making wise decisions about how to spend their resources, drug monographs and technology assessments are provided. Tech Flash, a just-in-time assessment can be requested by organizations focusing on a specific technology.

9.3.3.5 Hayes Inc.[128]

The Hayes Directory contains reports assessing a variety of new and emerging medical technologies. For each technology, an expert medical analyst evaluates the peer-reviewed scientific literature, gathering evidence in order to synthesize all of the published relevant data. All Directory reports provide the following information regarding the technology: safety and efficacy, indications and contraindications for use, patient selection criteria, and comparison to alternative technologies.

A Hayes Rating is assigned to each health technology for the specific clinical application assessed and reflects the strength and direction of the evidence. The ratings are scaled A through D and are defined as follows:

- A: Established benefit. Use of the technology is supported by a high level of positive published evidence regarding safety and efficacy for the cited application(s).
- B: Some proven benefit. Use of the technology is supported by a moderate level of positive published evidence regarding safety and efficacy for the cited application(s). Further research is required to fully clarify clinical indications, contraindications, treatment parameters, comparison with other technologies, and/or impact on health outcomes.
- C: Potential but unproven benefit. Use of the technology is supported by some positive published data regarding safety and/or efficacy for the cited application(s), but a beneficial impact on health outcomes has not been proven for one of two reasons: (1) Data are sparse and the level of evidence is low, or (2) Data are inconsistent or conflicting.
- D: No proven benefit and/or not safe. This rating conveys one of two conclusions: (1) Use of the technology has been shown to be unsafe and/or there is no evidence in the current scientific literature that its

[126] http://www.ecri.org
[127] http://www.uhc.edu/
[128] http://www.hayesinc.com/

use improves health outcomes; or (2) The research regarding use of the technology is so limited that an appraisal of safety and efficacy cannot be made.

9.3.3.6 Health insurance organizations

Some U.S. health insurance organizations, such as Blue Cross, Blue Shield and Aetna, are also sources of emerging technology assessments.

Blue Cross Blue Shield's Technology Evaluation Center[129]

The Technology Evaluation Center (TEC) was founded in 1985 by the Blue Cross and Blue Shield Association. TEC is now one of the 13 active EPCs and serves a wide range of clients in both the private and public sectors, including the Centers for Medicare and Medicaid Services (CMS). For technologies being assessed, a thorough review of the body of the clinical evidence available on the effectiveness of the technology is conducted. For emerging technologies, additional forms of research may include specialty society meeting abstracts and direct queries to investigators.

Aetna's Clinical Policy Bulletins[130]

Aetna is one of the providers of health, dental, group, life, disability and long-term care benefits in the US. Aetna's Clinical Policy Bulletins (CPBs) express their determination of whether certain services or supplies are medically necessary, experimental and investigational, or cosmetic. Aetna has reached these conclusions based upon a review of currently available clinical information. The Clinical Policy Bulletins (CPBs) are designed to be used by Aetna's professional staff in making clinical determinations in connection with coverage decisions.

9.3.3.7 Others

- The Office of Medical Applications of Research (OMAR): The Office of Medical Applications of Research (OMAR) is an administrative unit of the National Institutes of Health (NIH) Office of Disease Prevention. It is the focal point for evidence-based assessments of medical practice and state-of-the-science on behalf of the medical community and the public. A major responsibility of OMAR is the coordination of the NIH Consensus Development Program (CDP). Under this program, OMAR organizes major conferences on complex issues of medical importance to health care providers, patients and the general public. These conferences are open to the public, broadcast on the Internet and free of charge to participants. In conjunction with each conference, the Agency for Healthcare Research and Quality (AHRQ) provides a systematic review of literature on the conference topic through one of its Evidence-Based Practice Centers. The NIH Consensus Statements and State of the Science Statements produced by these conferences are disseminated widely to health care practitioners, policymakers, patients, the media and the general public. The purpose of a CDP conference is to evaluate the available scientific information on a biomedical issue and develop a statement that advances understanding of the issue under consideration and will be useful to health professionals and the public.[131]
- Medical Technology & Practice Patterns Institute (MTPPI): a nonprofit organization established in 1986 to conduct research on the clinical,

[129] http://www.bcbs.com/tec/tecassessments.html
[130] http://www.aetna.com/cpb
[131] http://odp.od.nih.gov/omar/

economic, and social implications of new and emerging health care technologies.[132]

- United Biosource Corporation: a global company (formerly MedTap International) focused on demonstrating effectiveness, minimizing safety risks, and documenting economic benefits.[133]
- RAND: The RAND Corporation is a nonprofit institution that helps improve policy and decisionmaking through research and analysis. Several divisions at RAND, including RAND Health, contribute to health and health care research.[134]
- Etc.

9.3.4 Regulation of medical devices[135]

The U.S. Food and Drug Administration (FDA) regulates medical devices to assure their safety and effectiveness and develops, and carries out a national programme designed to control unnecessary exposures to, and assure safe and efficacious use of, ionizing and non-ionizing radiation-emitting electronic products. The Center for Devices and Radiological Health (CDRH) is the component within the FDA that is responsible for this programme. The FDA's legal authority to regulate both medical devices and electronic radiation-emitting products is the Federal Food Drug & Cosmetic (FD&C) Act.

Medical devices are classified into Class I, II, and III. Device classification depends on the *intended use* of the device, e.g. a scalpel's intended use is to cut tissue, and also upon *indications for use*, e.g. for making incisions in the cornea. In addition, classification is risk based. Class I includes devices with the lowest risk and Class III includes those with the greatest risk. Regulatory control increases from Class I to Class III. Most Class I devices are exempt from Premarket Notification 510(k); most Class II devices require Premarket Notification 510(k); and most Class III devices require Premarket Approval. The basic regulatory requirements that manufacturers of medical devices distributed in the U.S. must comply with are:

- Premarket Notification 510(k), unless exempt, or Premarket Approval (PMA), investigational device exemption
- Establishment registration
- Medical Device Listing
- Quality System (QS) regulation,
- Labeling requirements
- Medical Device Reporting (MDR)

Among other things, CDRH's Office of Device Evaluation advises the Center Director and other agency officials on all premarket notification submissions (510(k)s), premarket approval applications (PMAAs), product development protocols (PDPs), device classifications, and investigational device exemptions (IDEs).

Product information on new and older approvals is provided by the CDRH.

[132] http://www.mtppi.org
[133] http://www.unitedbiosource.com
[134] http://www.rand.org/health
[135] http://www.fda.gov/cdrh/devadvice/

Table 8: Product information on new and older approvals[136]

Newest Approvals	Recently Approved Devices (5/12/2000-present)
Older Approvals	Monthly Listing of PMAs (1994-present) Monthly Listing of 510(k) Summaries (11/95-present) Premarket Approvals Application (PMA) Database (1977-present) Premarket Notification 510(k) Database (1976-present)

Parts of the procedure to put medical devices into the market are described underneath. Medical Device Reporting is discussed in the following part, i.e. post-market surveillance.

Pre-Market notification[137]

Each person who wants to market Class I, II and some III devices intended for human use in the U.S. must submit a 510(k) to FDA at least 90 days before marketing unless the device is exempt from 510(k) requirements. A 510(k) is a premarketing submission made to FDA to demonstrate that the device to be marketed is as safe and effective, that is, substantially equivalent (SE), to a legally marketed device that is not subject to premarket approval (PMA). Applicants must compare their 510(k) device to one or more similar devices currently on the U.S. market and make and support their substantial equivalency claims. A legally marketed device is a device that was legally marketed prior to May 28, 1976 (preamendments device), or a device which has been reclassified from Class III to Class II or I, a device which has been found to be substantially equivalent to such a device through the 510(k) process, or one established through Evaluation of Automatic Class III Definition. The legally marketed device(s) to which equivalence is drawn is known as the "predicate" device(s).

Applicants must submit descriptive data and, when necessary, performance data to establish that their device is SE to a predicate device. Again, the data in a 510(k) is to show comparability, i.e. SE of a new device to a predicate device and requires no demonstration of reasonable safety and effectiveness as in premarket approval.

Premarket approval[138]

Contrasting with the EU system the FDA premarket approval (PMA) requires the demonstration of a medical device's clinical effectiveness as a precondition for marketing. PMA is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. Class III devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury. Due to the level of risk associated with Class III devices, FDA has determined that general and special controls alone are insufficient to assure the safety and effectiveness of class III devices. Therefore, these devices require a PMA application under section 515 of the FD&C (Food, Drug, and Cosmetic) Act in order to obtain marketing clearance.

PMA is the most stringent type of device marketing application required by FDA. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s). An approved PMA is, in effect, a private license granting the applicant (or owner) permission to market the device. The PMA owner, however, can authorize use of its data by another.

[136] http://www.nlm.nih.gov/nichsr/ehta/chapter8.html
[137] http://www.fda.gov/cdrh/devadvice/314.html
[138] http://www.fda.gov/cdrh/devadvice/pma/

The PMA applicant is usually the person who owns the rights, or otherwise has authorized access, to the data and other information to be submitted in support of FDA approval. This person may be an individual, partnership, corporation, association, scientific or academic establishment, government agency or organizational unit, or other legal entity. The applicant is often the inventor/developer and ultimately the manufacturer.

FDA regulations provide 180 days to review the PMA and make a determination. In reality, the review time is normally longer. Before approving or denying a PMA, the appropriate FDA advisory committee may review the PMA at a public meeting and provide FDA with the committee's recommendation on whether FDA should approve the submission. After FDA notifies the applicant that the PMA has been approved or denied, a notice is published on the Internet (1) announcing the data on which the decision is based, and (2) providing interested persons an opportunity to petition FDA within 30 days for reconsideration of the decision.

The FDA pre-market approval of a subgroup of medical devices known as "combination products", the drug eluting coronary artery stent, demonstrates that the FDA approval can result in the delay deployment. As the demonstration for both the stent and the drug were required in the premarket approval process, the drug eluting coronary stent was introduced in the US two years after its release in Europe.[139]

Investigational device exemption[140]

An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval application or a Premarket Notification [510(k)] submission to FDA. Clinical studies with devices of significant risk must be approved by FDA and by an Institutional Review Board (IRB) before the study can begin. Studies with devices of nonsignificant risk must be approved by the IRB only before the study can begin.

Establishment registration[141]

Establishments involved in the production and distribution of medical devices intended for marketing or leasing (commercial distribution) in the United States (U.S.) are required to register with the FDA. This process is known as establishment registration. Registration provides FDA with the location of medical device manufacturing facilities and importers.

Registration of an establishment is not an approval of the establishment or its devices by FDA. That is, it does not provide FDA clearance to market. Unless exempt, premarketing clearance is required before a device can be placed into commercial distribution in the U.S.

Medical Device listing[142]

Most medical device establishments required to register with FDA must also identify to FDA the devices they have in commercial distribution including devices produced exclusively for export. This process is known as medical device listing and is a means of keeping FDA advised of the generic category(s) of devices an establishment is manufacturing or marketing. Listing of a medical device is not approval of the establishment or a device by FDA. Unless exempt, premarketing clearance is required before a device can be marketed (placed into commercial distribution) in the U.S. There is no fee for listing devices.

The database containing a list of medical devices in commercial distribution by both domestic and foreign manufacturers is updated monthly.

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[139] Lansing Kipp J. FDA regulation: The Dardanelles of new medical device availability. Book of proceedings of the 16th World congress on medical law. , 7-11 of august 2006, Toulouse, p. 843- 850.
[140] http://www.fda.gov/cdrh/devadvice/ide/index.shtml
[141] http://www.fda.gov/cdrh/devadvice/341.html
[142] http://www.fda.gov/cdrh/devadvice/342.html

Quality System (QS) regulation[143]

The quality system regulation includes requirements related to the methods used in and the facilities and controls used for: designing, purchasing, manufacturing, packaging, labeling, storing, installing and servicing of medical devices. Manufacturing facilities undergo FDA inspections to assure compliance with the QS requirements.

Labeling requirements[143]

Labeling includes labels on the device as well as descriptive and informational literature that accompanies the device.

9.3.5 Post-market surveillance

The most important post-market surveillance happens through the FDA's Medical Device Reporting and post-marketing surveillance studies. In this part only these systems will be discussed. However, we are aware that other safety warning systems exist (e.g. UHC's Patient Safety Net®, ECRI's Health Devices Alerts, etc.).

Medical Device Reporting (MDR)[144]

Since December 13, 1984, the FDA Medical Device Reporting (MDR) regulations have required firms who have received complaints of device malfunctions, serious injuries or deaths associated with medical devices to notify FDA of the incident. The Safe Medical Devices Act (SMDA) of 1990 provided FDA with two additional postmarketing activities, Postmarket Surveillance for the monitoring of products after their clearance to market and Device Tracking for maintaining traceability of certain devices to the user level. The MDR regulation provides a mechanism for FDA and manufacturers to identify and monitor significant adverse events involving medical devices. The goals of the regulation are to detect and correct problems in a timely manner. Although the requirements of the regulation can be enforced through legal sanctions authorized by the Federal Food Drug & Cosmetic (FFD&C) Act, FDA relies on the goodwill and cooperation of all affected groups to accomplish the objectives of the regulation. MDR data contains information from CDRH's former database, the device experience network (DEN). The reports include mandatory manufacturer reports on devices which may have malfunctioned or caused a death or serious injury. These reports were received under both the mandatory MDR Program from 1984 - 1996, and voluntary reports up to June 1993.

On July 31, 1996, the new MDR regulation became effective. The Manufacturer and User Facility Device Experience Database (MAUDE) represents reports of adverse events involving medical devices. The data consists of voluntary reports since June 1993, user facility reports since 1991, distributor reports since 1993, and manufacturer reports since August 1996.[145] Warning letters issued since 1996 are posted to a database on the FDA's web site that enables searches by company, subject, issuing office, date, and text content. Table 10 provides an overview of the available links for these post-marketing reports.

[143] http://www.fda.gov/cdrh/devadvice/overview.html
[144] http://www.fda.gov/cdrh/devadvice/351.html
[145] http://www.fda.gov/cdrh/maude.html

Table 10: post-marketing reports and warning letters issued by the Center for Devices and Radiological Health[146]

Post-Marketing Reports	Medical Device Reporting (MDR): http://www.fda.gov/cdrh/mdrfile.html (1984-1997) http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmdr/search.CFM (1992-1996) Manufacturer and User Facility Device Experience Database (MAUDE): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/Search.cfm (7/31/96-present)
Warning Letters	http://www.fda.gov/foi/warning.htm (11/96-present from FOI page)

Consumer or health professional can use the MedWatch programme for reporting significant adverse events or product problems with medical products. MedWatch is FDA's Safety Information and Adverse Event Reporting Program. It allows healthcare professionals and consumers to report serious problems that they suspect are associated with the pharmaceuticals and medical devices they prescribe, dispense, or use.147 User Facilities (e.g., hospitals, nursing homes) are required to report suspected medical device related deaths to both the FDA and the manufacturers. User facilities report medical device related serious injuries only to the manufacturer. Manufacturers report to the FDA. Time limits depend on the kind of adverse event. Table 11 gives a short overview.

[146] http://www.nlm.nih.gov/nichsr/ehta/chapter8.html
[147] http://www.fda.gov/medwatch/

Table 11: summary of reporting requirements for manufacturers and user facilities[148]

REPORTER	WHAT TO REPORT	TO WHOM	WHEN
Manufacturer	30 day reports of deaths, serious injuries and malfunctions	FDA	Within 30 calendar days from becoming aware of an event
Manufacturer	5-day reports on events that require remedial action to prevent an unreasonable risk of substantial harm to the public health and other types of events designated by FDA	FDA	Within 5 work days from becoming aware of an event
Manufacturer	Baseline reports to identify and provide basic data on each device that is subject of an MDR report. At this time, FDA has stayed the requirement for denominator data requested in Part II, Items 15 and 16 on Form 3417.	FDA	With 30 calendar, and 5 work day reports when device or device family is reported for the first time. Interim and annual updates are also required if any baseline information changes after initial submission.
Manufacturer	Annual Certification	FDA	Coincide with firm's annual registration dates.
User Facility	Death	FDA & Manufacturer	Within 10 work days
User Facility	Serious injury	Manufacturer. FDA only if manufacturer unknown	Within 10 work days
User Facility	Annual reports of death & serious injury	FDA	January 1

Post-market surveillance studies[149]

FDA may order a manufacturer to conduct postmarket surveillance of a medical device. Postmarket surveillance may be ordered for any class II or class III medical device that meets any of the following criteria:

- Failure of the device would be reasonably likely to have serious adverse health consequences;
- The device is intended to be implanted in the human body for more than 1 year; or
- The device is intended to be used to support or sustain life and to be used outside a user facility.

Postmarket surveillance means the active, systematic, scientifically valid collection, analysis, and interpretation of data or other information about a marketed device. The data can reveal unforeseen adverse events, the actual rate of anticipated adverse events, or other information necessary to protect the public health.

[148] http://www.fda.gov/cdrh/devadvice/351.html
[149] http://www.fda.gov/cdrh/devadvice/352.html

- **Several organizations (ECRI, UHC, Hayes Inc.) provide horizon scanning activities. These organizations also perform early assessments.**
- **On a federal level, technology assessment is performed by the Center for Devices and Radiological Health (CDRH) and the Agency for Healthcare Research and Quality (AHRQ). CDRH reviews requests to research or market medical devices. AHRQ's Center for Outcomes and Evidence (COE), which oversees the Evidence-based Practice Centers (EPC), conducts and supports research and assessment of health care practices, technologies, processes, and systems.**
- **Health insurance organizations (e.g. Blue Cross, Blue Shield and Aetna) are also sources of emerging technology assessments.**
- **The U.S. Food and Drug Administration (FDA) regulates medical devices.**
- **FDA registrations consist of both an establishment registration and medical device listing.**
- **Medical devices are classified into Class I, II, and III. Device classification depends on the intended use of the device, indications for use, and risk. Regulatory control increases from Class I to Class III.**
- **Most Class I devices are exempt from Premarket Notification 510(k); most Class II devices require Premarket Notification 510(k); and most Class III devices require Premarket Approval.**
- **A 510(k) is a premarketing submission made to FDA to demonstrate that the device to be marketed is as safe and effective, that is, substantially equivalent (SE), to a legally marketed device that is not subject to premarket approval (PMA). Contrasting with the EU system the FDA premarket approval (PMA) requires the demonstration of a medical device's clinical effectiveness as a precondition for marketing.**
- **An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a PMA application or a Premarket Notification (510(k)) submission to FDA.**
- **CDRH's Manufacturer and User Facility Device Experience Database (MAUDE) represents reports of adverse events involving medical devices.**
- **FDA may order a manufacturer to conduct postmarket surveillance of a medical device.**

9.4 CANADA

9.4.1 Health care system

Under the Canadian constitution, health care delivery and financing are a provincial responsibility. The federal government (Health Canada) has only jurisdiction for regulating the manufacturing, sale and import of therapeutic products (pharmaceuticals, medical devices).[150]

While responsible for the administration and funding of public health care, the provinces deliver very few health services directly. Most public health services are organized or delivered by regional health authorities that have been delegated the responsibility to administer services within defined geographic areas. This delegation of authority to health regions for health care delivery took place in the early 1990s, as part of a regionalization and decentralization move across Canada. Receiving global budgets from

[150] Marchildon GP. Health Systems in Transition: Canada. Copenhagen, WHO Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies. 2005.

the province, regional health authorities (RHAs) are expected to allocate health resources in a manner that optimally serves the needs of their respective populations. Prior to including a drug or medical device in a formulary and thereby making it eligible for coverage, provinces typically assess how such a decision will affect the public purse. Reviewing the therapeutic value and cost-effectiveness of new pharmaceuticals and medical devices on behalf of most provincial and territorial drug plans is the responsibility of the Canadian Agency for Drugs and Technologies in Health (CADTH). Given the existence of provincial health technology assessment organizations, this also means that the national CADTH coordinates the dissemination of existing studies throughout the country and provides original health technology assessments in areas not covered by the provinces.

9.4.2 Horizon scanning

CADTH[151] is a member of Euroscan and as such its mandate is to identify and alert decision-makers of the new and emerging health technologies (defined as medical procedures, devices, systems or pharmaceuticals used in the maintenance, treatment and promotion of health) that may have a significant impact on the delivery of health care in Canada. The CADTH Horizon Scanning Service started in 1997. Its aim is to help all Canadian jurisdictions monitor and stay abreast of rapid advances in health technology development.

Through active and ongoing literature scanning, CADTH identifies health technologies that are in the early development or adoption phase, and which may affect health care finances, facilities, operations, and patient care. The CADTH horizon scanning reports for drug (Emerging Drug List) and non-drug (Health Technology Update) health technologies help decision makers better anticipate, plan, and manage the introduction and diffusion of new technologies.

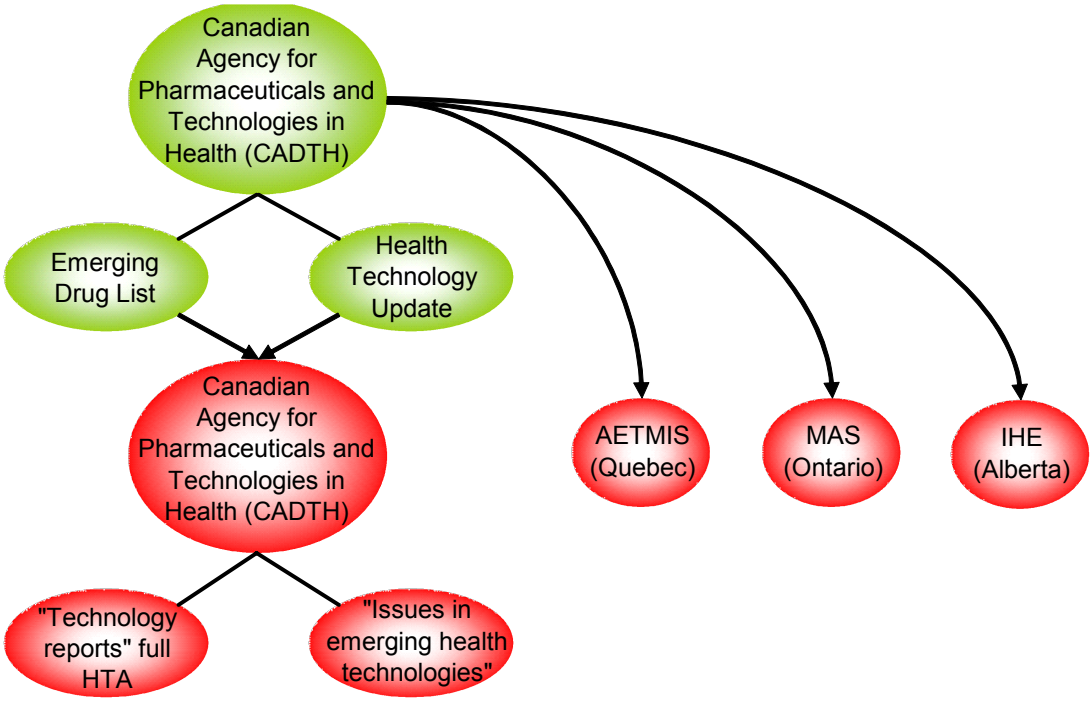
- "Emerging Drug List" is an online series that profiles new pharmaceuticals and vaccines while they are at an early stage of development, prior to Health Canada approval. Designed as a "heads up" for those who anticipate, plan, and manage drug coverage and prescribing decisions, these summaries identify pharmaceuticals that are expected to have a high impact on utilization, patient outcomes, hospital operations, or drug budgets. Summaries include a description of the drug, patient indications, regulatory status, alternative drug treatments, adverse effects, cost, a summary of the early evidence, and general comments.
- "Health Technology Update" is a newsletter whose aim is to provide the latest information on new and emerging medical devices, procedures and health systems to support health care decisions and policy making at the local, regional, provincial and national levels. The health technologies covered may or may not have Health Canada approval. Some of the technologies may already be licensed for use in the US or elsewhere, while others are being used only in clinical trials. Some not-so-new technologies are already licensed for use in Canada, but high costs or other factors may be influencing their rate of uptake and diffusion. The information included in the "Health Technology Update" is based on a limited literature review of the available evidence and as such is not advised to be used as a recommendation for or against the use of a particular health technology. This is because a lack of good quality evidence to support effectiveness does not necessarily mean a lack of effectiveness, particularly in the case of new and emerging technologies.

There does not seem to be any formal horizon scanning activities at the provincial level since most provinces work cooperatively with CADTH and monitor his work to inform their questions. In Ontario, for example, emerging technologies are identified through a

[151] http://www.cadth.ca/index.php/en/home

variety of methods including: applications for review of medical devices from users of technologies in the health care system (hospitals, community care centres, public health units etc.), requests from various divisions within the ministry, review of CADTH horizon scanning documents and industry information presented at research conferences.[152]

Figure 17: Horizon scanning and HTA in Canada



9.4.3 Health technology assessment

In Canada, both national and regional health technology assessment procedures exist (figure 17).

9.4.3.1 National procedure

The HTA activities at the CADTH examine technologies at all stages of their life cycle, from development through to maturity and obsolescence. At the start, the CADTH receives topics suggestions from Canadian policy makers, medical directors, managers, health care providers, industry, health care professional associations, and the public. Technology assessment topics may also be identified though the Horizon Scanning Program. Proposed topics are filtered and prioritized with the help of CADTH's Advisory Committee on Pharmaceuticals and the Devices and Systems Advisory Committee. Depending on the maturity of the technology (diffusion stage, evidence available) and on the timelines, a brief ("Issues in Emerging Health Technologies") or a thorough ("Technology Reports") assessment of the technology is performed. There is no separate procedure for the assessment of drug and non-drug technologies.

"Issues in Emerging Health Technologies" is a series of concise bulletins describing drug and non-drug technologies that are not yet used (or widely diffused) in Canada; in most cases, Health Canada's approval is anticipated in the next six to 18 months. Bulletins include a description of the emerging technology; patient indications; regulatory status; adverse effects; costs; anticipated diffusion rates; implementation issues; and a discussion of the reliability and quality of available evidence. While the bulletins analyze all available data, the evidence base is generally insufficient to permit a meta-analysis of

[152] Personal communication with Shirley Lee, MAS, Ontario [August 2006]

individual trials or other statistical analyses. Each bulletin is peer reviewed by two or more external clinical experts.

At a later stage, i.e. for more mature technologies, for which there is a larger and higher quality body of evidence available, CADTH produces "Technology Reports" which are a most comprehensive assessments of health care technologies and services. The technology's clinical effectiveness and cost-effectiveness are examined, as well as the social, ethical, and economic implications of its use, compared with alternative treatments. Information is also included about patient indications, current treatment practices, regulatory issues, adverse effects, and health services impact.

There is no systematic plan at CADTH to follow-up all the "Issues in Emerging Health Technologies" with full health technology assessments.[153] Further, note that field evaluation, though not formaly in place at the national level, is a component of the Pan-Canada Health Technology Strategy that is being developed in Canada.[154]

9.4.3.2 Regional procedure

Québec (AETMIS) [155]

The Agence d'Évaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) was established in Quebec in 1988. The Agency receives several requests for assessment originating mainly from the Ministry of Health and its decisional authorities. Assessment, as carried out by the Agency, involves instruments, devices (including technical aids for the disabled), medications and substances. Each assessment proposal is subject to a preliminary analysis conducted with a view to determining its relevance. This analysis is then transmitted to the Board of Members, which selects the topics to be evaluated. The assessment method used by the Agency consists in summarizing the scientific publications on the topic and analyzing how applicable the proposed recommendations are for Québec. The assessment takes into consideration numerous parameters affecting the effectiveness, security and efficiency of the technologies or intervention methods involved, as well as their ethical, social, organizational and economic repercussions. If one of the topics proposed by the Ministry of Health is about an emerging technology, it will be assessed following the general AETMIS HTA process. The completeness of the analysis and the length of the report will however vary according to the priority level of the technology, the availability and quality of the scientific evidence and the timelines. There is no systematic re-assessment of the technology at a later stage. Further, a system of "field evaluations" to gather additional evidence about emerging technologies is not yet in place in Quebec.[156]

Ontario (MAS) [157]

The Medical Advisory Secretariat (MAS) is a division within the Ontario Ministry of Health and Long-Term Care (MOHLTC). The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of new health technologies and health services in Ontario to the ministry and other government agencies. Through systematic reviews of scientific evidence and consultation with experts in the medical community, MAS provides up-to-date evidence-based assessment and advice to government health care decision-makers about emerging health technologies and health services. Technologies encompass interventions used at any point in healthcare delivery. However, they do not examine pharmaceutical products or information systems in isolation.

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[153] Personal communication with Leigh-Ann Topfer, CADTH [August 2006]
[154] http://www.hc-sc.gc.ca/hcs-sss/pubs/ehealth-esante/2004-tech-strateg/index_e.html
[155] http://www.aetmis.gouv.qc.ca/
[156] Personal communication with Jean-Marie R. Lance, Conseiller scientifique principal, Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) [August 2006]
[157] http://www.health.gov.on.ca/english/providers/program/mas/mas_mn.html

When a new health technology is identified through application from users of technologies, from the ministry or through horizon scanning, MAS prepares a vignette which provides background information on the technology and indicates the type and extent of evidence available. The vignette is sent to the Ontario Health Technology Advisory Committee (OHTAC) that reviews and discusses the vignette, and decides whether a full systematic review is necessary.

OHTAC is an advisory committee appointed by MOHLTC that provides advice to the Deputy Minister of Health regarding the introduction and diffusion of health technologies in Ontario. MAS provides a secretariat support to OHTAC by preparing vignettes, conducting & presenting evidence-based analyses on effectiveness, economic analysis and policy analysis all within a context that is relevant to Ontario utilisation and patterns of practice, and potentially to policy decision makers.

After considering the information prepared by MAS, OHTAC makes recommendations to the Deputy Minister and finally to the entire health system. Recommendations form OHTAC may be:

- introduction of the technology as an insured health service,
- against the introduction of the health technology,
- re-evaluation on a later date (i.e. if publications of major trials are pending),
- conditional introduction within a field evaluation.

The conditional introduction recommandation made by the OHTAC refers to temporary funding provided to specified academic health centres for a new health technology to be used in a specific target group (e.g. high risk vs low risk, meeting certain clinical criteria) under specified conditions (e.g. following protocol of the field evaluation, collecting & reporting required data etc.) as part of a field evaluation. Such conditional introduction tend to be for technologies that have evidence of effectiveness, have a significant impact on patient outcomes, and have significant budgetary impact, but for which there is still uncertainty regarding their utility, cost, or potential disruption to the health system (e.g. target population, health human resource impact, real time cost-effectiveness, or generalisability to Ontario for published randomized controlled trials). Example of technologies that have field evaluations include PET scans for which 5 clinical trials were developed together with registry studies. The ministry provides funding and selects the appropriate sites for the field evaluation. An arms-length research organization such as the Program for Assessment of Technologies in Health (PATH) at McMaster University develops the protocol with the evaluation sites, coordinates the study working with experts and academic health science centres from across the province, analyzes the data, and provides a report to OHTAC and the ministry. OHTAC may make new recommendations or revise previous recommendations based on outcomes of the field evaluation.[158]

Alberta (IHE)[159]

In order to strengthen HTA in Alberta, the HTA programme of the Alberta Heritage Foundation for Medical Research (AHFMR) has been integrated in July 2006 with the HTA groups at the Institute for Health Economics (Alberta). IHE is a unique partnership of government; academia and industry representatives committed to providing relevant research that will help policy makers formulate decisions regarding the best means of delivering health care while ensuring optimal use of resources. The Institute is a member of the International Network for Health Technology Assessment and the Health Evidence Network of the World Health Organization.

Alberta has formal horizon scanning activity yet. The IHE of Alberta works cooperatively with CADTH and monitors CADTH work to inform their questions.

[158] Personal communication with Shirley Lee – MAS – Ontario [August 2006]
[159] http://www.ihe.ca/index.html

9.4.4 Regulation of medical devices

Medical devices in Canada are divided into four classes based on the level of risk associated with their use (table 12). Class I devices present the lowest potential risk and do not require a medical device licence for their sale in Canada. However, manufacturers of Class I devices must ensure they are designed and manufactured to be safe as defined under the Medical Devices Regulations. Manufacturers of Class II, III and IV devices must obtain a medical device licence before their products can be legally sold in Canada. The license is awarded by the Therapeutic Products Directorate (Health Canada). As the risk level of the device increases, more data is required from the manufacturer to demonstrate that it is safe and effective for its intended application.[160]

Table 12: medical devices classification

	Risk	Examples
Class I	Lowest risk	Reusable surgical scalpel, Band-Aids, culture media
Class II	Low risk	Contact lenses, epidural catheters, pregnancy test kits, surgical gloves
Class III	Moderate risk	Orthopedic implants, glucose monitors, dental implants, haemodialysis systems, diagnostic ultrasound systems
Class IV	High risk	HIV test kits, pacemakers, angioplasty catheters

- **Horizon scanning routinely performed since 1997 by the national CADTH. Production of two reports: "Emerging drug lists" for pharmaceuticals "Health technology update" for medical devices.**
- **National assessment: Full or succinct assessment of drug and non-drug technologies by CADTH depends on the level of evidence available, diffusion stage and timelines. "Issues in Emerging Health Technologies" is a concise bulletin describing drug and non-drug technologies that are not yet used (or widely diffused) in Canada.**
- **Regional assessment: AETMIS (Quebec), MAS (Ontario) and IHE (Alberta) are provincial HTA agencies. MAS only allows a "conditional reimbursement as part of field assessments" of new technologies to obtain additional evidence.**
- **Field evaluation is a component of the Pan-Canada Health Technology Strategy that is being developed in Canada.**

9.5 THE NETHERLANDS

9.5.1 Health care system

The Dutch health care system is insurance based. Health care financing is done by a mix of public and private health insurance. Health care providers however are usually independent practitioners or non-profit institutions. Because the separation between payers (insurers or sickness funds) and providers, the Dutch health care system has always some form of entitlement – setting mechanism. Consequently, a majority of health policy decisions are discussed at the level of the central government, particularly the Ministry of Health, Welfare and Sports.[161]

[160] http://www.hc-sc.gc.ca/ahc-asc/pubs/hpfb-dgpsa/access-therapeutic_acces-therapeutique_e.html

[161] http://www.ehma.org/_fileupload/File/Projects/Benefit_Report_Netherlands.pdf

The introduction of new health technologies can be divided in several subdomains that are treated by several institutions.

For a brief overview of the different organisations:

- Gezondheidsraad (Health council): Information on the current state of affairs of medical science (horizon scanning)
- RVZ[162] (Raad voor volksgezondheid en zorg – council for public health and care): independent advising institution on organisational issues
- Stichting DBC (diagnostics treatment combination) onderhoud [163] : introduction and adjusting of existing DBC's for hospital care
- CTG/ZAio[164] (college tariffs health care): controlling price-fixing and regulation
- CVZ (college for medical insurance): advising on decisions regarding the insertion, adaptation or removal of health care provisions from the insured package.

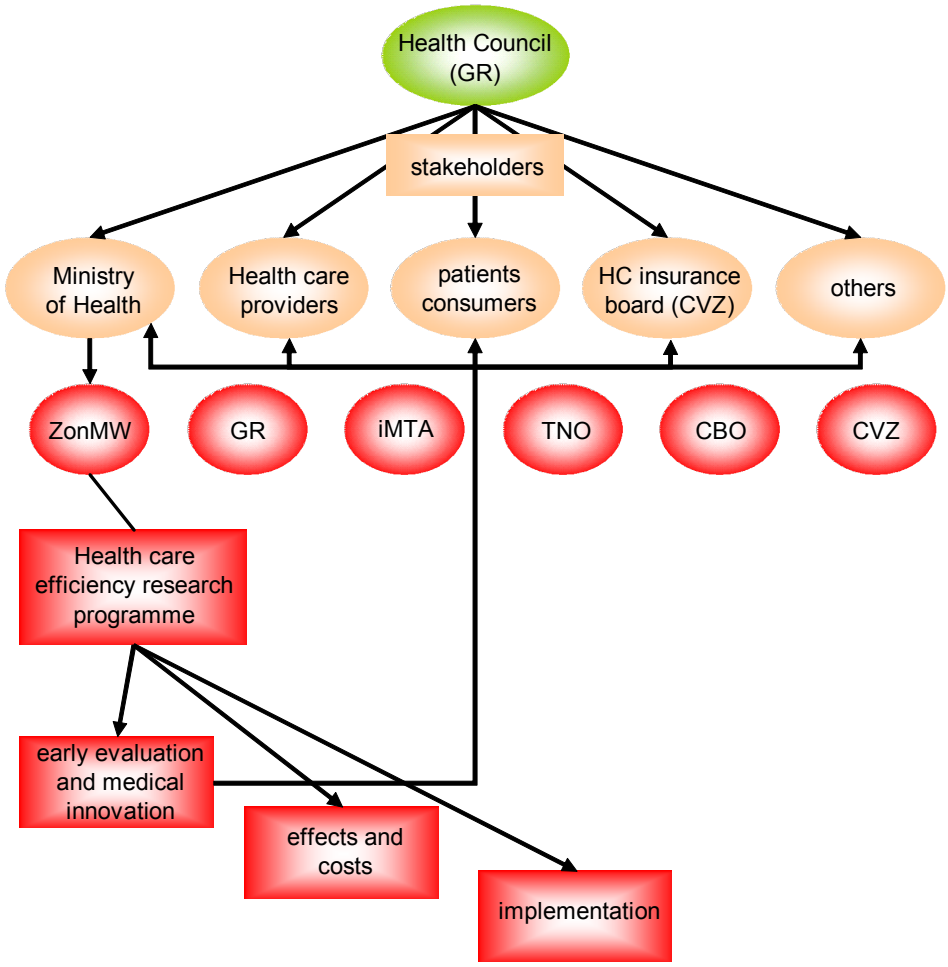
9.5.2 Horizon scanning

The Health council is engaged in identifying and studying emerging technologies. In the domain of signalisation of new health technologies 3 steps can be distinguished.[165]

- Horizon scanning: since the Health council is a member of Euroscan, INAHTA and other associations, the largest amount of information comes from those sources. Apart from these sources there are eight consultation groups (e.g. for medicine, for infectious diseases, genetics, ethics and law,…) and some permanent working groups (e.g. for screening, blood products, etc..) and individual members, external sources who can also provide information on new health technology.
- Filtrating the information: The system developed by Euroscan is used as a starting point. Then the system is adapted to the Dutch situation according to the relevance for policy within the legislation in force. The following criteria for selection are used: public interest (quality of care, accessibility, cost containment and efficacy), surveillance of the ethical limits, national character and technologies that will enter the market within 3 to 5 years.
- Indication and reporting of new health technologies in order to allow proactive policy to the Ministry of Public Health and Sports (VWS), the College for Medical Insurance (CVZ), professionals, patients, organisations developing guidelines (CBO, NHG, etc.), individual health insurers, ZonMw (cfr. infra) etc…

[162] http://www.rvz.net/cgi-bin/rvz_p.pl?id=2
[163] http://www.dbconderhoud.nl/organisatie/index
[164] http://www.ctg-zaio.nl/index.php
[165] http://www.gr.nl/pdf.php?ID=1247&p=1

Figure 18: horizon scanning and HTA in the Netherlands



9.5.3 Health technology assessment

The process of efficiency research/HTA in the Netherlands is cyclical. Organisations such as the Health Council and the Health Care Insurance Board (CVZ) are responsible for highlighting inefficiency. The "Raad voor Gezondheidsonderzoek" (RGO) then responds by setting certain priorities for HTA. Using the advice of the RGO and others, the ministry of health, welfare and sports (Ministerie voor volksgezondheid, welzijn en sport (VWS)) commissions parties, such as ZonMw, to execute research programmes.

After VWS has approved a programme, research is performed within the agreed framework. The results are actively disseminated and implemented among health care practitioners and other stakeholders, such as professional associations, care insurers, CVZ and VWS. A re-evaluation is carried out after some time, which might highlight further inefficiencies, and so the cycle is complete.

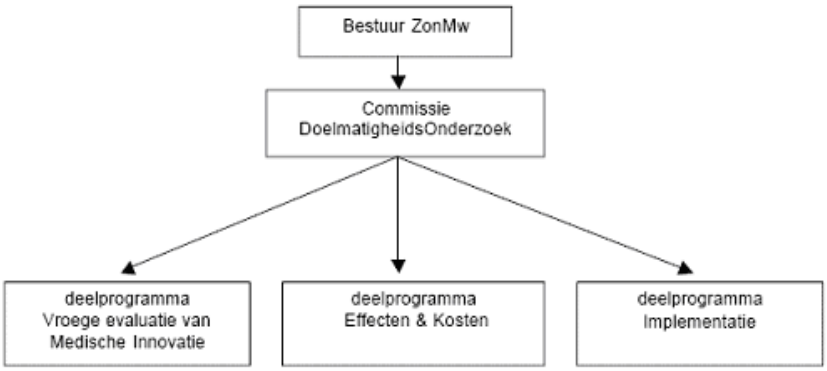
There are also other institutes involved in health technology assessment (figure 18).

9.5.3.1 *Nederlandse organisatie voor gezondheidsonderzoek en zorginnovatie (ZonMw)* [166]

ZonMw is a national organisation that promotes quality and innovation in the field of health research and health care, initiating and encouraging new developments. All the activities in the Health Care Efficiency Research programme are carried out in close consultation with VWS and other relevant organisations, such as the CVZ, VAZ, RGO and the Health Council. At international level, there is collaboration with the INAHTA.

One example of a research programme commissioned by the VWS to ZonMw is the Health Care Efficiency Research programme (figure 19). This is a structural, layered programme that provides a research budget for policy problems which knowledge derived from research could help to solve. The emphasis is on health technologies and the organisation of health care.

Figure 19: Health Care Efficiency Research programme



The current focus of the Health Care Efficiency Research programme is narrow. Many potential applications are not submitted or are rejected because they do not meet the conditions of the programme. The large amount of preliminary research required presents a particular obstacle. Experience has shown that the main reason for rejecting applications is a failure to prove their likely efficacy. The field consultation highlighted 450 potential efficiency studies, but the submissions showed that often many important questions need to be addressed before actual efficiency research can commence. The conclusion is that the current efficiency research programme has been unable to foster important developments in the form of scientific innovation and exploration of the potential of new technology and its application that could enhance the efficiency of care. Therefore the Ministry's commissioning letter of 12 April 2002 left room for practical development and innovation matters that need to be assessed in terms of their societal relevance. The idea was to launch a new Innovation sub-programme,[167] which allows for targeted fostering of developments that could enhance the efficiency of health care. It focuses on new technologies in their second or third stage of development, where their safety has been established, there is some indication as to their efficacy, but there is insufficient information to underpin a cost-effectiveness study. Existing interventions are also eligible; in so far questions have been raised about the feasibility of research. The organisation of professional practice also falls within the parameters of this sub-programme, including forms of organisation that have proved useful in other countries but have yet to be introduced in the Netherlands.

[166] http://www.zonmw.nl/nl/programmas/doelmatigheids-onderzoek/opzet-programma/deelprogrammas/vroege-evaluatie-van-medische-innovatie.html

[167] According to the "Wet bijzondere medische verrichtingen" the minister can decide that medical interventions are subsidized by the government in the scope of a project of development medicine (= the current Innovation program of ZonMW). Subsidies will only be provided to the institution that is concerned in the project if this is justified by ethical, societal of legal reasons, or if major concerns are involved.

More specifically the general conditions to be included in the subprogramme Innovation are:

- The evaluation applies to medical interventions that are part of the domain of the regulated system of financed care.
- The safety of the innovative intervention must be reasonable.
- The maximum term for the project is 2 years.
- Project costs are up to maximally 250.000 Euro. Half of the costs of the project are subsidized by ZonMw. The other 50 % has to be financed by the institutions performing the study or another source of financing. The budgeting has to be set for the entire project.

According to the relevance the research may not solely be "technology driven" but also aims at application in society. Consequently the research subject has to be closely linked to the inefficacy signals in society.

With regard to quality there are some specific conditions for the subprogramme innovation:

- The study design or the types of the study has to be described
- The outcome of the research has to be formulated on patient level
- (health / quality of life).
- Some expertise and experience with regard to the innovative intervention is necessary.
- The Programme can not be used for products in the phase of development
- Economic analysis has to be assessed.

The results of the studies under the innovation programme are actively disseminated and implemented among health care practitioners and other stakeholders, such as professional associations, care insurers, CVZ and VWS. A structured follow-up trajectory after the research performed in the scope of the innovation programme similar to the procedure in UK however does not exist[168]. Moreover there is no formal link between assessment of new technologies and reimbursement policy.

9.5.3.2 The institute for Medical Technology assessment

Nearly all medical faculties and university hospitals in the Netherlands are to some extent involved in HTA activity.[169] Some of these became established centers. Special mention should be made of The institute for Medical Technology Assessment (iMTA), founded in 1988, at the Erasmus University Rotterdam which is closely linked to the institute for Health Policy and Management (iBMG). The main activities of the iMTA are:

- applied scientific research in medical technology assessment (MTA);
- development of new methods and techniques on behalf of MTA research;
- dissemination of our knowledge about MTA through workshops, conferences, courses and publications;

[168] http://www.zonmw.nl/fileadmin/cm/kwaliteit_en_doelmatigheid/documenten/DO07-09_programmatekst.pdf

[169] http://www.eunethta.net/upload/IJTAHC%20HTA%20Projects%20articles/p.485-The%20Netherlands.pdf#search=%22Health%20technology%20assessment%20in%20the%20Netherlands%22

- to advise health care parties with regard to MTA research and about its application in policy and daily practice;
- to teach students with regard to MTA research (for iBMG students, postgraduate education, and courses for profit and nonprofit organizations).

iMTA's mission is to support the development and application of MTA-research and its main products are therefore:

- cost-effectiveness research;
- developing methods and techniques for MTA-research;
- implementation of evaluation studies;
- education.

The iMTA is a scientific institute and the priority therefore is to deliver independent studies of a high quality standard. The iMTA is largely financed through contract research. Research is funded by the government and government-related institutions, from the European Commission, from health care organizations and foundations and from the pharmaceutical industry. To date, over 100 projects have been completed in various areas of medicine.

The iMTA offers all the expertise necessary for tackling the various aspects of a comprehensive MTA-study and it provides the infrastructure for carrying out prospective evaluation studies linked to clinical trials.

9.5.3.3 De Gezondheidsraad/The Health council[170]

The Health Council is the statutory body advising the government on the scientific state of the art with respect to medicine, health care, public health, and environmental protection in the Netherlands. Its involvement in health technology is based on this responsibility. Reports on specific technologies and families of technology have been done for many years, before the term "technology assessment" was coined. To carry out its task, the council brings together groups of experts on specific topics, at the request of the government. It can also initiate studies on its own. The council has broad interests, covering most fields of the natural sciences and medical research, as well as environmental issues and, lately, nutrition. A large number of experts from the Dutch scientific community, as well as foreign experts, representing many different medical specialties and other scientific disciplines, can be consulted by the council. Committees of the Health Council usually evaluate the effectiveness, efficiency, safety, and availability of health technologies. Some committees also examine epidemiologic and economic aspects and—in specific cases—ethical, legal, or social issues.

9.5.3.4 Nederlandse organisatie voor toegepast natuurwetenschappelijk onderzoek (TNO)

TNO's technology assessment activity is small, but it does maintain a well established centre (the Medical Technology Section) for the evaluation of medical devices' safe, efficient, and reliable use. The Medical Technology Section provides information and acts as a consultant. Areas of expertise include electrical and physical safety of medical devices, safety of electrical installations in hospitals, electromagnetic compatibility, electrosurgery, ultrasound, infusion systems, lung function, laser technology, diagnostic technology, dialysis, pacemakers, beds and related products, and information on medical products. TNO also has a long-established programme on preventive medicine that has published a number of reports related to technology assessment (for example, the 1990 report, *Setting Priorities in Prevention*). TNO's HTA programme started in 1990 and was formally established in 1994. It has focused on policy aspects of technology development and diffusion, home care technology, and minimally invasive therapy. TNO's technology

[170] http://www.gezondheidsraad.nl/

assessment unit is actively involved in coordinating HTA projects on a Europe-wide scale, in collaboration with the European Commission.[171]

9.5.3.5 National Organization for Quality Assurance in Hospitals [172]

The National Organization for Quality Assurance in Hospitals (CBO) has been active in both quality assurance and technology assessment. It was established as an independent foundation in 1979 by the National Specialists Organization and the Dutch Association of Medical Directors of Hospitals. The CBO deals primarily with established or widespread medical practice concerning safety, effectiveness, appropriate use, and physician acceptance. It has an ongoing consensus development programme that produces reports that are used as a basis for quality assurance activities, primarily for hospital-based audits. Consensus reports have dealt with a wide variety of topics, including hypercholesterolemia, mammography, blood transfusion, prevention and treatment of bedsores, osteoporosis, and total hip prostheses. The CBO is considered to be one of the most expert organizations in Europe concerning quality assurance.

At present, the CBO is developing a concerted European effort on quality assurance with the support of the European Commission. The CBO is also a WHO Collaborating Centre.

9.5.3.6 College voor Zorgverzekeringen/Health Care Insurance (CVZ)[173]

It is the task of CVZ to supervise, coordinate, and improve the health insurance and financing system, and to guarantee accessible and appropriate health services. A natural element of this mission is to perform HTA of both new and established technologies.

9.5.4 Regulation for medical devices

The European Directives have been transposed into Dutch legislation.[174] The competent authority that supervises the respect of the national legislation on medical devices is the ministry of Health. The cluster medical technology of the health care inspectorate supervises the medical devices.[175]

A Dutch manufacturer has to notify the address of his registered place of business and the category of the device at stake to the competent authority.[176] The manufacturers also have to report possible incidents to the health care inspectorate.

- **Horizon scanning in the Netherlands is one of the tasks of the Health council/Gezondheidsraad.**
- **Several organisations perform HTA in the Netherlands.**
- **New technologies can be subsidized by the new innovation programme of ZonMw. There is no follow- up trajectory for the results of the research performed under the innovation programme.**

9.6 DENMARK

9.6.1 Health care system

The development of HTA activities in Denmark reflects the decentralised nature of the health care system. Denmark disposes of a public health care system, which implies that public authorities own, plan, manage and finance the system. The payment to individual

[171] http://www.tno.nl/industrie_en_techniek/producten_en_diensten/
[172] www.cbo.nl
[173] http://www.cvz.nl/
[174] Wet op de medische hulpmiddelen, Besluit gesteriliseerde medische hulpmiddelen in ziekenhuizen, Besluit in-vitro diagnostica, Besluit medische hulpmiddelen; see http://www.wetten.overheid.nl
[175] http://www.igz.nl/
[176] Art. 5 besluit medische hulpmiddelen

heath care institutions is not related to the number of patients that are treated in those institutions. The administration of the system is decentralised through regional and district structures but the national budgetary system gives the central government very strong control over total spending on health care. National tax finance is supplemented by local taxation and the service is managed by the counties. The budgetary system is similar for hospitals. They have control over the use of the funds but the overall size of the budget is controlled centrally.

The public hospitals in Denmark outside central Copenhagen are owned and managed by the 14 county councils. They are funded largely by local income taxes raised by the counties, with a smaller contribution from the state as a part of the general redistribution to even out economic differences between different parts of Denmark. The county councils consist of directly elected politicians who have overall responsibility and control for both providing and financing the hospitals and other health care services. Executive management is carried out by the counties' health administrations, collaborating with the administrations of the individual hospitals.

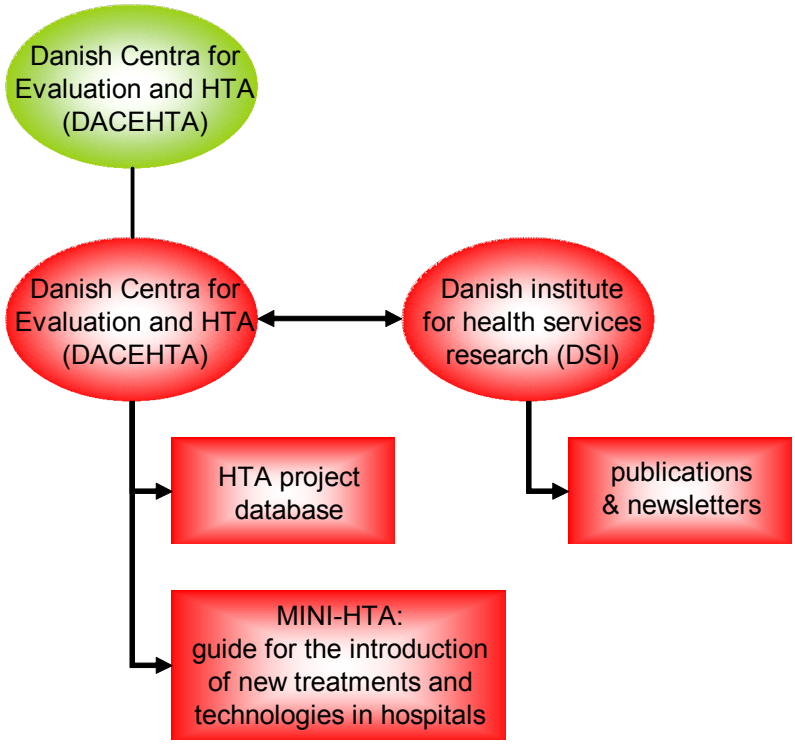
For the introduction of new health technologies no formal barriers exist. Consequently hospitals can decide themselves what technology will be offered. The diffusion of technology however is limited by budget constraints.

9.6.2 Horizon scanning

In the early warning process, the Danish Centre for Evaluation and Health Technology Assessment (DACEHTA) identifies new and emerging health technology by systematically searching the Internet, and by input from expert groups or other international agencies dealing with HTA (figure 20).[177] The target groups include health professionals, health managers and political decision makers. Technologies to be assessed are selected, the prioritisation criteria being that the technology is expected to lead to considerable health improvements for a large group of patients, and that substantial economic or organisational consequence are to be expected. The subsequent broad assessment is based on the best available evidence. However, as the technology is very new, usually large randomised controlled trials are not at hand. The emerging technology alerts are published on the website and can be downloaded.

[177] http://www.sst.dk/Planlaegning_og_behandling/Medicinsk_teknologivurdering/Tidlig_varsling.aspx?lang=en

Figure 20: horizon scanning and HTA in Denmark



9.6.3 Health technology assessment

9.6.3.1 The Danish institute for Health Services research[178]

The Danish Institute for Health Services Research (DSI) is an independent not-for-profit research organisation established in 1975 by the Danish Government, the Association of County Councils in Denmark, and the City Councils of Copenhagen and Frederiksberg.

The aim of the institute is to provide an improved basis for the work of the planning and management authorities within the health services. Collecting, examining and disseminating information, carrying out research and development tasks and theoretical and practical counselling does this. The main areas of work are hospitals, primary health care, community health services and the pharmaceutical sector.

In general, DSI performs research and provides advisory services within the areas of Health Services Research including Health Systems Research and Health Policy Research. The main areas of competence include Health Economics (economic evaluation and planning, financing and organisation, and measurement of productivity and effectiveness), Pharmacoeconomics, Health Technology Assessment, Health and Hospital Planning, Health Informatics, Management (Quality Assurance and Development, Consumer Involvement, and Human Resource Development) and Organisation.

For many years, DSI was the Danish centre for development of the broad health technology assessments (HTAs). The HTAs have now got their own national institute under the National Board of Health and are becoming more and more integrated in the planning and operation of health care institutions. Therefore, DSI's role today is primarily to undertake the management and carrying through of specific health technology assessments for the Danish counties, hospitals and the Danish Institute for

[178] http://www.dsi.dk/engelsk.html

Health Technology Assessment (DACEHTA). DSI has a collaboration agreement with DACETHA regarding the provision of expert advice in relation to HTA projects. Typically, DSI will carry out the economic evaluation, but they also carry out analyses of the patient perspective and organisational element in health technology assessments.

9.6.3.2 The Danish Centre for evaluation and health technology assessment[179]

DACEHTA is situated as a separate entity within the framework of The National Board of Health and is headed by a director. DACEHTA is served by two boards: The Centre Advisory Board and The Scientific Advisory Board.

The key aims of DACEHTA include carrying out HTA's and evaluations of public health services with the aim of improving quality, standards and value for money. It is also an objective to integrate HTA-principles into the running and planning of the public health service at all levels.

DACEHTA promotes the use of health technology assessment in Denmark, which includes doing, commissioning and granting HTA, and providing information, advice, education and training concerning HTA. Through these activities the centre contributes to quality development and effective utilization of resources within the health care system.

They make analyses and assessments in relation to new and existing methods of examination, investigation, treatment and care, methods of rehabilitation, health education and preventive health care work – including devices and pharmaceuticals.

The centre primarily targets health professionals and decision-makers at all levels as well as related research communities. DACEHTA is charged with employing those activities and methods that will contribute most effectively to quality, efficiency and standards of care in the Danish health service.

9.6.3.3 The mini-HTA

In 2000 DACEHTA prepared a form and a guide on the acquisition of medical devices for hospitals aimed at inspiring to a systematic assessment before new investments are made. Later the use of HTA forms has been enlarged to the introduction of new treatments and technologies.

Since it's impossible to undertake a comprehensive HTA when a new technology, treatment, device etc. is planned to be introduced, The Copenhagen Hospital Corporation elaborated the concept of a mini HTA. It is a decision support tool based on the reasoning of health technology assessment, which can be used by hospital management locally and regionally when contemplating the introduction of new health technology. It can be made in a limited timeframe (less than 3 months) and offers a contribution to decisions at the time when needed. Therefore it is easy to adapt to local or regional budget and planning process.

Nowadays many Danish hospitals dispose of a local version of the mini HTA. In order to harmonize and uniform the use of mini-HTA's the DACEHTA has developed a common national decision support tool to be used locally and regionally. The intention is to offer a guiding tool for decision makers and applicants proposing new technology.

The tool is a form of a check list with a number of questions concerning the prerequisites for and consequences of using (new) health technology, in which:

- the questions are grouped according to four HTA perspectives: technology, patient, organisation and economy
- the answers to the questions provide a brief, written basis for decisions (2-5 pages) and takes, based on experience, 5-15 hours, excluding the time spent on information retrieval and assessment, and economic calculations

[179] http://www.sst.dk/Planlaegning_og_behandling/Medicinsk_teknologivurdering.aspx?lang=en

- the purpose is to provide (part of) the decision-making basis for a proposal to introduce a specific new health technology or, for the use of existing technology for new indications.
- both the preparation and the use of the decision-making basis may take place at local or regional level and be adapted to local or regional objectives, decision criteria and time schedules

A non–exhaustive list of possible applications of the mini-HTA is summarised by DACETHA. For instance, mini-HTA can be used for

- New treatments. There is however no definition of the concept "new treatment".
- A new indication for the application of existing technology
- New medical devices
- Draft budgets or activities with increasing cost pressure

Although a mini-HTA is undertaken within a limited timeframe and with limited resources high quality and credibility must be assured. Therefore:

- Literature search and assessment remains essential
- Interdisciplinary work is indispensable
- Independent quality check by impartial professionals must be organised
- Identified weaknesses and uncertainties should be reported

Some applications concerning the use of the mini-HTA are the county of Funen and the Copenhagen Hospital Corporation. In the county of Funen the mini HTA is mandatory when department managements submit draft budgets for hospital management or centre management. The Copenhagen Hospital Corporation uses the mini-HTA concept primarily in connection with:

- New treatments and diagnostic initiatives for which it is possible to document a significant clinical effect
- Approval of special subsidies at national and regional level implying reimbursement of the department's expenses for particularly expensive pharmaceuticals or implants for a small well-defined group of patients.

If a proposal for a new treatment has been described in mini HTA format, it must be approved by the centre managements and the executive board of the hospital. Then it is submitted to the management board of the Copenhagen Hospital Corporation which is comparable to a county health service. Finally the proposal is considered by the political governing body to which the mini-HTA material is submitted for decision-making purposes. The treatments expected to be carried out on patients from other counties will also be presented to the members of the counties' health committees.

If a proposal is approved, the expenses and activities are included in the budgets of the hospital departments, distributed between the Copenhagen Hospital Corporation and county activities. Since the mini-HTA procedure is closely linked to the annual budgeting procedure, a new treatment cannot be introduced until the beginning of a new budget year.

The approved interventions are evaluated annually for the purpose of examining whether the original conditions for introducing new treatments have turned out to be relevant in practice.

9.6.4 Regulation of medical devices

The European Directives have been transposed in Danish legislation.[180] The Ministry of the Interior and Health Affairs and the Danish Medicines Agency (DMA) act as the competent authority for medical devices.[181] The agency's principal function is to implement the regulatory systems for the safety and performance of medical devices on the market.

The agency's activities include:

- Implementation and enforcement of the regulations for medical devices
- investigation of adverse/serious incident reports from manufacturers and users
- operating the vigilance system for notifications affecting medical devices on the market
- designating and monitoring of the notified bodies in Denmark
- contributing to the European work programmes for the safety and quality of medical devices
- provision of advice to users, manufacturers and interested parties
- maintaining the register of Danish manufacturers of Class I, custom made devices and procedure packs
- issuing export certificates to Danish manufacturers of medical devices.

From the 1st January 2006 the DMA assumes the role as competent authority with respect to the technical aspects of clinical investigations of medical devices from the Scientific Ethical Committee System. From this date there is a requirement for authorisation, from the DMA, for the clinical investigation of medical devices on human subjects. The investigation may be initiated when the DMA has granted authorisation and the Scientific Ethical Committee has approved the investigation.

The regulatory requirements for application for authorisation for the conduct of clinical investigation pertain to the clinical investigation of non CE-marked devices and CE-marked devices, if the objective of the investigation is application of the device for an intended use for which the device is not CE-marked for.

Clinical investigations notified to the Scientific Ethical Committee prior to 1 January 2006 do not require authorisation from the DMA.

Clinical investigation of CE-marked devices utilised for their intended purpose do not require authorisation by the Danish Medicines Agency. However, this type of investigation may require notification to the Scientific Ethical Committee.

The general costs of medical devices are provided by the local authorities or clinics with which the manufacturer has established the agreement of supply for medical devices.[182] The reimbursement scheme for medicinal products operated by the Danish Medicines Agency is not applicable to medical devices. However in specific cases the private user of some medical devices e.g. technical aids, hearing aids and glasses may be reimbursed. The relevant local authority must be contacted directly regarding its provision, service and maintenance, where appropriate.

[180] http://www.medicaldevices.dk/1024/visArtikel.uk.mu.asp?artikelID=3890
[181] http://www.medicaldevices.dk
[182] http://www.medicaldevices.dk/1024/visArtikel.uk.mu.asp?artikelID=3912

- **Horizon scanning in Denmark is performed by the Danish Centre for Evaluation and Health Technology Assessment (DACEHTA). One of the key aims of DACEHTA includes carrying out HTA's.**
- **The Danish Institute for Health Services Research (DSI), an independent not-for-profit research organisation established by the Danish Government also performs HTA's. Moreover DSI has a collaboration agreement with DACEHTA regarding the provision of expert advice in relation to HTA projects.**
- **The Copenhagen Hospital Corporation elaborated the mini HTA being a decision support tool based on the reasoning of health technology assessment, which can be used by hospital management locally and regionally when contemplating the introduction of new health technology.**
- **European legislation on medical devices has been transposed into Danish legislation**

9.7 FINLAND

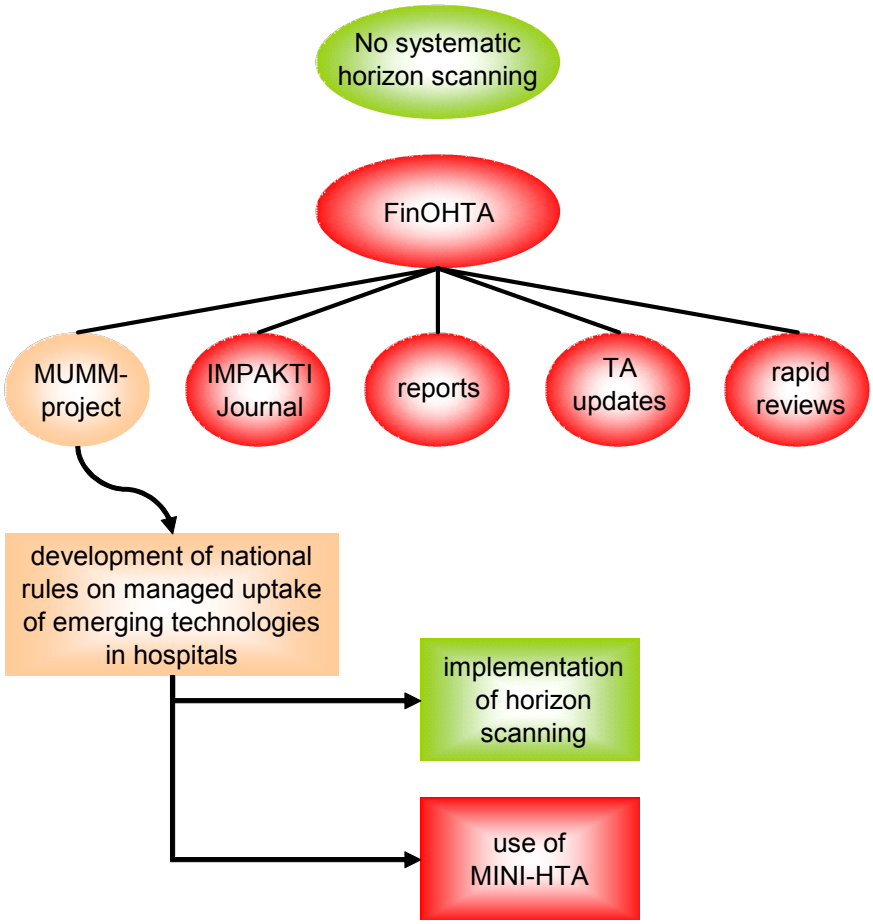
9.7.1 Health care system

In Finland decisions about health care are made in at about 400 municipalities that individually or in small groups provide primary care in some 250 primary care centres. Hospitals conglomerated into 21 hospital districts provide specialised care. 5 university hospitals provide tertiary care. Management of national health care is primarily a case of management of information and recommendations. Only a few selected areas are governed by law. There is no organ for the decision making. The uptake of new technologies may vary in that a method may be in routine use in one hospital, being only considered exceptionally in another one while the rest are somewhere in between. There are always a number of stakeholders with vested interests like the producer, possibly the clinicians, the patients, sometimes patient advocacy groups, … Hence, a lot of forces working to increase expenditure and uptake of the newest of new.

9.7.2 Horizon scanning

Currently there's no systematic horizon scanning in Finland.

Figure 21: horizon scanning and HTA in Finland



9.7.3 Health technology Assessment

9.7.3.1 Finnish Office for Health Technology Assessment

The Finnish Office for Health Technology Assessment (FinOHTA) is an independent, public assessment agency working as a part of STAKES the National Research and Development Centre for Welfare and Health (figure 21). FinOHTA tends to produce, support and co-ordinate HTA in Finland. Furthermore, assessment results and experiences are disseminated, both nationally and internationally, within the health care system. The results of international and domestic HTA research are disseminated by means of four series of publications: the Impakti journal consisting of articles written by our staff, consultants and other experts, dealing with HTA, new research results and also lighter subjects, the reports containing the inquiries and assessment studies commissioned or funded by our unit, the TA updates containing summaries translated into Finnish of the reports published by HTA units operative in other countries and the rapid reviews that are usually based on foreign assessment reports the findings of which are critically appraised and applied in the Finnish context.

9.7.3.2 Managed uptake of medical methods

The Managed Uptake of Medical Methods or MUMM project was launched in a workshop with representatives of 19 hospitals together with FinOTHA. The aim of the project is to develop collectively national rules for the uptake of new medical technologies.

Hospitals have been visited in order to gather ideas and experiences. From a draft list of about 60 topics some have been selected for review. The next step is the review of the selected topics, i.e. a literature review is conducted, in a mini-HTA.

There have been requests to set up common rules for bringing out new equipment for testing, because the current control of equipment has repeatedly been described as "the wild west". For the uptake of new technologies, some kind of horizon scanning will have to be built in. Moreover, the mini-HTA procedure developed in Denmark (cfr. supra) will be translated and disseminated for use.

9.7.4 Regulation of medical devices

The Finnish National Agency for Medicines (NAM) as competent authority is responsible to maintain and promote the safety and safe use of pharmaceuticals, medical devices and blood products. According to medical devices, there is some specific legislation[183] conform to the European legislation. In that scope the function of the NAM is to monitor the compliance of medical devices with the legislation and regulations.

Hazardous incidents reported to NAM relating to medical devices represent an important means of market surveillance.[184] Of the 584 hazardous incidents addressed during 2005, a total of 402 concerned Finland. One hundred of these were severe incidents, 36 had severe sequelae and 22 were near misses. NAM carried out 20 inspections relating to medical devices. Domestic manufacturers were specifically targeted. The inspections revealed a few non-conformities which did not, however, compromise the safety of use of the devices. The operations and competence of a Finnish Notified Body, the Technical Research Centre of Finland, Department for Products and Manufacture, were assessed during one round of inspection. The present safety status of medical devices was examined by carrying out a survey. The majority of the medical and healthcare units gave a general score of 8 or higher out of 10 for the safety of the medical devices in use. Half of the respondents considered the safety of the medical devices and accessories in use in their own unit to have improved during the past two years. Nearly half felt that safety had remained unchanged. In its role as a medical devices regulator, NAM passed with distinction. Scope for improvement was found in communications and the availability of information. NAM was deemed to have expertise, be reliable and expedient.

9.7.4.1 Product registry[185]

A Finnish manufacturer must send a notification to the product register stating the name and address of his company, place of business, identification data of the medical device, details of the certificates or rejections by the notified body and other information required for market control. Notification must also be made when the information referred to previously in this section changes. An authorised representative established in Finland must submit a corresponding notification. The notification shall be sent to the National Agency for Medicines. The National Agency for Medicines may require that a notified body submits the details of medical devices referred to previously when it has participated in their conformity assessment.

The National Agency for Medicines shall send the registration data of *in vitro* diagnostic medical devices referred to in Directive 98/79/EC on *in vitro* diagnostic medical devices to the European database, which is accessible to the competent authorities. The data collected in the database may only be used for purposes of control by the authorities.

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[183] http://www.nam.fi/english/medical_devices/legislation_medical_devices/index.html
[184] http://www.nam.fi/uploads/julkaisut/vuosikertomukset/Laakelaitos_vk_05.pdf
[185] art. 15 Medical devices act

- **There's no systematic horizon scanning in Finland**
- **HTA is carried out by FinOHTA, an independent, public assessment agency working as a part of STAKES the National Research and Development Centre for Welfare and Health.**
- **The MUMM project aims at the development of collectively national rules for the uptake of new medical technologies. In that scope a system of horizon scanning will be built in and the Danish mini HTA will be used**
- **European legislation on medical devices has been transposed into Finnish legislation. The competent authority performing the post market surveillance is the Finnish National Agency for medicines.**

9.8 FRANCE

9.8.1 Health care system[186]

The French health care system is currently undergoing a reform that aims to establish a casemix-based system of payment for health care delivery ("Système de tarification à l'activité" or activity-based financing system). This casemix-based system applies to all medical or surgical activities: in-patient care (one-day or long-term hospitalisation) and out-patient care. The French casemix-based system is a mixed financing system including on one side a general annual funds endowment to ensure the routine public health activities and, on the other side, a specific per-activity payment that varies according to the nature and the volume of this activity ("Classification en groupe homogène de malades – GHM" or DRG-based system).

Innovative technology payment is a difficult issue within a DRG-based financing system as integration in the DRG tariffs can take years, the following steps having to be followed:

- Initiating the CE Mark process (delays vary by application);
- Obtaining a positive reimbursement decision from the national authorities;
- Obtaining of coding assignment;
- Collecting data with a view to DRG re-weighting.

As a response to this issue, the French health authorities have established a system of "exclusion lists" ensuring that some innovative technologies are reimbursed within a shorter delay. A limited number of pharmaceuticals and medical devices will then be reimbursed unit by unit (on top of DRG's tariffs) each time they are prescribed by a hospital, provided they fulfill the following criteria:

- Previous positive reimbursement decision by the health authorities (i.e. being on the "Liste des Produits et Prestations Remboursables (LPPR) or on the "Base des Medicaments Remboursables")[187];
- A high cost per unit and/or a non-generalized use, resulting in an great heterogeneity of costs within the DGR tariff to which they are attached.

Upon fulfillment of these criteria, the technologies are registered on an exclusion list published yearly by the French Ministry of Health. There are actually two distinct lists, one for pharmaceuticals and the other for medical devices They are elaborated and updated on decision of the Ministry of Health, and made public through an official decree.

[186] http://www.sante.gouv.fr/htm/dossiers/t2a/
[187] Personal communication with Sophie Casanova, CEPS [August 2006]

These two lists are by definition limitative, meaning that only the pharmaceuticals and devices listed on them can be reimbursed to the hospitals additionally to the DRG tariffs. What is more, these two lists will in principle evolve in the same fashion, i.e. towards a gradual integration of each item to the DRG tariffs as soon as its use becomes the standard treatment, and as soon as the classification and tariffs can be adjusted to fit this change. The lists will thus be revised and adapted permanently in a continuous process, being enriched with new elements when new costly therapeutics appear, and losing elements when those become the standard and are integrated to the DRG tariffs.

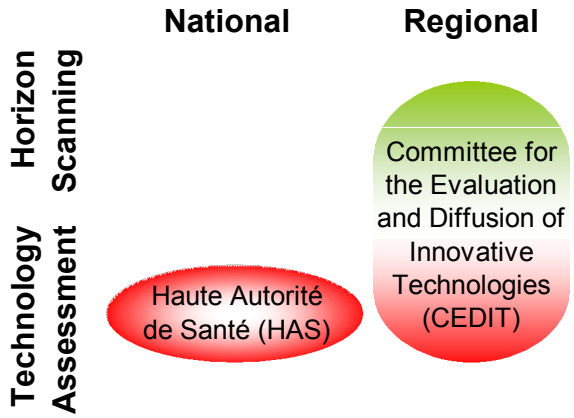
In 2004, there were 26 categories of medical devices on these lists, which in fact represent most implantable devices, esp. cardiovascular and orthopedic devices.

Besides this system of "Exclusion lists" ensuring the reimbursement of selected innovative therapies, the French Ministry of Health calls each year applications for a programme supporting innovative and expensive technologies that are prior to- or in their phase of adoption, and that are not yet included in one of the "exclusive lists" (i.e. not yet reimbursed unit per unit, on top of DRG's tariffs). The French name of this programme is "Programme de soutien aux techniques innovantes et coûteuses" (STIC).

9.8.2 Horizon scanning

The CEDIT (Committee for the Evaluation and Diffusion of Innovative Technologies, a regional HTA agency) is a member of Euroscan and as such sends its reports on innovative technologies. Although it is one of its missions, the CEDIT does not perform actually any formal horizon scanning activity. This activity is however planned for the near future and is at least discussed in meetings. Further, the Haute Autorité de Santé (HAS) plans also to join Euroscan in 2007 (figure 22).

Figure 22: horizon scanning and HTA in France



9.8.3 Health technology assessment

9.8.3.1 National procedure: LPPR

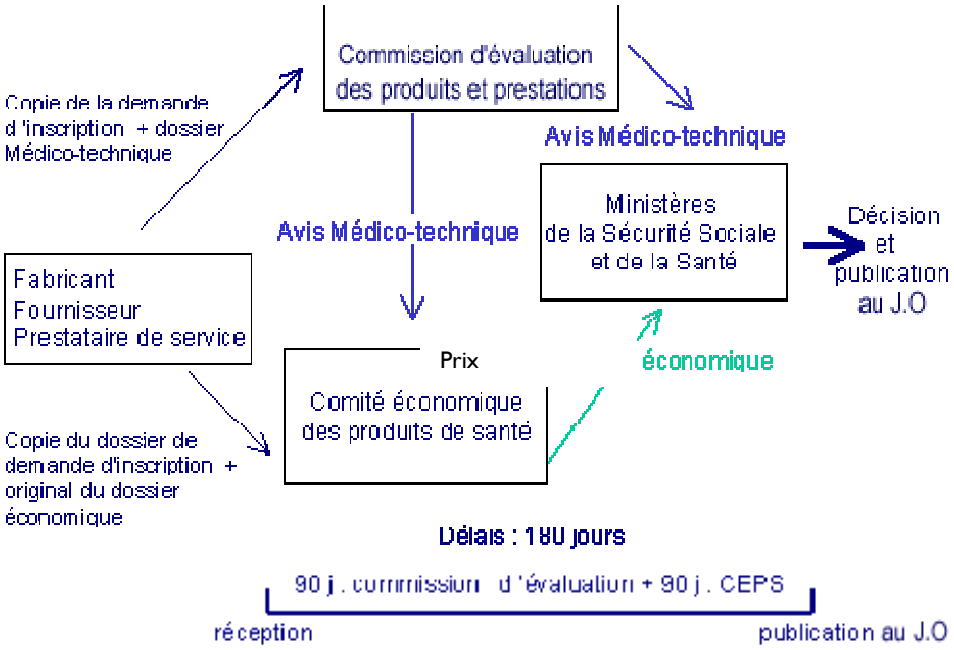
In 2001, the medical device sector underwent a reform of its reimbursement system. The 2000 funding law of the Social Security Code and its enforcement decrees n°2001-256 and 2001-257 of March 2001, have created the CEPP (Commission d'Evaluation des Produits et Prestations) and have substituated the Liste des Produits et Prestations Remboursables (LPPR) for the Tarif Interministériel des Prestations Sanitaires (TIPS) for:

- medical devices for individual use (MDIU)
- tissues and cells from the human body and their derivatives

- healthcare products other than medicines
- associated services and adaptations

Each applicant (manufacturer or distributor) wishing to register his product or service on the LPPR must apply to the CEPP for the analysis of medical and clinical evidence on the product, and to the CEPS (Comité Economique des Produits de Santé) for the analysis of the economic evidence. The procedure is illustrated below (figure 23).

Figure 23: National HTA procedure



For the registration of products or services not yet included in the reimbursement list, the following four scenarios are possible:

- Scenario 1: The applicant considers that the characteristics of his product or service correspond to one of the generic lines of the existing list (technical specifications, and where applicable therapeutic or diagnostics indications, particular intended conditions of prescription and use). The applicant does not claim either an improvement in service rendered compared to this generic line or a price or tariff higher than those fixed for the generic line. In this case, there is no application to submit. However, a voluntary notification may be submitted by the applicant to the CEPS in order for them to have a better overview of the market.
- Scenario 2: The applicant considers that the characteristics of his product or his service correspond to one of the generic lines of the existing list. However, because of the innovative aspects of his product or service, he claims an improvement in service rendered («Amélioration du servie rendu »), which he wishes to use to ensure a higher tariff or price than those fixed for the existing line.
- Scenario 3: The applicant considers that the characteristics of his product correspond to one of the generic lines of the existing list but he wishes to make modifications to the registration terms of the existing generic line of the list (i.e. extension of indication(s),...).

- Scenario 4: The applicant does not find any generic line in the list to which his product or service corresponds. The product or service of the applicant presents thus innovative aspects.

For the last three scenarios (scenarios 2, 3 and 4), the applicant submits his requests for initial registration to the CEPP and the CEPS. The application is made up of three parts: a description of the application, a medico-technical file and an economic file.

Description of the application

The description of the application consists in:

- An application letter to the Ministry of Social Security
- An information form
- A summary form

The information form collects detail about: the apllicant, the type of request (initial registration, registration renewal, request for changes in registration terms…), the scope of the request (description of the product or service, identification of the product or service, details of the product CE mark, date of first placing of product on any market and market name, packaging).

Medico-technical file (Commission d'évaluation des produits et prestations – HAS)[188]

The CEPP is a specialised commission of the Haute Autorité de Santé (HAS) that examines products and services (plasters, defibrillators…) for them to be reimbursed by the National Health Insurance. Among the products studied, medical devices are evaluated after they are CE marked. The CEPP is in charge of the medico-technical evaluation of the applications for initial registration, for registration renewal or for changes in the registration of the products and services on the LPPR.

The medico-technical file submitted to the CEPP by the manufacturer or any other applicant, for his product or service to be registered in the reimbursement list (LPPR), should contain the following information: the product or service characteristics, the evaluation of the service provided («evaluation du service rendu») (seriousness aspects, ratio of performance to adverse effect, presentation of the alternatives, contribution to public health), the improvement of the service provided ("amelioration du service rendu" – ASR) in comparison to other products or services already registered, the procedure for using the product/service, the target population and the predicted sales volume. It is therefore the responsibility of the applicant to provide the relevant information for his application

The medico-technical file is evaluated by CEPP members after internal expertise (by the «Service Evaluation des Dispositifs et Technologies de Santé de la Haute Autorité de santé») and, if needed, after external expertise (by specialists of the therapeutic domain). The CEPP then formulates a recommendation regarding the reimbursement of the product/service for each of its therapeutic indications. The recommandation comprises among others:

- The product or service description.
- The CEPP opinion about the relevance of the registration of the product/service on the the LPPR, taking into account its service provided.
- If relevant, the therapeutic indications for which the CEPP allows the registration on the LPPR ; the recommandations about the judicious prescription and utilisation of the product or service ; and the minimal technical requirements for being listed on the LPPR.

[188] http://www.has-sante.fr/has/cepp/index.htm

- The duration of the registration on the LPPR and, if relevant, the additional studies required to allow a re-assessment of the service provided at the time of registration renewal.
- A comparison of the service provided by the product or service with other comparable products or services (or therapeutic alternatives) already listed on the LPPR.

According to the epidemiological evidence available, an estimation of the number of patients reached by the product or service listed (per indication)

Economic file (Comité Economique des Produits de Santé – Ministry of Health)[189]

The mission of the "Comité Economique des Produits de Santé" (CEPS) is to make a proposition regarding the reimbursement tariffs and the prices of the products and services belonging to the List defined by article L. 165-1 (Social Security Code).In order to set those tariffs, the CEPS may liaise with the applicant and set up conventions on, among others, sales volumes. The CEPS periodically reviews those expenses.

The economic file submitted to the CEPS by the manufacturer or any other applicant for his product or service to be included in the reimbursement list, should contain the following information: data related to the application (public sale price and tariff foreseen, forecast of market shares and sales volume estimated in France), justifications of the sales forecast (potential market, market achieved in France or abroad), justification of the requested price and tariff (saving or excess achieved by the product compared to other therapeutic strategies, break-down of the public sale price, data on the market prices in France and abroad), identification and information about the applying company. It is therefore the responsibility of the applicant to provide the relevant information in his application form. Further, no formal economic evaluation is required in the economic file.

Article R 165-4 of the Social Security Code related to the tariff setting of medical devices states that products or services that do not bring improvement to the service provided or savings in the treatment cost, or that are likely to give rise to unjustified expenses for the health insurance scheme, cannot be listed on the LPPR. The tariffs setting mainly takes into account the service provided, its possible improvement (ASR), the tariffs and prices of comparable products or services registered on the list, the projected sales volumes, and the foreseeable and actual conditions of use of the product of service. The CPS distinguishes between three main scenarios for setting the tariffs of innovative medical devices (product with an ASR).

Neutral or positive impact on the health insurance budget: In the simplest cases, it is possible to show that the price proposed or accepted by the company, and therefore regarded by it as a reasonable valuation of its discovery, results in costs for health insurance that are lower, or at worst equivalent, to the savings produced by its use (account is only taken in such cases of direct costs incurred by health insurance, whatever their character). Registration thus poses no problem. But this illustrated how important it is to have reliable and compelling medicoeconomic studies at hand.

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Small impact on the health insurance budget and modest but fairly frequent ASR: It is frequent in the medical devices sector that improvements in terms of service provided are achieved by "incremental" innovations, i.e. modest but fairly frequent improvements.

[189] http://www.sante.gouv.fr/ceps/

Where it appears that the prospect of an increased market share for the new product does not constitute a satisfactory valuation of the innovation, and that a price advantage is necessary, the Committee may propose temporary tariffs that are higher than those of comparable products already registered. In case of registration of another equally innovative device some time later, the committee agrees to give the new device the same price/tariff advantage as its predecessor for the remainder of the period of advantage attributed first. The reward for innovation is thus secured for a generally short term, at the end of which the innovation can be expected to be technologically outdated. This system, initiated by the Committee in charge of pacemakers pricing, allows an adequate compensation of the ASR status devices and avoids tariff escalation.

This leaves the most difficult cases, those of innovations which are both crucial in terms of ASR and costly; and for which the (sometimes considerable) additional expenditure to be supported by the health care budget is only compensated by non-financially measurable improvements in patient care. Cost effectiveness studies may inform decision-makers but are not of a straightforward use. Under this scenario, the discussion about the price level (highly constrained by the existence of international markets), is actually replaced by the quantitative issue of limiting the innovation delivery only to the patients for whom the expected advantage of the innovation is well established. This requires that the following concerns have been answered: identification and screening of the target populations and possibility (by any means) to reach that particular population such that only they can benefit from the innovation. Registration is accompanied systematically in such cases by contractual provisions concerning the limitation of volumes and the compensation paid by companies in case of overrun; as well as the introduction of follow-up studies (mainly therapeutics).

9.8.3.2 National procedure: STIC

Since 2000, the French «programme supporting expensive innovations» («programme de soutien aux innovations coûteuses» or STIC) allows to finance national research projects involving thousands of patients each year. The aim of this programme is to foster hospitals' initiatives in the field of innovative and expensive techniques. This programme comes right after clinical research.

The objectives of the programme are three-fold:

- To encourage the diffusion of some expensive innovations (medical devices, pharmaceuticals and organisational, diagnostic and therapeutic techniques) by providing funds to hospitals participating in a multi-centre research study selected by the programme
- To specify how to use the innovation ("conditions d'utilisation") for the care of the patients and to evaluate the medical and economic impact of the innovation.
- To increase exchanges and consensus between the health professionals implied in the programme.

The results of the studies funded by the programme provide decision-makers information to decide upon the most relevant diffusion terms of the innovation in the health care system.

The research studies funded aim to answer pragmatic questions. They must relate to innovative techniques that are already validated by clinical research and that are at the early beginning of their diffusion period. As an example, past research studies tried to answer the following questions:

- What are the therapeutic indications, validated by clinical research, for which the use of the innovation is relevant in comparison with other well-established diagnostic and therapeutic alternatives?
- What is the financial impact, on the hospital's and the health care system's budget, of reimbursing the innovation (increase in the costs or savings)?

- What is the impact of the innovation in terms of operational working teams required, given the number of patients implied in France?
- What should be the technical level required for professionals using the innovation?
- How should the innovation be spread on the national territory?
- Should practitioners be trained for them to use the innovation? What training and how?
- What is the minimum number of medical acts (related to the innovation) required from the practitioner in order to guarantee a good level of know-how?

The funds are given for a limited period that cannot exceed two years. The funds allocated can only be spent for the extra cost generated by the use of the innovation. They do not constitute an alternative source of hospital funding.

9.8.3.3 Regional procedure: CEDIT

The CEDIT was created by Assistance Publique-Hôpitaux de Paris (AP-HP, regional university hospital group for Paris area, 40 hospitals) in 1982. The CEDIT is responsible for formulating opinions for the general manager of AP-HP on opportunities for the dissemination of technological innovations and the extent and mode of dissemination desired in the AP-HP hospitals. The mission is threefold:

- Assessment of new technologies in terms of technical, clinical, economic, organizational, legal and ethical aspects
- Aid in technology implementation and use
- Identification of potentially valuable emergent technologies.

The CEDIT's field of expertise is medical devices and procedures for diagnosis and treatment used by health-care professionals in the care and management of individuals, and the systems in which this care is administered. Medications are not assessed by the CEDIT.

Step 1: "Saisine"

The CEDIT acts upon request from any member of the AP-HP (whether administrative, medical or paramedical staff. A specific form must then be introduced to the CEDIT (i.e. a so called "saisine").

STEP 2: Selection committee

A Selection Committee, composed of some members of the CEDIT, assesses each "saisine" in terms of medical, economic and organisational criteria. The committee selects then the "saisines" for which a thorough assessment will be performed. Dossier selection takes 10 weeks on average.

STEP 3: Production of a technology evaluation report

A report synthesising all the available information (medical, technical, economic, regulatory, legal and ethical) is prepared by the Scientific Secretariat of the CEDIT for each technology selected. To produce the report, scientific secretariat members conduct an extensive search and analysis of the literature and hold meetings and consultations with experts in the field. The mean time taken to build a report (delay between selection of the technology and presentation of the report to the CEDIT plenary meeting) is on average four and a half months.

STEP 4: Plenary meeting of the CEDIT and recommendations

The evaluation report is presented to a plenary committee by a member of the Scientific Secretariat:

- If the information is sufficient at the outset, the CEDIT makes a recommendation of diffusion or non-diffusion of the technology within AP-HP hospitals,
- If the information is insufficient for the committee to make a recommendation on diffusion, it may request additional information (see Step 5) to be provided.

The rapidity of diffusion of certain technologies may render obsolete recommendations issued from a complementary evaluation that takes too long. The search for a balance between the delays necessary for a high-quality analysis and the speed of diffusion of the technology is thus one of the constant concerns of the CEDIT.

STEP 5: Additional information

The provision of additional information may take one of three non-mutually-exclusive forms:

- waiting for information from outside AP-HP, for example the results of an international study,
- the constitution of a working group and
- the setting up of a complementary evaluation within AP-HP hospitals for which the CEDIT specifies the direction of the research and indicates its level of financial involvement, if appropriate. These studies generally focus on the true medical value of the technology concerned, and may go as far as clinical research if no such studies have been carried out. They may also deal with questions on economic, technical or organisational aspects. A single dossier may lead to several studies. CEDIT assistance to evaluation studies may be methodological, financial or logistic.

Once collected, the additional information is presented to the plenary committee for recommendation about the diffusion of the technology within AP-HP hospitals.

The recommendations of the CEDIT are systematically sent to the general management of AP-HP, to the management of AP-HP hospitals, to the biomedical engineers and to the physicians of the specialties concerned. The technology evaluation reports are sent systematically to the expert of each dossier.

- **Horizon scanning is one of the missions of the CEDIT. CEDIT is a member of Euroscan.**
- **HTAs in France are performed at the national (HAS) and regional levels (CEDIT).**
- **Reimbursement of innovative technologies, on top of DRG tariffs, is ensured by a system of "exclusion lists" (Ministry of Health).**
- **The Ministry of Health calls each year applications for a programme supporting innovative and expensive technologies that are prior to- or in their phase of adoption, and that are not yet included in the "exclusion lists".**
- **The CEDIT may finance field evaluations (within AP-HP hospitals) of technologies with insufficient information. The collected information helps making a recommendation about their diffusion.**

9.9 BELGIUM

9.9.1 Health care system

In Belgium regulation and supervision of the health insurance system takes place at federal level and the national government also transfers some funding (drawn from general taxation) to the insurance system. Thereafter the flow of services, payments and reimbursements takes place at sub-national level between independent health care providers, sickness funds and patients.

The system is characterized by its heterogeneity and fragmentation. Ever since its foundation, an essential principle of the Belgian health care system has been the patient's freedom of choice between a wide range of independent providers. Health care is therefore privately managed and delivered (mainly by a range of non-profit organizations) whilst responsibility for the funding of health care and oversight of its organization are in the public sector, and are shared out between numerous public authorities.

This division of responsibilities is mirrored by the fragmented structure of the Belgian state. Since the early 1980s elements of responsibility for health care have been devolved to the communities; but there are many exceptions (especially in curative medicine) for which the federal authorities remain responsible).[190]

9.9.2 Horizon scanning

Currently there is no organised horizon scanning, neither a process of review of other horizon scanning sources in Belgium.

9.9.3 Health technology assessment

Previously, assessment was mostly done by individual experts of sickness funds, universities or professional societies participating in the advisory bodies of the RIZIV/INAMI. Health technology assessment using systematic methods to assess clinical effectiveness and cost-effectiveness has legally been introduced in 2002 by the foundation of the Belgian Health Care Knowledge Centre[191] (KCE) that since 2003 published several publicly accessible HTA reports. KCE tries to complement and to work in collaboration with the existing expertise at the RIZIV/INAMI and the sickness funds as well as other stakeholders. The reports serve as a guiding tool for the decision making of political decision makers and competent bodies of the RIZIV/INAMI and the Ministry of Health.

9.9.4 Regulation of medical devices

The European directives on medical devices have been transposed into Belgian legislation. [192] In Belgium the "Dienst medische hulpmiddelen van het DG Geneesmiddelen/DG médicaments"[193] is the competent authority for the directives 90/385/EC and 93/42/EEG. For the medical devices in vitro diagnostics (Directive 98/79/EC) the "Wetenschappelijk Instituut Volksgezondheid (WIV/ISP), afdeling Klinische Biologie" is competent[194].

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[190] For an overview of the Belgian Health care system: Schokkaert E, Van de Voorde C. Health care reform in Belgium. Health Econ. 2005;14:S25–S39.

[191] http://kce.fgov.be/ (Federaal Kenniscentrum voor Gezondheidzorg/Centre Fédéral d'Expertise de Soins de Santé)

[192] K.B. van 18 maart 1999 betreffende de medische hulpmiddelen, *B.S.* 14 april 1999; K.B. van 15 juli 1997 betreffende de actief implanteerbare hulpmiddelen, *B.S.* 1 augustus 1997 ; K.B. van 14 november 2001, *B.S.* 12 december 2001.

[193] https://portal.health.fgov.be/portal/page?_pageid=56,513091&_dad=portal&_schema=PORTAL

[194] http://www.iph.fgov.be/ClinBiol/bckb33/activities/competent_authority/_nl/competent_authority.htm

The most important task of the competent authorities is market surveillance:

- Notification of the putting in the market of medical devices (for classes I and custom made)[195]
- Notification of distributors and exporters[196]
- Notification of clinical studies on medical devices in Belgium[197]
- Notification of incidents with medical devices in Belgium[198]
- Notification of notified bodies and supervision of the bodies.
-

In the scope of post market surveillance the draft legislation on implants and invasive devices states that every dysfunction or adverse event as well as the measures that have been taken to solve the problems and the removing of the device from the market will have to be reported to the "Commission for reimbursement of Implants and invasive medical devices" (RIZIV/INAMI).

With regard to clinical trials the European clinical trials directive[199] has been transposed in Belgian legislation. The Belgian law concerning experiments on the human person however has a broader scope than the directive. The Belgian law also applies to research which involves non – pharmaceuticals such as the testing of a new health technology or medical device whereas the European legislation only aims clinical trials with pharmaceuticals[200].

The Belgian law (art .5) states that clinical trials can only be performed if:

- It is scientifically justified and based on the current state of scientific knowledge and on an adequate pre-clinical experiment.
- The aim of the experiment is to improve knowledge or the means to improve the health of men.
- There are no alternative methods with a similar efficacy and which can give the same results
- There's a (continuing) proportionality between the risks and the benefits for the participant and for third persons (right to privacy etc.)
- The protocol has been approved by an ethical commission (Art. 11). The ethical commission considers the relevance of the experiment, the adequacy of the assessment of the anticipated benefits and risks and the soundness of the conclusions, on the therapeutic level and in the scope of public health. Moreover they consider adequate: the protocol, the competence of the researcher and his/her team, the research file, the adequacy of the facilities, de adequacy and the completeness of the written information that will be provided to the participant, the compensation in case of an injury linked with the experiment or in case

[195] art. 10 K.B. van 18 maart 1999 betreffende de medische hulpmiddelen; Art. 16 § 4 of the K.B. however states that the DG Pharmaceuticals, section medical devices can require that notified bodies give information on the attributed, refused or removed certificates, the details of the class II a, II b and III devices and the active implants that obtained the CE mark and data allowing to identify the manufacturer.
[196] art. 10bis K.B. van 18 maart 1999 betreffende de medische hulpmiddelen
[197] art. 9 K.B. van 18 maart 1999 betreffende de medische hulpmiddelen
[198] art. 11 K.B. van 18 maart 1999 betreffende de medische hulpmiddelen
[199] Directive 2001/20/EC http://eudract.emea.eu.int/docs/Dir2001-20_en.pdf#search=%22clinical%20trials%20directive%22
[200] Interpretation of art. 2, 11° Wet 27 december 2005 houdende diverse bepalingen, *B.S.* 30 december 2005; The Belgian law of 7 may 2004 regarding clinical trials on the human body, *B.S.* 18 may 2004 implements the directive 2001/20/EC; See also C. Trouet, *Clinical trials in Belgium*, Intersentia, Antwerp. 2004.

of death, the presence of an insurance covering the researchers' liability, the way of selection of participants.

- Written Informed consent has been given by the participant (art. 6)

A copy of the ethical commissions' advice is sent to the minister (Art. 11 § 13).

Since clinical effectiveness does not have to be proven in order to put medical devices into the market, the implications of this legislation are rather limited. It can even discourage to perform clinical trials on medical devices.

- **There's no organised horizon scanning in Belgium**
- **HTA including public reporting has been formally introduced in 2002 by the creation of the Health Care Knowledge Centre (KCE).**
- **There is a procedure for the conditional reimbursement of new implants**
- **The European directives on medical devices has been transposed into Belgian legislation.**
- **The European directive on clinical trials is transposed in Belgium but the field of application is larger. The protection mechanisms are also applicable to research involving the testing of new health technologies, medical devices, …**

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Wettelijk depot : D/2006/10.273/50

KCE reports

1. Effectiviteit en kosten-effectiviteit van behandelingen voor rookstop. D/2004/10.273/1.
2. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid (fase 1). D/2004/10.273/2.
3. Antibioticagebruik in ziekenhuizen bij acute pyelonefritis. D/2004/10.273/5.
4. Leukoreductie. Een mogelijke maatregel in het kader van een nationaal beleid voor bloedtransfusieveiligheid. D/2004/10.273/7.
5. Het preoperatief onderzoek. D/2004/10.273/9.
6. Validatie van het rapport van de Onderzoekscommissie over de onderfinanciering van de ziekenhuizen. D/2004/10.273/11.
7. Nationale richtlijn prenatale zorg. Een basis voor een klinisch pad voor de opvolging van zwangerschappen. D/2004/10.273/13.
8. Financieringssystemen van ziekenhuisgeneesmiddelen: een beschrijvende studie van een aantal Europese landen en Canada. D/2004/10.273/15.
9. Feedback: onderzoek naar de impact en barrières bij implementatie – Onderzoeksrapport: deel 1. D/2005/10.273/01.
10. De kost van tandprothesen. D/2005/10.273/03.
11. Borstkankerscreening. D/2005/10.273/05.
12. Studie naar een alternatieve financiering van bloed en labiele bloedderivaten in de ziekenhuizen. D/2005/10.273/07.
13. Endovasculaire behandeling van Carotisstenose. D/2005/10.273/09.
14. Variaties in de ziekenhuispraktijk bij acuut myocardinfarct in België. D/2005/10.273/11.
15. Evolutie van de uitgaven voor gezondheidszorg. D/2005/10.273/13.
16. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid. Fase II : ontwikkeling van een actuarieel model en eerste schattingen. D/2005/10.273/15.
17. Evaluatie van de referentiebedragen. D/2005/10.273/17.
18. Prospectief bepalen van de honoraria van ziekenhuisartsen op basis van klinische paden en guidelines: makkelijker gezegd dan gedaan.. D/2005/10.273/19.
19. Evaluatie van forfaitaire persoonlijk bijdrage op het gebruik van spoedgevallendienst. D/2005/10.273/21.
20. HTA Moleculaire Diagnostiek in België. D/2005/10.273/23, D/2005/10.273/25.
21. HTA Stomamateriaal in België. D/2005/10.273/27.
22. HTA Positronen Emissie Tomografie in België. D/2005/10.273/29.
23. HTA De electieve endovasculaire behandeling van het abdominale aorta aneurysma (AAA). D/2005/10.273/32.
24. Het gebruik van natriuretische peptides in de diagnostische aanpak van patiënten met vermoeden van hartfalen. D/2005/10.273/34.
25. Capsule endoscopie. D/2006/10.273/01.
26. Medico–legale aspecten van klinische praktijkrichtlijnen. D2006/10.273/05.
27. De kwaliteit en de organisatie van type 2 diabeteszorg. D2006/10.273/07.
28. Voorlopige richtlijnen voor farmaco-economisch onderzoek in België. D2006/10.273/10.
29. Nationale Richtlijnen College voor Oncologie: A. algemeen kader oncologisch kwaliteitshandboek B. wetenschappelijke basis voor klinische paden voor diagnose en behandeling colorectale kanker en testiskanker. D2006/10.273/12.
30. Inventaris van databanken gezondheidszorg. D2006/10.273/14.
31. Health Technology Assessment prostate-specific-antigen (PSA) voor prostaatkankerscreening. D2006/10.273/17.
32. Feedback : onderzoek naar de impact en barrières bij implementatie – Onderzoeksrapport : deel II. D/2006/10.273/19.
33. Effecten en kosten van de vaccinatie van Belgische kinderen met geconjugeerd pneumokokkenvaccin. D/2006/10.273/21.
34. Trastuzumab bij vroegtijdige stadia van borstkanker. D/2006/10.273/23.
35. Studie naar de mogelijke kosten van een eventuele wijziging van de rechtsregels inzake medische aansprakelijkheid (fase III)- precisering van de kostenraming. D/2006/10.273/26.
36. Farmacologische en chirurgische behandeling van obesitas. Residentiële zorg voor ernstig obese kinderen in België. D/2006/10.273/28.
37. HTA Magnetische Resonantie Beeldvorming. D/2006/10.273/32.
38. Baarmoederhalskankerscreening en testen op Human Papillomavirus (HPV). D/2006/10.273/35
39. Rapid assessment van nieuwe wervelzuil technologieën : totale discusprothese en vertebro/ballon kyfoplastie. D/2006/10.273/38.
40. Functioneel bilan van de patiënt als mogelijke basis voor nomenclatuur van kinesitherapie in België? D/2006/10.273/40.
41. Klinische kwaliteitsindicatoren. D/2006/10.273/43.
42. Studie naar praktijkverschillen bij electieve chirurgische ingrepen in België. D/2006/10.273/45.
43. Herziening bestaande praktijkrichtlijnen. D/2006/10.273/48.
44. Een procedure voor de beoordeling van nieuwe medische hulpmiddelen. D/2006/10.273/50.