HAUTE AUTORITÉ DE SANTÉ

Assessment of medical devices

Assessment principles established by the Medical Device and Health Technology Evaluation Committee (CNEDiMTS) to determine the reimbursement eligibility of medical devices for individual use

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Sommaire

Abbreviations and acronyms

ANSM	Agence Nationale de Sécurité du Médicament et des Produits de Santé (French health products safety agency)
ACB	Actual clinical benefit
CCAM	Joint classification of medical procedures
CEESP	Commission d'évaluation économique et de santé publique (Commission for Economic and Public Health Evaluation)
CEPS	French Healthcare Products Pricing Committee
CNEDiMTS	Medical Device and Health Technology Evaluation Committee
CNP	French National Council for Healthcare Professionals
CME	Health Care Organisation Medical Committee
DFSMP	Dietary food for special medical purposes
DEMESP	Medical Device and Health Technology Evaluation Committee
MD	Medical device
IVDMD	In vitro diagnostic medical device(s)
PDI	Public Declaration of Interests
GHS	Groupe homogène de séjours (diagnosis-related group)
HAS	Haute Autorité de santé
PHB	Public health benefit
LPPR	List of products and services qualifying for reimbursement
PCH	Allowance for disability compensation
RP	Early dialogues
CAV	Clinical added value
SAHOS	Obstructive sleep apnoea-hypopnoea syndrome
SNITEM	National Union of the Medical Technology Industry (France)
UNCAM	French Association of Health Insurance Funds

Preface

We all aspire to live longer and in good health. Therefore, innovation in the health sector is more than simply a requirement.

And tomorrow, even more than today, the healthcare applications of the digital revolution and of electronic miniaturisation, the automatic processing in record time of billions of bits of data, along with genome sequencing and the arrival of 5G, will transform the future of medicine.

However, if society wants innovation, it also has a legitimate need for confidence.

In expressing an opinion in response to requests from manufacturers looking to gain access to reimbursement for their devices, the CNEDiMTS has a dual obligation: to recognise and to measure with discernment the useful, incremental or breakthrough innovation, whether in terms of medicine or quality of life, for French patients or people with disabilities – especially since medical devices are evolving as fast as technologies and are tending to increase their portion of the therapeutic arsenal, and of the care and life pathways.

The CNEDiMTS and the HAS Medical Devices Assessment Department are proud to be contributing to this scientific assessment. They are also aware of their responsibility with regard to the issues at stake, which is all the more onerous when the relevant scientific evidence, in terms of both benefit and risk, is not as exhaustive as it should be.

In carrying out this assessment mission, the CNEDiMTS relies on HAS's three values: independence, scientific expertise, transparency.

As regards transparency, the deliberations are accessible and the opinions are publicly available. In addition, the CNEDiMTS is required to specify the methods and principles it follows in implementing the assessment criteria for health products with a view to their adoption by the French health insurance scheme (Art. L. 161-37 of the French Social Security Code).

This is the purpose of this document, which covers medical devices for individual use and which has been supplemented by another, specifically tailored to the assessment of "connected" medical devices.

The CNEDiMTS's intention is to provide useful benchmarks because, over and above its legal obligation, it is very much committed to giving visibility to the principles on which its assessments are founded and thus to develop a predictability for manufacturers whose business relies on the reimbursement approach.

Happy reading.

I. ADENOT
Chair of the CNEDiMTS

Introduction

European Regulation 2017/745[1] defines a medical device (MD) as "*any instrument, apparatus, appliance, software, implant, reagent, material, or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:*

- the diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of a disease;
- the diagnosis, monitoring, treatment, alleviation or compensation of an injury or a disability;
- the investigation, replacement or modification of the anatomy or of a physiological or pathological process or state;
- providing information by means of an in vitro examination of specimens derived from the human body, including organ, blood and tissue donations;

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

Great diversity of the sector

This definition underlines **the considerable diversity** of the MD world, including products as diverse as dressings, corrective glasses, cardiac pacemakers, medical imaging equipment. This diversity is also to be found in the companies that market MDs, in both their number (1300 companies in 2017)[2] and their size.

The sector's diversity does ultimately make it difficult to estimate the number of devices on the market (probably somewhere between 800,000 and 2 million).

CNEDiMTS's activities, between CE marking and the French Healthcare Products Pricing Committee

European Directives 93/42[3] and 90/385[4] and Regulation 2017/745 (2017/746 for in vitro diagnostic medical devices- IVD-MDs) bring a measure of consistency to the marketing of MDs in Europe through CE marking, a procedure that assesses conformity with the general requirements relating to safety and performance. **Nevertheless, each Member State is free to decide whether any MD is covered by its own national health insurance scheme.**

The Medical Device and Health Technology Evaluation Committee (CNEDiMTS) is the HAS Committee responsible for evaluating medical devices for individual use, healthcare products other than medicinal products and associated services, with a view to determining their eligibility for reimbursement by the French health insurance scheme. Its task of scientific assessment kicks in once CE marking has been obtained.

This Committee[5,6] is independent and multidisciplinary. It is made up of:

- voting members who are healthcare professionals and patient representatives, that is to say:
  - 22 full members with **voting rights**, including two representatives of patients' and users' associations,
  - 7 substitute members, including one representative of a patients' and users' association;
- 8 members in an **advisory role** (representatives from the departments of the Ministry of Health, the ANSM and the UNCAM).

The role of the CNEDiMTS is to give health authorities an advisory opinion, recommending or otherwise the reimbursement of MDs, to help determine the conditions of good use and their place in the therapeutic, diagnostic or preventive strategy. Where appropriate, it decides on the conditions for optimising the use of technology in terms of user competence and necessary environment.

1. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. 2017. Official Journal of the European Union 2017.
2. www.snitem.fr/le-marche-des-dm [consulted on 07/05/2019] (in French).
3. Directive 93/42/EEC of the Council of 14 June on medical devices. Official Journal of the European Union 1993.
4. Directive of the Council of 20 June 1990 concerning the approximation of the laws of the Member States relating to active implantable medical devices (90/385/EEC). Official Journal of the European Union 1990.
5. Regulation of the CNEDiMTS. HAS, 13 March 2019 (in French).
6. Composition de la CNEDiMTS.

The Committee's opinion provides answers to the following questions:

- Whether used in hospital or in community medicine, should this MD be paid for by the taxpayer?
- What is the added value of the MD for the patient, in other words what therapeutic benefit in the broader sense does it offer in comparison with existing treatment methods?
- What is the size of the population for which reimbursement is justified and in which the MD has an added value?
- What is the impact of this MD on public health?

In the cases of an initial application for inclusion, a request to have the conditions of inclusion varied or an application for inclusion renewal,the CNEDiMTS assesses the actual clinical benefit (ACB) and, if this is sufficient, the clinical added value (CAV).

The opinion of the CNEDiMTS is then sent to the French Healthcare Products Pricing Committee. Ultimately, the decision on reimbursement rests with the Minister for Social Security and the Minister for Health. This process is subject to a tight schedule: in application of the French Social Security Code (art. R. 163-9), the time between submission of the application for reimbursement and publication of inclusion in the LPPR (list of products and services qualifying for reimbursement) in the JO is 180 days.

Principles of assessment

In conducting an assessment, the Committee takes into account the scientific and medical background. Within the regulatory framework entrusted to it, it relies on the available data, applies a scientific analysis methodology and a reasoning that together **constitute its principles of assessment, which are the subject of this document.**

Note: to make it easier to read, we shall be using the term "medical device". However, these general principles apply equally to other products falling within the scope of the CNEDiMTS's assessment, such as dietary foods for special medical purposes (DFSMPs) and assistive products to compensate for disabilities, as well as the services associated with these healthcare products.

This information document, whose objective is to provide some practical benchmarks regarding the CNEDiMTS's principles of assessment, is aimed at manufacturers, as well as at the National Councils of healthcare professionals (CNPs). It is also aimed at patients, who can get involved in the assessment of MDs since they are often users.

Neither is it a binding document. It should be regarded as a methodological aid and is complementary in its approach to the following guides:

- "Methodological choices for the clinical development of medical devices". HAS 2013;
- "Guide to the specific features of clinical evaluation of a connected medical device (CMD) in view of its application for reimbursement". HAS 2019;
- "Choices in methods for economic evaluation". HAS 2011.
- "Post-inclusion studies on healthcare technologies (medicinal products, medical devices and procedures) – Principles and methods". HAS 2011 (in French);

In addition to these guides, general information documents and support measures are available:

- "Medical device assessment in France". HAS 2017;
- + link to the submission guide "Early dialogue with HAS about a medical device undergoing clinical development". HAS 2017;
- " Procedure for applying for a pre-submission appointment and sequence of events". HAS 2017;
- "Contribution of patients' and users' associations to the assessment of medical devices. Guide for patients' and users' associations". HAS 2017.

This document is divided into **three main parts**. The first part summarises the regulatory framework for the reimbursement of medical devices in France. The second part deals with the determinants of the ACB/CAV assessment at the time of inclusion and for inclusion renewals.

Finally, the third part deals with the conditions of assessment (patient contribution, clinical research, endpoints, equivalence, comparators, etc.).

1. Regulatory framework for the reimbursement of medical devices and other healthcare products

When an application for reimbursement by the French health insurance scheme is received, the MDs are submitted to assessments over and above those relating to CE marking. The procedure for gaining access to reimbursement depends on the financing arrangements and the types of inclusion in the LPPR. They are summarised here before moving on to the principles of assessment.

1.1 Financing arrangements

The coverage of MDs by the French health insurance scheme varies depending on the sector concerned and the type of product.

In the ambulatory sector, MDs for individual use in the patient's home (with no hospitalisation involved) can be covered by including them in the LPPR (list of products and services qualifying for reimbursement). It should be remembered that MDs linked to a procedure performed by a healthcare professional are not subject to any individualised pricing structure, but are included in the fee for the procedure. The latter is included in the joint classification of medical procedures (CCAM).

In the case of hospitalised patients, the MDs used are mainly financed by the hospital stays (in homogeneous groups in healthcare establishments / intra-GHS) according to the pricing principle of the activity. For these MDs, it is the responsibility of the Health Care Organisation Medical Committees (CMEs) to draw up the list of sterile devices recommended for use in the establishment. The tariff for the MD is negotiated directly with each purchaser or hospital purchasing group. Some MDs are financed separately, in addition to hospitalisation benefits (extra-GHS). In such cases, they are included in the list of products and services qualifying for reimbursement in addition to hospitalisation benefits, more commonly referred to as an "additional list".

In order to increase the health safety of health products, Law No. 2011-2012 of 29 December 2011 and its implementing decree published on 15 September 2012 (Article L. 165-11 of the French Social Security Code) have **also extended the scope of the CNEDiMTS assessment to certain homogeneous categories of products financed through hospitalisation benefits (intra-GHS). A 2013 Order[7] defined the first categories to be assessed:**

- intracranial stents used in angioplasty of atheromatous stenosis;
- conventional implantable cardiac defibrillators: with endocardial lead (single-, dual-, and triple-chamber);
- implantable cardiac defibrillators without endocardial lead;
- biological surgical heart valves.

An order published in February 2019[8], stipulated another 5 categories required to undergo assessment by the CNEDiMTS **with a view to inclusion** in the "intra-GHS" list:

- implantable devices for the treatment of pelvic organ prolapse by the vaginal route;
- implantable devices for the treatment of urinary incontinence by the vaginal route;
- devices for the treatment of pelvic organ prolapse by the abdominal route;
- intracranial flow diverter stents;
- thrombectomy devices.

Note: some MDs may be covered by specific aid measures. This is the case, in particular, with some devices financed by departmental allocations to compensate for a disability in certain patients (allowance for disability compensation – PCH).

1.2 Types of inclusion in the LPPR

Two LPPR inclusion arrangements coexist.

→ Inclusion under the **generic description** identifies a product group according to its indications and its technical specifications without mention of a company or trade name. If the manufacturer considers that their MD meets the definition of a generic description, he/she takes responsibility for including it under this description. The product is then

7. Order of 28 November 2013 fixing for 2013 the homogeneous categories of health products referred to in Articles L. 165-11 and R. 165-49 of the French Social Security Code (in French).
8. Order of 22 February 2019 laying down for 2019 the homogeneous healthcare product categories mentioned in Articles L. 165-11 and R. 165-49 of the French Social Security Code.

covered according to the conditions defined on the LPPR for this generic description. The MD is not assessed by the CNEDiMTS, but the manufacturer (or distributor) is obliged to declare the use of the LPPR code for their product to the ANSM (French National Agency for Medicines and Health Products Safety).

Note: Since 2015, a new type of generic description - the enhanced generic description has been introduced as one of the ways to include MDs in the LPPR with the aim of both enhancing health safety and reducing the costs unduly borne by the French health insurance scheme. To date, this provision has not been used.

→ Inclusion under **brand name** (or trade name) is the process used in the case of innovative products or where the impact on the French health insurance scheme expenditure, public health imperatives, control and/or difficulty in defining minimum technical specifications necessitate special product monitoring. It is up to the manufacturer to request inclusion under brand name. It is required to submit a well-argued dossier (medico-technical dossier) that the CNEDiMTS will use to assess the MD. This type of inclusion is necessary in particular when an MD:
- does not match any generic description in the LPPR;
- or is subject to specific indications;
- or has a special benefit in terms of efficacy or tolerance that justifies it being treated individually under a specific LPPR code.

→ A framework agreement was concluded in 2011 between the CEPS and the professional organisations concerned by the products and services listed in the LPPR. In particular, this document stresses the quality of the content of dossiers submitted to the CNEDiMTS. It also contains other useful information, including pricing principles and the implementation of studies on products included in the list.

Inclusion under brand name in the LPPR is guaranteed for a maximum period of 5 years, and under a generic description for 10 years, which implies periodic assessments for inclusion renewal

2. Assessment by the CNEDiMTS: general principles

In its opinions, the CNEDiMTS assesses the **actual clinical benefit** of an MD or other healthcare product (sufficient or insufficient ACB), particularly on the basis of clinical data. In its opinions, it issues recommendations aimed at decision-makers.

If the actual clinical benefit is sufficient, the Committee then specifies **the clinical added value** (CAV can be absent, minor, moderate, important or major).

→ The ACB serves to determine whether an MD should be reimbursed or not (sufficient or insufficient).
→ The CAV has an impact on the fixing of the price of the MD, negotiated by CEPS with the manufacturer.

The main determining factors underpinning the assessment are the patient and their illness or disability, how the MD fits into the therapeutic strategy and into the healthcare system, and the quantity of its effect.

Knowledge of the illness or disability, their various forms and their grading in levels of severity are taken from the available scientific literature, including the recommendations and the advice of experts.

The ACB assessment[9] is carried out, for each of the product's indications, according to:

- the product's benefit as regards:
  - its place in the therapeutic, diagnostic or disability compensation strategy, given all the other available therapies or diagnostic or compensation methods,
  - its therapeutic, diagnostic or disability compensation effect, as well as undesirable effects or risks associated with its use;

9. Article R. 165-2 of the French Social Security Code (in French).

- its public health benefit, including in particular:
  - its impact on the health of the population, in terms of mortality, morbidity and quality of life,
  - its capacity to meet a therapeutic, diagnostic or disability compensation need that is not covered, in view of the severity of the pathology or of the disability,
  - its impact on the healthcare system,
  - its impact on public health policies and programmes.

The actual clinical benefit is assessed, where appropriate, according to the technical specifications and the specific prescribing and use conditions on which inclusion depends.

essment of the CAV is based on the improvement afforded by the product, assessed in relation to a comparable product, procedure or service or to a precisely designated group of comparable products, procedures or services, considered as a reference according to current scientific data and whether or not accepted for reimbursement[10].

This assessment is done on a given date in an ever-changing environment.

2.1 Clinical data: the basis of the assessment

The general principle behind the assessment of MDs is based on a rigorous analysis of the clinical data (see chapter 6).

All assertions relating to the data on the MD **claimed by the manufacturer** need to be scientifically demonstrated. **The data are analysed according to the criteria used in evidence-based medicine.**

However, the Committee's experience has led it to highlight four specific elements of MD assessment:

- the difficulty of setting up studies for certain MDs;
- the fact that the performance of the MD varies over time: the short life cycles of MDs with frequent incremental changes can call into question the validity of results already obtained with earlier versions;
- the target population which is sometimes small;
- the operator-dependent nature of the MD and the environment in which it is used: when drafting a protocol, account should be taken of the learning curve of operators, the experience of the team, the technical facilities, etc.

2.2 Reliance on expertise

The general principle of MD assessment is also based on the clinical and scientific expertise of healthcare professionals.

In addition to the members of the Committee, in certain cases, the CNEDiMTS Chair may call on **outside expertise**, in particular for MDs relating to professional specialities not represented among the Committee members. This outside expertise sheds light on the pathophysiological background, the reference therapeutic strategy and on clinical practice.

After analysis and validation of their public declaration of interest (PDI) by the HAS Ethics Committee, and only then **the expert, subject to confidentiality rules, receives the medico-technical dossier**. The expert's contribution takes the form of a written report. He/she may also, at the request of the Committee Chair, attend the meeting in order to give their point of view on the dossier for which (s)he has been approached and to answer questions from members of the CNEDiMTS. However, **the outside expert does not take part in the deliberations of the members or the voting**.

2.3 Stakeholders involvement

► National Councils of healthcare professionals

As an alternative or in addition to outside expertise, the Committee may wish to question the National Councils of healthcare professionals. In this case, the medico-technical dossier is not sent to them. The object here is to listen to the national councils of the specialities concerned on their positioning in terms of recommendations and professional practices, particularly in the event of discrepancies or a lack of published recommendations.

10. Article R. 165-11-3 of the French Social Security Code (in French).

► Patients' contribution to the assessment

Patients have special knowledge about their disease. Their experience of living with the disease, and with existing treatments, care pathways and needs, adds a rich perspective to the assessment of healthcare products.

In consequence, the CNEDiMTS **does take into account the patients' point of view in its assessments**.

The contribution of patients to the work of the CNEDiMTS can take several forms:

- in accordance with Article R. 165-18 of the French Social Security Code, **three voting members** of the Committee are chosen from among the members of an association of patients and users of the healthcare system (associations mentioned in Article L. 1114-1 of the Public Health Code);
- at the initiative of the Committee, users may be consulted as **stakeholders**;
- at their own initiative, associations that so wish may, via a patient contribution process, transmit their spontaneous contribution concerning a medical device under assessment using a generic questionnaire.

These different ways in which patients contribute to the work of the CNEDiMTS allow the Committee's members to have a broader perspective of:

- the impact of the disease or of the health state on the patients, their lifestyle, their quality of life (or that of their relatives);
- the experience of patients treated with therapies other than those assessed;
- the experience of patients with the product being assessed (provided that patients have had experience of using the products or that the association is familiar with the results of clinical trials relating to the product).

Patients' contribution may include MDs for which an assessment is planned, for the initial inclusion or the inclusion renewal. Also, the views of users may be sought, as stakeholders, within the framework of reviews of homogeneous product categories. **Thus, with these different ways of being involved, all the devices assessed are likely to benefit from patients' insights, whether the products are included under "brand names" or "generic descriptions".**

3. Actual clinical benefit

The ACB of a healthcare product is assessed in each one of the claimed indications according to the following two criteria: the benefit of the MD and its public health benefit[9]. The criterion here is a binary one: sufficient or insufficient. If the actual clinical benefit is sufficient, the opinion goes in favour of the MD being included in the LPPR. If the ACB is insufficient, the opinion goes against the MD being included in this list.

3.1 Product benefit

Product benefit is the first criterion on which the Committee has to give a verdict. This concerns, firstly, *"its therapeutic, diagnostic or disability compensation effect and adverse effects or risks associated with its use and, secondly, its place in the therapeutic, diagnostic or disability compensation strategy, taking into account the other available therapies or means of diagnosis or compensation"*[9]. In other words, with this criterion it is possible to measure the MD's contribution according to its effect at an individual level and in the pathophysiological setting.

► Pathophysiological setting and the reference therapeutic strategy

The first step of the assessment involves taking the pathophysiological setting in account together with the usual ways of dealing with the disease or the disability.

When assessing the reference therapeutic strategy, the CNEDiMTS takes into account:

- French and foreign **recommendations** together with the **opinion** of healthcare professionals. The value of these recommendations and opinions is determined on the basis of how they were developed;
- **the medical and organisational context**, by adjusting its level of requirements according to the category of the MD and by assessing the transferability of the results of the clinical studies supplied to the actual conditions of use of the MD;
- **the available therapeutic arsenal**, especially in those cases where the alternatives are few and where the therapeutic need is not covered adequately or at all. The CNEDiMTS specifies in its opinion whether the product is a first-, second- or even third-line product relative to the alternatives. It also indicates which populations are most likely to benefit from the product.

The severity of the disease or disability (in terms of mortality and morbidity, in particular) is an essential parameter in the assessment. However, **its severity alone does not justify a sufficient ACB**.

▶ Therapeutic/diagnostic/disability compensation effect compared to the risks associated with use

The benefit of the MD is assessed as regards its therapeutic, diagnostic or disability compensation effect, as well as undesirable effects or risks associated with its use.

The risk/benefit ratio of the MD, the ratio between one or more benefits and one or more risks established on the basis of scientific evidence, is a **major element of the assessment.**

The assessment takes into account the results observed in the course of clinical trials and possible limits to their extrapolation to the population likely to be treated with this MD in a current use situation.

▶ Place of the MD in therapeutic strategy

The MD needs to find a place in the therapeutic arsenal that is available to the pathology concerned. The reference strategy can be determined from **literature data** (systematic reviews, reports by French or international assessment agencies, meta-analyses, randomised controlled studies) and/or the recommendations of healthcare professionals

For example: in the etiological diagnosis of ischaemic strokes in certain patients, the Committee relied especially on the recommendations of HAS, the American Heart Association and the American Stroke Association to define the reference diagnostic strategy and, in particular, the place of implantable cardiac monitors.

This reference strategy can be **another MD, a medicinal product, a surgical intervention, or other form of cover**. In the absence of valid scientific evidence, the reference strategy is defined as that used in practice on expert advice. This reference strategy should be the one that, in the absence of the new MD, is expected to yield the **best results** in patients having the disease.

3.2 Public health benefit

The public health benefit (PHB) is the second criterion on which the Committee has to give an opinion. In contrast to the product benefit that sets out to assess the contribution that technology offers on an individual level, the PHB takes the collective dimension into account..

▶ Disease epidemiology

Epidemiological data, when they are of use in the medical context of the MD, enable the Committee to get a picture of the incidence and the prevalence of the disease. The Committee takes into account all of the available epidemiological data, including those published in the literature or extracted from medico-administrative databases.

▶ Impact of the MD on public health

The product's impact on public health is dependent on:

- its potential effect on the health of the population (mortality, morbidity, disability compensation, quality of life, etc.);
- its foreseeable effect on the organisation of care, on individual or collective expenditure (number of consultations, number or length of hospital stays, number of procedures, etc.);
- its compatibility with the objectives of public health programmes defined by law or by other recommendations of the bodies concerned.

▶ Target population – estimate

In order to forecast the volumes of legitimate prescriptions involved, the CNEDiMTS estimates the target population for the MD likely to be treated in France. **The estimate is made for each one of the indications** in which the medical device and/or service is proposed for reimbursement.

For example: the Committee has accepted two different indications for:
- a dietary food for special medical purposes in children:
  - diagnosis and treatment of allergy to protein hydrolysates (including allergy to cow's milk proteins);
  - treatment of eosinophilic oesophagitis.
- an implantable cardiac monitor:
  - etiological diagnosis of syncope;
  - etiological diagnosis of ischaemic stroke.

In each example, the target population was thus estimated in both the indications separately, based on epidemiological data.

As a general rule, the determination of the target population(s) is based on epidemiological data or data from practice (medico-administrative or other databases). It is expected that French data be used as a priority; failing that, foreign data can be used, on condition that such data can be extrapolated to the French context. On the basis of these data, an approach based on the population affected by the disease or disability will be able to lead, step by step, to the population eligible for reimbursement, i.e. the population that is likely to be treated by the MD.

When the target population cannot be estimated due to a lack of available epidemiological data, the CNEDiMTS then tries to estimate the population reached, which corresponds not to the theoretical population likely to be treated (target population) but to the population actually treated by the MD or other products from the same category. The Committee uses all the data at its disposal to produce this estimate; usually analyses conducted by HAS on medico-administrative databases are used.

In some cases, in particular when registering an MD belonging to a new category, the CNEDiMTS can use the sales data or the sales forecasts sent in by manufacturers, as well as the estimate produced by the experts tasked with examining the dossier.

For example:
- in the case of energy storage and return prosthetic feet, the Committee considered that it was not possible to determine the target population for each class of foot on the basis of the epidemiological data. It therefore relied on the French health insurance reimbursement data for this type of equipment and so estimated the population actually treated by the MD;
- in the case of deep brain stimulators used in Parkinson's disease, the Committee considered that the population needing deep brain stimulation could not be determined on the basis of the epidemiological data. This type of stimulation is in fact reserved for the severe stage of the disease, though still responding to dopa therapy and subject to several selection and exclusion criteria. The Committee accordingly resorted to data relating to procedures classified under the National hospital discharge database (PMSI) to estimate the population actually treated by the MD.

► Some factors leading to an insufficient actual clinical benefit

A low level of efficacy, with no clinical relevance

For example: in the treatment of first-degree mild to moderate early presbycusis (hearing loss of between 30 and 55 dB), the Committee estimated that the actual clinical benefit of a hearing aid was insufficient compared to the conventional hearing aids listed in the LPPR. One of the criticisms made about the studies related to the absence of documentation concerning the clinical relevance of the difference observed for the hearing assessment score used.

A low level of efficacy, with no clinical relevance as regards significant adverse effects

For example: in the case of a topical ophthalmic solution containing a preservative known to be irritant, the Committee deemed the ACB insufficient because the studies provided did not demonstrate a clinically relevant amount of effect, i.e. a quantity of effect that outweighed the disadvantages associated with the use of a preservative for this type of product.

A demonstrated efficacy in a population whose transferability to the population actually concerned is in doubt

For example: in the case of a hydrocellular dressing, the Committee judged that the ACB was insufficient because the available data did not establish the benefit of these dressings in preventing the occurrence of bedsores in a homecare setting. Indeed, the application was based on a study conducted in patients at high risk of developing bedsores, hospitalised in intensive care units. Even though the results of this study were favourable to the product, as the rate of bedsores that developed was statistically different between the control group and the treatment group, it was not possible to extrapolate its results to the home treatment of patients at high risk of developing bedsores.

An indication different from that claimed in the application for reimbursement

For example: in the case of a topical sterile ophthalmic solution for use in the symptomatic treatment of dry eyes, the Committee estimated that the ACB was insufficient since all the studies provided were conducted in indications other than those claimed, without justification of transferability by the manufacturer.

A study provided whose objective is not to assess the effect specific to the product that is the subject of the reimbursement application

For example: in the symptomatic treatment of pain associated with oral mucositis caused by radiotherapy and/or chemotherapy, the study provided was not constructed to demonstrate the specific effect of the product subject to the request for inclusion (product + an active substance versus product alone).

A study provided not meeting the standards of the CNEDiMTS

For example: in the case of a dressing with an antiproteinase effect, the primary outcome measure of the pivotal study provided was the reduction in wound surface area and not the outcome measure recommended by the Committee, i.e. complete would closure.

The placing of several MDs in a single pack when not justified by care practice or usability

For example:

- in the case of a self-monitoring kit for blood glucose and blood pressure, the Committee deemed the ACB insufficient because no benefit could be established in combining an autotensiometer with a blood glucose monitor in the same kit;
- in another case involving blood glucose self-monitoring kits, the Committee judged that the ACB was insufficient because their packs did not allow self-monitoring of blood glucose on account of the lack of any test strips;
- in the case of sets of dressings for chronic deep/cavity, moist or exudative wounds in the budding phase, the Committee deemed the ACB insufficient because it believed that primary dressings should properly be prescribed separately from the sets, in order to be better able to take into account the characteristics of the wound and how it develops.

A lack of demonstrable equivalence with a clinically-proven MD (earlier model or version in the range from the same manufacturer or a competitive MD)

For example: in the case of a polyethylene bone prosthesis for craniofacial or maxillofacial reconstruction, the Committee deemed the ACB insufficient in light of the lack of any specific clinical data. The application was, in fact, based on an argument of equivalence and on non-specific studies for which the products used were not described, which made it impossible to establish the transferability of the data provided.

4. Clinical added value

When the actual clinical benefit is sufficient to justify registration for reimbursement, the Committee **assesses the clinical added value (CAV) relative to an appropriate comparator**. This involves assessing the additional benefit afforded by the new product in relation to precisely designated therapeutic strategies, considered as a reference according to current scientific data, whether accepted or not for reimbursement.

This improvement is assessed on a given date in an ever-changing environment.

It is up to the applicant to justify the choice of comparator and the claimed level of clinical added value.

4.1 Choice of comparator

The comparator favoured by the Committee stems from the reference strategy based on current scientific data. It is defined for **a given indication and may be accepted or not for reimbursement**.

Several scenarios can be identified:

- the comparator used in the study/studies supporting the application is the relevant comparator;
- the study comparator is not or is no longer the reference comparator or in the absence of a comparative study: the Committee will then need to define a comparator based on the reference therapeutic strategy[11];
- 2when the need is not covered, the comparator is the absence of any alternative.

The very nature of this comparator may be very variable:

- a product (medical device, medicinal product or other healthcare product) or a homogeneous category of products;
- and/or a procedure or a group of procedures;
- and/or a service.

In some cases, the Committee may choose several comparators. In particular, this is the case when an MD is not superior to the other MDs in the same category (Level V CAV for the various MDs in the same category); the Committee may also provide an insight with respect to the available therapeutic arsenal by allocating a "class" CAV.
E.g.: cochlear implants

The relevant comparator is at the same place in the therapeutic strategy[11] as the product being evaluated and must match the comparator(s) identified in methodologically good-quality comparative clinical studies. It may be the one claimed by the manufacturer or a comparator that the Commitee defines as being more relevant.

Several examples of comparators may be identified

1. **First device(s) in a new class**[12]

→ On inclusion, the comparator may be a product, and/or a procedure, and/or a service occupying the same place in the therapeutic strategy[11].

For example:

- in the area of disability, the Committee assessed an externally-powered myoelectric prosthetic full hand belonging to a new device class (no prosthesis with these functionalities is included in the LPPR). The comparator used by the Committee was the one occupying the same place in the disability compensation strategy, namely an end-effector (hand) from a myoelectric upper-limb prosthesis.
- in hip joint replacement revision surgery in a situation of massive bone loss, the Committee assessed a new acetabular revision system. The comparator that it chose was a massive structural allograft combined with a supporting ring (reference therapeutic strategy in this indication).

→ **On inclusion renewal with no other device of the same class**[12] **listed in the LPPR**[13]: the comparator may be the one chosen during the initial application for inclusion, in the absence of any change in the therapeutic strategy[11].

For example: for a scleral lens used in the event of corneal deformation or destruction, the comparator selected by the Committee was the absence of alternative, since no device with the same indication has been reimbursed.

→ If, between the time an opinion is given relating to inclusion and to inclusion renewal, one or more devices in the same category have been assessed by the Committee: it/they can become the comparator(s), in the absence of any other relevant comparators coming from comparative clinical studies.

For example: for the assessment of carotid endoprostheses, the comparator chosen by the Committee in its opinion on inclusion was the absence of any alternative. In its opinion on inclusion renewal, the Committee chose other carotid endoprostheses as comparators.
For a blood glucose and ketone meter, the comparator chosen by the Committee in its opinion on inclusion concerned systems for assay of urinary ketone bodies. In its opinion on inclusion renewal, the Committee chose another system of the same type having been included in the LPPR in the intervening period, as the comparator.

11. Therapeutic strategy: reference therapeutic, diagnostic or disability compensation strategy, or strategy used in current practice in the absence of scientific evidence.
12. In the remainder of the text, the term "class" will refer to a homogeneous category of products.
13. Included or awaiting inclusion (sufficient ACB granted).

→ In the event that two medical devices of the same class have been developed concurrently (within approximately 3 years of each other), given the difficulty of obtaining comparative clinical data between these two products, another comparator occupying the same place in the therapeutic strategy may be taken into account, subject to comparative data being available.

For example: in the case of active balloons used in the treatment of peripheral vascular diseases, the comparator chosen by the Committee was the uncoated balloon. Studies comparing drug-eluting balloons with uncoated balloons were provided. No study comparing the active balloons was available.

2. **First application for registration and one or more medical devices of the same class[12] already included in the LPPR and having identical indications:** the comparator may be the device(s) of the same class[12].

For example:
- when an application was made to include an insulin pump that did not meet the technical specifications of the generic description for insulin pumps, the comparator selected by the Committee was the generic description of insulin pumps;
- in the case of custom-made bone substitutes, devices used in cranial vault reconstruction, the comparator chosen by the Committee corresponds to other custom-made bone substitutes, included in the LPPR.

3. **Expanding the range:** the comparator may be the device(s) from the previous generation assessed by the CNEDiMTS.

For example, the comparator chosen by the Committee was the previous generation, included in the LPPR, to expand the range of the following products:
- implanted wide-diameter bone-anchored hearing aids;
- implantable, refillable bone marrow stimulation systems.

4. **Extension of indication:** the comparator may be the one from the same class[12] of devices with the same indication. In the absence of a device of the sameclass[12] and the same indication, the comparator may be the one having the same place in the therapeutic strategy[11].

For example: for an INR self-monitoring device, when applying for an extension of indication in adult patients with a mechanical heart valve under treatment with vitamin K antagonists, the comparator chosen by the Committee was the one occupying the same place in the diagnostic strategy, i.e. the INR measurement carried out only in a medical laboratory. This comparator was also the comparator used in comparative clinical studies.

5. **Other changes in the conditions of inclusion (technical specifications, packaging):the comparator concerns the references[14] of the device already assessed by the Committee.**

For example: to add new diameters or new lengths for abdominal aortic endoprostheses, the comparator chosen by the Committee was the other references of the range included in the LPPR.

4.2 Determining the CAV level

The CAV claimed by the manufacturer is documented by the clinical data supporting its application.

In theory, the CAV level is determined on the basis of the results of clinical studies demonstrating the clinically relevant superiority of the MD assessed versus a comparator that is also relevant. The improvement may concern variable criteria depending on the purpose of use of the MD, in particular, efficacy, reduction of a risk, convenience of use, quality of life, organisational impact, etc.

Where appropriate, if the manufacturer feels unable to provide comparative studies with a high level of evidence, they should explain and substantiate this in the medico-technical dossier.

14. Included or awaiting inclusion (sufficient ACB granted).

Major CAV (level I) applies in particular to an MD that has demonstrated appreciable efficacy in relation to the mortality criterion for MDs with therapeutic or disability compensation objectives and affording a major benefit in the medical domain concerned.

Important (level II), moderate (level III) or minor (level IV) CAV qualifies the additional clinical benefit in terms of efficacy, risk reduction or disability compensation and/or quality of life, according to its intensity.

In the absence of any demonstration of the superior benefit of a product in relation to the reference strategy, the Committee generally concludes that there is an absence of CAV (CAV V). This is especially the case when an application:

- is not based on any comparative clinical study or is based on comparative data that cannot be interpreted;
- is based on a claimed equivalence to another MD in the same category;
- or is based on study results demonstrating non-inferiority.

For example:

- in the case of a transapically implanted aortic valve, given that the pathologies involved are serious and the need is not covered (absence of any alternative therapy), the Committee decided in favour of a major CAV (CAV I) for this valve compared to palliative care;
- in the endoscopic drainage of pancreatic fluid collections (pseudocyst), the Committee decided in favour of an important CAV (CAV II) for a luminal biliopancreatic apposing implant and its electrocautery-enhanced delivery system, enabling the creation of an anastomotic duct facilitating the drainage of pancreatic fluid collections. The comparators chosen were "double pigtail" plastic stents, also used during endoscopic drainage;
- in malignant primary bone tumours of the pelvis, requiring surgical resection, the Committee granted a moderate CAV (CAV III) for a custom-made surgical guide enabling the surgeon to locate and perform the resection(s). The comparator selected is the conventional bone tumour resection method, i.e., without intraoperative assistance;
- in the adjuvant treatment of high-risk non-muscle-invasive bladder cancer (NMIBC), the Committee decided in favour of a minor CAV (CAV IV) for a radiofrequency-induced thermochemotherapy system, in the absence of an alternative;
- for triple-chamber implantable cardiac pacemakers, combined with remote medical monitoring, only the data concerning previous versions of single and double-chamber pacemakers and of the transmitter used for the remote monitoring system were available. The Committee therefore ruled that there was no CAV (CAV V) compared to the other triple-function implantable cardiac pacemakers with a remote monitoring function already listed in the LPPR.

For one and the same category of MD, **the CAV levels assigned by the CNEDiMTS evolve to reflect changes in the available therapeutic arsenal and as new data comes to hand**. As a general rule, the CAV is assigned in relation to the existing therapeutic, diagnostic and disability compensation strategy. The first MD in a category often constitutes the reference when manufacturers of competing MDs subsequently seek inclusion of their MD in the LPPR. The other MDs from this same category will then be compared with each other.

For example:

- the Committee granted a major CAV (CAV I) for an intracorporeal electrical continuous-flow left-univentricular mechanical circulatory support device (MCSD), in the absence of any alternative. When renewing inclusion, the Committee compared this device with other continuous-flow MCSDs listed in the LPPR, thus assigning it an absence of CAV (CAV V) compared to these latter devices;
- in the case of mandibular advancement orthotics, the first device assessed by the Committee received sufficient ACB and was compared to two different treatments, the reference therapeutic strategy varying according to the severity of the obstructive sleep apnoea-hypopnoea syndrome (SAHOS), with one:
  - minor CAV (CAV IV) compared to the absence of treatment, for the treatment of severe SAHOS and
  - absence of CAV (CAV V) compared to continuous positive airway pressure devices, for the treatment of mild to moderate SAHOS.

  The following devices were compared with the first one, and the Committee decided in favour of an absence of CAV (CAV V) compared to the mandibular advancement orthotics already listed in the LPPR.

Since the medico-technical dossier is examined in the light of the manufacturer's application, the CAV level awarded by the Committee cannot be more favourable than that claimed by the applicant if the Committee selects the same comparator.

5. Inclusion renewal

When renewing the inclusion of an MD, the information on which to base the assessment of the ACB and CAV is comprised of the new available data: the results of post-inclusion studies requested by the CNEDiMTS at the time of the initial assessment, materiovigilance data and all other available new clinical data.

In addition, the Committee examines the inclusion renewal application against the medical background, the therapeutic arsenal available, the therapeutic strategy and the good practice recommendations, **which may have changed since the initial assessment of the MD**.

For example: for the inclusion of a coronary endoprosthesis with a specific coating, the Committee granted a CAV IV compared to uncoated stents, while at the same time requesting a post-inclusion study. The results of this study were taken into account by the Committee when assessing the new generation of this endoprosthesis (the previous one was taken off the market). Since the results of this study did not reveal any difference in the rate of major cardiac events at 24 months, the Committee decided on a CAV V for this new version of coronary endoprosthesis compared to uncoated stents.

It should be noted that the Committee may, at its own initiative or following a request from the ministers of health and social security, reassess the actual clinical benefit of a product listed in the LPPR.

5.1 Request for a post-inclusion study

During assessment of a medical device, the CNEDiMTS can ask for additional data to be collected via the performance of a post-inclusion study, with the aim of enabling patients to access reimbursed new technologies with a controlled level of risk. Depending on the case, the objective may be to confirm the benefit of the MD in a real-life situation - particularly when the organisation of care in routine MD use conditions differs from the standardised organisation of care in studies, or to confirm their benefit for patients in the long term. This is the case, for example, when only short-term data are available at the time of assessment by the Committee.

It is on the basis of missing data identified during its initial assessment of the MD that the CNEDIMTS formulates its expectations with respect to post-inclusion studies (confirmation of benefit, complication rate, quality of life, etc.). The data from the post-inclusion study requested must be available at the time of reassessment of the MD; they are then taken into account.

For example:

- for inclusion renewal of dual mobility acetabular cups, the CNEDiMTS would like to have data relative to the dislocation rate (intra- and extra-implant) and long-term survival of these implants (making a distinction between revision for any cause and revision for aseptic loosening), on the basis of follow-up of an exhaustive cohort;
- for inclusion renewal of a dietary food for special medical purposes – adult parenteral nutrition – the CNEDiMTS wished, in particular, to see the results of the requested multicentre study under actual conditions of use, as well as a reassessment at 2 years.

The methods to be used when conducting these studies are described in "Post-inclusion studies onhealthcare technologies (medicinal products, medical devices and procedures) – Principles and methods". HAS – November 2011.

To make it easier for manufacturers to understand what it expects, the Committee structures its post-inclusion study request process:

- identifying the missing data that will be required for assessment of the actual clinical benefit, or clinical added value, and which must be submitted at the time of inclusion renewal;
- formulating the expected objectives and outcome measures;
- ensuring the feasibility of the study in view of the data sources during the inclusion duration (ad hoc data collection vs use of databases).

The Committee stresses that when a post-inclusion study is requested, the results of this study will be decisive for reassessment of the MD at the time of renewal of its inclusion for reimbursement. Given the arrangements available to promote the implementation of post-inclusion studies (exchange with the HAS, guide), non-performance of such a study may logically lead, apart from in exceptional circumstances, to modification of the conclusions of the opinion at the time of product inclusion renewal (depending on the cases, modification of the actual clinical benefit, reduction in the actual clinical added value, etc.).

The Committee therefore draws the attention of the manufacturers concerned to the importance of their commitment to implementation of the studies requested.

In all cases, and independently of any post-inclusion study request, it will be expected to see an update of the data, as recommen ded in the practical guide for inclusion of products or services.

6. Evidence-based assessment: methods and criteria

6.1 Clinical research

The scientific data submitted by the manufacturer are analysed according to the criteria of evidence-based medicine. The CNEDiMTS determines the clinical relevance and the transferability to the French healthcare system.

A randomised controlled trial designed and conducted in double-blind (or at least with an independent observer) is the study offering the highest level of evidence. However, in some situations, this type of study may not be an option when it comes to assessing MDs, and the Committee takes this context into account and adapts its requirements, subject to one condition: **the CNEDiMTS expects the manufacturer to explain and justify this impossibility.**

The CNEDiMTS has identified situations in which conventional randomised controlled trials are not possible and has identified methods and conditions for allowing clinical quality assessment in the "Methodological Choices for the Clinical Development of Medical Devices". Above all, the study must be appropriate to the applicant's claims.

In the event of a study of non-inferiority of a new MD compared to the reference MD already assessed by the Committee, the latter shall pay attention to the methodology of the studies provided and, in particular, to the choice of the non-inferiority threshold and its justification.

For example: in the case of a rechargeable implantable spinal cord neurostimulator, the Committee selected a randomised controlled study specific to this device that showed the non-inferiority of burst stimulation compared to tonic stimulation on the parameter for assessing overall pain in the follow-up at 3 months.

The CNEDiMTS's expectations can vary depending on:

- **the category of the MD:** for example, the Committee takes into account the inherent context of certain assistive products, whether it is an MD or not. The clinical assessment of products, focused on the needs of the person with disabilities, their lifestyle, life plan and environment is always preferable. For a certain number of categories of products (bedsore prevention aids, energy storage and return prosthetic feet, for example), however, a technical assessment, subject to compliance with standards, may be sufficient.

For example:
- in the case of propulsion assistive devices and scooters, the Committee has proposed inclusion under generic description for these two categories of devices. It has defined minimum technical specifications that constitute a technical evaluation reference frame for applications for inclusion under a brand name pending the transfer of each of the nomenclatures that it has recommended to the LPPR.
- in the case of transcatheter aortic valve implantation (TAVI) devices, the Committee has adopted a reference framework outlining its level of requirements in terms of the minimum clinical data to be supplied for a new device, for acceptance of a new indication or for the renewal of a new device already accepted for reimbursement.

- **the life cycle of the MD:** it can be shorter than that of the clinical research. With any device it is essential, as far as possible, to anticipate the incremental evolution in the clinical development plan of the MD. This is a key element for taking clinical data into account for new ranges (new models);

For example: in the case of a rechargeable implantable spinal cord neurostimulator, the Committee selected a randomised controlled study specific to this device that showed the non-inferiority of burst stimulation compared to tonic stimulation on the parameter for assessing overall pain in the follow-up at 3 months.

- **the limited chances of recruitment** in a clinical study: the Committee insists that in such cases, conducting international multicentre studies increases the number of subjects that can be included. In all cases, a favourable opinion can only be delivered on the basis of the expected benefit for the patient when the risk inherent in these MDs is sufficiently characterized and limited according to the type of MD.

For example: in the case of an external prosthesis replacing the hip in patients amputated at the hip joint, the Committee found that this device offered a benefit in the claimed indications despite the major limitations of the studies performed in support of the manufacturer's application. The Committee has accordingly taken into account the fact that: i) this technology was targeting an extremely limited population (fewer than 60 persons annually); ii) it expanded the available therapeutic arsenal; iii) and its functional characteristics should allow a gait that was more closely matched to the physiological gait and thus limit the repercussions for the spine and the risk of falling.

6.2 Endpoints

► Primary endpoint

It is proposed to identify **a single primary endpoint** in conformity with the main aim of the study. It should be defined before the protocol is drawn up and make it possible to quantify the therapeutic effect of the new MD in comparison to the control treatment.

The choice of primary endpoint should be consistent with the disease being treated and the clinical action of the new MD and of the control treatment. In order to have a convincing demonstration of the clinical benefit of the new MD, the chosen endpoint must be relevant and valid. At best it should be a clinical endpoint or one denoting convenience of use, with clinical benefit for patients.

Note: if the medical device is associated with a telemedicine procedure (remote medical monitoring, for example), apart from individual clinical benefit and patient acceptability, HAS introduced the principle of a multidimensional assessment, based on the following criteria: accessibility, organisation of care, quality of care and safety of care, costs.

A medico-economic assessment may be built into the multidimensional assessment, subject to adequate efficacy and cost data being available. The principles and the methods adopted by HAS to respond to this mission can be found in the guide "Choices in methods for economic evaluation".

The endpoints of the studies in support of applications for inclusion in the LPPR must thus be adjusted to the type of technology **and be consonant with the manufacturer's claims**.

Endpoints the most frequently observed in studies supporting dossiers submitted for assessment:

- mortality reduction in the short, medium or long term;
- reduction or improvement in morbidity (pain, healing, decrease in relapses, pain reduction, etc.);
- compensation of disability (degree of dependence and autonomy, resumption of lifestyle, mobility, socio-professional insertion, etc.);
- reduction in complications or adverse events attributable to the surgical technique or procedure: duration or number of hospital stays, infections, bleeding, reinterventions, etc.;
- improvement in the patient's quality of life;
- impact on the organisation of care: reduction in the length of hospital stay, decreased consumption of healthcare products or decrease in the number of procedures, less reliance on medically-equipped transportation.

► Intermediate or surrogate endpoints

It is possible to use intermediate endpoints. They can be useful in cases where it takes a long time for the value of the clinical endpoint to be known. However, the use of a validated intermediate endpoint is crucial in order to avoid any risk of it being called into question at the end of the study. Endpoints that are robust and predictive of the long-term outcome are difficult to determine. They need to rely on a validity of the predictive nature of the expected clinical effect. In practice, **an intermediate endpoint is validated if the literature provides evidence that the endpoint is a surrogate endpoint**.

For example:

- the Committee used the glycated haemoglobin level, a validated predictive surrogate endpoint of the onset of degenerative complications in diabetic patients;
- when assessing new vascular endoprostheses, the Committee has already encountered "late luminal loss of the vascular lumen" as an angiographic intermediate endpoint, often used in trials. This endpoint criterion has not been shown to be formally predictive of the onset of relevant clinical events, such as myocardial infarction or recurrence of angina requiring revascularisation.

► Patient-centred endpoints: PROMs/PROs

In some cases, patients themselves are involved in the collection of clinical data. PROs (Patient related outcomes) or PROMs (Patient related outcome measures) are tools that measure a patient's perception of their medical condition or quality of life. The parameters taken into consideration may be variable, single or multiple. The specific characteristic is that the data are collected by patients themselves. The objective is to question patients about how they cope with their disease, its impact on their daily, social or professional life and on their family, their experience of the care pathway, their symptoms, their perception of treatment side effects, etc.

PROs are generally used as a secondary endpoint in parallel with clinical measurement of a medical result.

For example, the Committee examined a request for inclusion for a web application-based software, intended for remote medical monitoring and early detection of relapses and complications in cancer patients. In one of the studies provided, the primary endpoint was overall survival and the secondary endpoints included specific follow-up of patients: in parallel with clinical and imaging follow-up, the patients completed a weekly questionnaire (i.e. a PROM) via a dedicated application. The algorithm on which the operation of the device was based uses symptoms directly reported by the patient and generates alerts in the event of detection of a risk of recurrence or complication.

6.3 Clinical relevance of the effect

Regardless of the endpoint used, the Committee pays particular attention to the magnitude of the effect. Thus, the results of the clinical studies supporting an application are analysed with regard to the clinical relevance of the difference in effect obtained compared to the reference treatment. The relevance of the effect is assessed with respect to clinical practice and the available recommendations.

6.4 Equivalence

Equivalence can be claimed with respect to a product that has undergone one or more clinical studies. Consistency in the approach of the manufacturer making the equivalence claim is essential. In particular, the product to be assessed must be used in indications and conditions strictly similar to the product for which equivalence is being claimed. This approach is especially applicable to range expansions.

The European regulation on medical devices uses three different and cumulative dimensions to demonstrate such an equivalence:

- **technical:** the device is of similar design; it is used under similar conditions; it has similar specifications and properties, including physicochemical properties such as energy intensity, tensile strength, viscosity, surface properties, wavelength and algorithms; it uses similar installation methods, where applicable; it is subject to the same operating principles and critical performance requirements;
- **biological:** the device uses the same materials or substances in contact with the same human tissues or bodily fluids for the same type or same duration of contact, and release characteristics relating to similar substances, including degradation products and leachable substances;
- **clinical:** the device is used for the same clinical condition or same destination, including similar severity and stage of the disease, in the same part of the body, in a similar population, particularly with regard to age, anatomy and physiology; it has the same type of user; it has similar critical performance relevant to the expected clinical effect for a given destination.

The CNEDiMTS finds that this equivalence approach is often used by manufacturers for very many products, such as hip or knee prostheses, cardiac defibrillators, pacemakers…

If there are any differences, the manufacturer must be able to show that they do not impact the clinical, technical or biological dimension of the MD. The Committee takes into account and analyses the applicant's arguments, including that which enabled him to obtain CE marking or approval by the Food And Drug Administration via the 510(k) submission process. In addition, it would like to have all the data specifically relating to the new product, **including those concerning materiovigilance.**

The specific characteristics of the manufacturing, materials and use of an MD necessarily make them unique and potentially innovative.

Thus, a specific clinical assessment of the MD is expected if its equivalence with another MD has not already been demonstrated or if the manufacturer claims some additional action or efficacy over and above the reference strategy.

For example:

- in the treatment of Parkinson's disease, the Committee agreed to data from an earlier device in the range being extrapolated to the stimulator undergoing assessment in light of the technical arguments. Nevertheless, it declined to accept extrapolation of these data to another indication;
- in the case of a transanal irrigation device, the Committee concluded that the ACB was insufficient on the basis of the claim for technical equivalence with another device in the same category. Indeed, the technical data provided revealed differences whose repercussions had not been assessed either in terms of efficacy and safety or in terms of ease of use for the patient and caregivers.

6.5 Assessment of connected medical devices (CMDs)

The connected medical devices area is vast. Those assessed by the CNEDiMTS only account for a small proportion of connected medical devices (CMDs). These consist of those that are CE marked, for individual use - i.e., implanted or used by patients themselves - and are candidates for individual funding by the French health insurance system.

For example, the Committee has already assessed several types of CMD, for:

- medical remote monitoring purposes (e.g. an implantable cardiac defibrillator and remote medical monitoring);
- self-treatment or self-monitoring purposes (e.g. nerve stimulator to treat pain connected to a smartphone application allowing the patient to manage their treatment themselves);
- transmitting information with a view to treatment optimisation (e.g., an insulin pump combined with a sensor for the continuous measurement of interstitial glucose using the patient's electronic diary to optimise their treatment).

For these technologies, the regulatory assessment criteria for their reimbursement by the French health insurance system are the same. To be able to reach a decision in terms of ACB and CAV, the Committee expects demonstration of their benefit by clinical trials. While no methodological specificity as such was identified following the study[15] conducted in 2018 by HAS, the characteristics of CMDs can have an impact on the way the CNEDiMTS assesses the CMD. These MDs can have specific characteristics related, in particular, to their very rapid technological development, their interaction with other devices/objects/platforms, and the algorithms on which their operation is based. These specific features can have an impact on various aspects, such as the patient's health, quality of life or treatment organisation.

For the clinical assessment component as such, the first challenge for the company in question is to create a development programme that is consistent with the CMD's intended ultimate purpose. Hence, for all CMDs for individual use, the evaluation of their impact in terms of clinical benefit, acceptability or improvement of quality of life for users is necessary. Other impacts can also be looked for, especially in terms of access to treatment, standard of care and treatment organisation.

Since these are connected technologies potentially involving interactions between several products and users, the scope of the technological solution to be assessed must be questioned at an early stage by the manufacturer concerned in order to optimise its development plan: in theory it is the technological solution as a whole that should be considered, that is to say all elements collecting, processing and transmitting information from a remote site, taking treatment organisation into account.

For example, if a CMD is combined with remote medical monitoring, the evaluation will cover the "CMD and remote medical monitoring system" in its context of use.

15. Guide to the specific features of clinical evaluation of a connected medical device (CMD) in view of its application for reimbursement, HAS January 2019.

In some cases, especially where certain components are self-operating, evaluation of the effect specific to the CMD can be a challenge for developers.

Clinical trials supporting applications for registration on the LPPR are to be in keeping with the claims of the manufacturer or supplier of the technological solution.

7. Quality of life

It is the Committee's view that it is essential to measure the quality of life of patients and people with disabilities. This makes it possible to assess the impact of the condition and treatments from the patients' perspective.

Quality of life is considered a relevant criterion for the CNEDiMTS assessment. It is particularly used to assess patient compliance with respect to device use. A general HAS document contains the general principles of this criterion.

The main limitation encountered by the CNEDiMTS for taking quality of life into consideration in the submissions that it receives is the lack of data or weakness of the data collection methodology in respect of this endpoint in the clinical studies submitted. As such, the challenge is to collect, whenever this measure is deemed relevant, quality-of-life data in clinical studies supporting submissions made by companies for National Health Insurance cover of the medical devices marketed by these companies.

Therefore, the CNEDiMTS encourages companies to provide clinical data indicating this parameter, as often as possible, using generic scales (such as EQ-5D, SF-36, etc.) or specific scales that have been the subject of a thorough methodological validation. Examples of specific and generic scales identified in submissions made to the CNEDiMTS are given below.

Examples of satisfaction and quality of life scales

Generic scales	
European Quality of Life Instrument (EQ-5D)	5 dimensions (with 3 or 5 levels of severity for each dimension): pain/discomfort, anxiety/depression, mobility, self-care, usual activities
Medical outcome study short form-36 item health survey (SF36)	36 items covering 8 dimensions: physical functioning, physical role functioning, physical pain, general health perception, vitality, social role functioning, emotional role functioning, and mental health
Specific scales for a given disease/population	
Chronic obstructive pulmonary disease assessment test (CAT)	Chronic obstructive pulmonary disease (COPD) • 8 items on a 6-point scale (0 to 5) describing the impact of COPD on health status (coughing, sleep, etc.) Overall score out of 40 (Positive low score)
Disabilities of the Arm Shoulder and Hand (DASH)	Overall functional index of both upper limbs • 23 items covering regular daily activities assessed on a 5-point scale and 7 items covering symptom severity assessed on a 5-point scale Overall score out of 100 (Positive low score)
Specific scales for a given disease/population	
Diabetes quality of life measure (DQoL)	Diabetes • 46 items covering 5 dimensions: satisfaction with treatment and life in general, impact of diabetes on daily life, worries about social and vocational issues, worries about future effects of diabetes, and well-being. Each item is assessed on a scale of 0 to 5
Diabetes treatment satisfaction questionnaire (DTSQ)	Diabetes • 8 items assessing patient satisfaction on a scale of 0 to 6 Overall score out of 36 points
Intermittent Self-Catheterization Questionnaire (ISCQ)	Urinary self-catheterisation • 24 items covering 4 dimensions: ease of use, convenience, discreetness, well-being evaluated on a 5-point scale Overall score out of 100
Pshychosocial impact of assistive devices (PIADS)	People with disabilities • 26 items covering 3 dimensions: competence, adaptability and self-esteem. Each item is assessed on a 7-level ordinal scale
Quality of life in epilepsy inventory-form 31 (QOLIE-31-P)	Epilepsy (patients >18 years) • 38 items covering 7 dimensions: seizure worry, overall quality of life, emotional well-being, energy/fatigue, cognitive functioning, medication effects, social functioning, health status
Quality of life in epilepsy inventory for Adolescents (QOLIE-AD-48)	Epilepsy (adolescents of 11-18 years) • 48 items covering 8 dimensions: health perception, physical functioning, memory/concentration, school behaviour, social support, epilepsy impact, attitudes towards epilepsy, stigma, and an optional section for seizures Total score out of 100
St George's respiratory questionnaire french (SGRQ)	Chronic respiratory diseases • 50 items categorised under 3 dimensions: symptoms over the last 12 months (cough, sputum, shortness of breath, wheezing, chest trouble), disturbances to daily activity and impact on the patient's life (working, social, family life, etc.) Total score out of 100 (Positive low score)
Trinity Amputation and Prosthesis Experience Scales – revised (TAPES-R)	Amputee prosthesis users • 33 items categorised under 3 dimensions: psychosocial adjustment, activity restriction and satisfaction with the prosthesis
Wheelchair Outcome Measure (WhOM)	Mobility aid users • 2 parties : ❶ two series of questions aimed at expressing not more than five goals in respect of mobility aid intervention in the home and five goals outside the home ❷ three items relating to organic functions (comfort when seated, positioning, skin condition) Each item is assessed on a scale of 0 to 10

The general principles for the assessment of quality of life data by the CNEDiMTS aimed at helping companies optimise their development programmes, in relation to the quality of life measure, are described below and illustrated using various examples.

7.1 Quality of life: an assessment criterion

The relevance of the «quality of life» endpoint, in relation to other endpoints such as mortality or morbidity in particular, is dependent on the end-purpose of the medical device.

→ For devices intended to treat patients with a **life-threatening or health-impairing** disease, quality of life is generally presented as a secondary endpoint. In these situations, measuring patient perception nonetheless sheds further light which is helpful in assessing the benefit of the device.

In a number of situations, the Committee has considered that quality-of-life data supported the efficacy data available on objective endpoints.

For example,

- For a first inclusion application of a sacroiliac joint arthrodesis implant, in its assessment, the Committee took into consideration the quality of life of subjects after implantation of this device. This technology is intended for patients for whom conservative analgesic treatments are ineffective. No alternative is available. The clinical findings reported clinical efficacy data particularly in relation to pain (component of the primary endpoint defined by the success rate).

  Additionally, data assessing quality of life post-surgery by means of generic questionnaires **(EQ-5D and SF-36)** were available as secondary endpoints. Due to the improvement in the success rate (composite primary endpoint) associated with the improvement in quality of life, the actual clinical benefit provided by this implant was deemed to be sufficient. Its benefit was validated for the second-line treatment of pain in cases of sacroiliac joint dysfunction for patients for whom conservative treatment provided no pain relief.
- For a first inclusion application of an implantable endobronchial valve system, in its assessment, the Committee took into consideration the impact on patients' quality of life in view of the severity of severe and very severe emphysema. This device helps regulate air flow so as to improve pulmonary function in patients with hyperinflation associated with severe emphysema and/or to reduce air leaks.

  The comparative and observational clinical studies available reported efficacy data by way of primary endpoint in favour of the valves compared to the control group, particularly in terms of pulmonary capacity (percent change in FEV1) and survival (perioperative and postoperative mortality rate). Quality of life and functional capacity criteria were also assessed as secondary endpoints between inclusion and the end of follow-up. As such, an improvement in the **SGRQ** score and the **CAT** questionnaire with respect to inclusion was reported in the group treated with bronchial valves with differences deemed to be clinically significant.

  Based on all of the data provided (clinical and quality of life), the actual clinical benefit of the endobronchial valve system for a severe or very severe stage COPD patient population in France was deemed to be sufficient.

→ In some situations, the medical device is intended to **compensate for a deficiency**, and enable the subject to perform tasks and have a social role. This particularly applies to devices designed as prosthetic equipment for people with disabilities. In this situation, quality of life can be considered as a primary endpoint. The same applies for mobility aid devices. To illustrate this statement, two examples are cited below:

For example,

- For a new class of external myoelectric prosthetic hand, in its assessment, the committee took into consideration the quality of life of patients with acquired or congenital total hand amputations. Two specific questionnaires **(DASH and TAPES-R)** were used and completed by device users via a platform, within the framework of a specific device survey (unpublished data). These questionnaires were completed before fitting, immediately after fitting, and then at 3-month intervals. Patient satisfaction with the prosthesis was also surveyed. This section related to the cosmetic aspect of the prosthesis (colour, shape, appearance).

  Even though this study provides exploratory data with a low level of evidence, the committee was of the opinion that this prosthesis was of benefit for the compensatory strategy of the disability by enabling functional and cosmetic compensation for total hand amputation. In addition, the Committee made the renewal of this device conditional on the transmission of new specific follow-up data reporting the benefit of this prosthesis compared to other myoelectric prostheses with termino-terminal pinch only.
- For a request for inclusion on request for inclusion on reimbursement lists in respect of a protective coating for a tibial prosthesis, an intermediate report from an observational study based on the **PIADS** self-reported questionnaire was furnished to measure the impact of the use of assistive products on quality of life. As such, the committee considered the psychosocial impact for patients equipped with this coating as an assessment criterion and acknowledged a benefit of this device for amputees needing to use their prosthesis in the presence of water. Indeed, despite limitations, the initial data available demonstrate the positive impact of the use of this coating particularly in terms of quality of life despite the lack of clinical data and given the cosmetic need met by this type of coating.

Through these 2 examples, the committee established that, in the field of disability, the benefit of these devices in view of their added value may be assessed using patient quality-of-life data. In some situations and despite the lack of clinical studies assessing the impact on the subject's quality of life, the Committee also took into consideration the psychosocial impact (self-esteem, perception by others) as a criterion.

For example,

- Within the framework of the reassessment of external prosthetic upper limbs, the Committee approved the inclusion of custom-tinted cosmetic prosthetic upper limb coatings, focusing on the added value in terms of patient quality of life. As such, it assigned these devices a moderate clinical added value (CAV III) compared to standard tint cosmetic coatings.

A frequent question that arises for the collection of these data is that of the choice of scale. Validated generic scales (such as EQ5D and SF36) are routinely used in clinical trials and may be applied to various types of populations or conditions. On the other hand, specific scales target either a clearly defined condition or a specific population and offer superior impact measurement sensitivity.

7.2 Quality of life: an evaluation criterion

Of two technologies of recognised clinical benefit, and of identical clinical efficacy, one may offer other advantages (comfort, convenience, safety, etc.). In other words, where the actual clinical benefit is sufficient, the added value provided by a technology in terms of quality of life may be taken into consideration in the determination of the CAV with respect to the conventional therapeutic strategy or to other devices of the same class.

For example,

- For an intermittent urinary catheter, in its assessment, the committee took into consideration the quality of life of subjects performing self-catheterisation. A specific questionnaire **(ISC-Q)** in respect of this procedure and the use of these probes was used as the primary endpoint within the framework of a randomised clinical study. The catheter was deemed to be superior in terms of quality of life compared to conventional catheters and was assessed as such by the CNEDiMTS. A CAV rating of IV (minor) was assigned based on this criterion.
- A request for inclusion on reimbursement lists was submitted in respect of an interstitial flash glucose self-monitoring system for type 1 or 2 patients treated with intensive insulin therapy. The benefit of this system was demonstrated for the treatment of diabetes based on data from 2 randomised studies. The primary endpoint was a validated biological surrogate endpoint. For the determination of the CAV, the committee took into consideration the added value in terms of satisfaction and quality of life measured based on specific questionnaires **(DTsQ and DQOL)** reported by patients. As such, it was assigned a moderate improvement in clinical added value (CAV III) compared to glucose self-monitoring using a capillary glucometer alone.

7.3 Quality of life and post-registration study (renewal)

Post-registration studies are devised to address queries raised during the initial CNEDiMTS assessment. The data required are, in this case, generally based on a **real-life** medium- and long-term assessment for which it may be essential to seek to improve a subject's quality of life compared to their daily life.

By way of example:

- Within the framework of a second inclusion renewal application of an electric stair-climbing wheelchair, the committee took into consideration the increased self-care for subjects with functional tetraplegia. This increase in self-care was assessed using the specific **WhOM** questionnaire after one year of use, within the framework of a post-registration study commissioned by the Committee.
  Quality of life assessed using the generic **EQ-5D** scale was measured in this study as a secondary endpoint at different time intervals (D0-M1-M6 and M12). The benefit of the wheelchair was demonstrated in view of the expected increase in independent mobility. Failing a comparator and given the increase in self-care, the committee assigned this device a high clinical added value (CAV II).
- For a renewal inclusion application in respect of vagus nerve stimulation electrodes indicated for patients diagnosed with refractory epilepsy, in its assessment, the committee took patients' quality of life into consideration. These data are taken from a French registry, compiled in 15 centres and including prospective follow-up of over 100 patients (approximately 50% of patients implanted in France). Following this registry, the data in relation to the primary endpoint, i.e. reduction of over 50% in frequency of seizures during follow-up, are in favour of these electrodes. Quality of life (secondary endpoint) measured using the specific **QOLIE 31P** scale up to 24 months post-implantation reports an improvement for adults. The **QOLIE 48 AD** scale used for children indicates an improvement of the overall score at 18 months of follow-up. These data collected post-registration enabled the committee to confirm the benefit of the device; it assigned this device a sufficient actual clinical benefit (ACB) as a last-line treatment for invalidating, drug-resistant epilepsy.

In summary,

In the opinion of the CNEDiMTS, quality of life assessment represents a key factor in completing the evaluation of the medical added value of a technology. It may be of particular significance for subjects with chronic diseases or people with disabilities. This parameter reflects the patient's perspective in terms of perceived benefit, a key decision-making factor.

Therefore, companies are encouraged to incorporate an appropriate QOL scale, which has been the subject of a thorough validation in terms of clinical and/or economic approach, in the development programme in respect of their MDs.

This measure must play its rightful role depending on the technology. For the assessment of invasive technologies aimed at improving patient survival, quality of life is no substitute for morbi-mortality endpoints, but may shed further light on the matter. On the other hand, it has a vital role in assessing equipment technologies designed for people with disabilities, for example.

Each company may incorporate, into its development programme, a case-by-case analysis of the benefit of measuring the impact of the technology provided in terms of quality of life. To optimise this process, the company must address key questions, such as:

- → Which validated (generic or specific) measurement scale is best suited to obtaining their quality of life data in the context of use of the MD in question?
- → Which difference would, at first glance, be considered clinically relevant?
- → Is the questionnaire completed by the patient or not (self-reported questionnaire or questionnaire reported by another person depending on the patient's ability to respond, particularly in the case of cognitive disorders or young children)?
- → Should this criterion be the primary or secondary endpoint of the planned study depending on the mode of action of the product, the type of technology, the condition and the target indications?
- → Will collecting quality-of-life data be used to justify an evaluation of the devices in terms of IECB in view of the conventional strategy (this question is based on the planned study schedule: superiority/non-inferiority, ranking of quality of life as primary or secondary endpoint, etc.)?

8. Future prospects

In assembling the major principles of assessment together in this document, the CNEDiMTS has sought to provide guidance for companies. Moreover, whenever it has the opportunity to do so, the CNEDiMTS tries to shed a little more detailed light, by type of medical device, especially when a homogeneous product category is undergoing review. Relying on the contributions of specialist healthcare professionals in the implemented working groups set up, the Committee has sought to outline what the expectations in terms of clinical studies are in order to guide manufacturers on various evaluation parameters, including clinically relevant endpoints or expected clinical hindsight.

Some of these expectations that emerge in the course of individual assessments are presented, by way of example, in an appendix to this document.

9. Medico-technical dossier strong points

When putting together the medico-technical dossier on an MD, the CNEDiMTS recommends that the manufacturer thinks ahead about its strategy in terms of indications and of the ensuing clinical development programme.

Thinking ahead in this way will enable to:

- determine the indications to be claimed in a clear and precise manner;
- define the conditions of use: depending on the case, environment in which it is used (outpatient setting, healthcare establishment), technical facilities, operator expertise, professionals involved in follow-up, user training, etc.
- carry out a rigorous analysis of the reference therapeutic strategy so as to be able to propose a clinically relevant comparator;
- look ahead to the possibility of developing the MD;
- put together a correctly-proportioned clinical study in the right population so as to support the CAV level that the manufacturer would like to obtain for their product;
- substantiate the product's place in the therapeutic strategy;
- decide on the target population corresponding to the claimed indications.

The recommendation given to the manufacturer is to explain and substantiate every one of their choices. Namely, if a clinical study cannot be conducted, it shall be well-argued in the medico-technical dossier.

10. Support from HAS

10.1 Pre-submission appointments

Manufacturers, service providers or distributors of equipment for home use who wish to **obtain information about the technico-regulatory aspects necessary to prepare the medico-technical dossier** can request a pre-submission appointment (in French).

These meetings are arranged by HAS (on request) prior to the submission of a dossier in support of inclusion in the LPPR. **No CNEDiMTS members are present at these interviews**.

This type of appointment is not intended as a means of obtaining advice about the company's strategy. They are optional, non-binding, confidential and free of charge. A distinction should be drawn between these interviews and the early dialogues designed to give an insight into the methodological elements regarding the device development.

10.2 Early dialogues

With devices undergoing clinical development, HAS's Medical, Economic and Public Health Assessment Division (DEMESP) has offered the possibility of arranging early dialogues (in French). **No CNEDiMTS members are present at these interviews.**

The company or the developer may request an early dialogue on matters connected with the **clinical development of the healthcare product** concerned or a joint early dialogue also touching on issues relating to the performance of a medico-economic study, if an assessment of the product's effectiveness is due.

The early dialogues organised by HAS are optional, non-binding, confidential and free of charge.

The answers given by HAS departments to companies or developers during the course of these early dialogues do not in any way constitute an assessment and should not be taken as predicting the conclusions of any assessment by the Committees concerned, i.e. the CNEDiMTS and, where applicable, the CEESP, at the time of submission of the dossier.

Regulatory and documentary references

► Regulatory references

Decree No. 2004-1419 of 23 December 2004 concerning the acceptance of the products and services mentioned in Article L. 165-1 of the French Social Security Code and amending said Code.
www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000000425016

Decree No. 2009-1088 of 2 September 2009 concerning Committees mentioned in Articles R. 5212-7 of the Public Health Code and L. 165-1 of the French Social Security Code**.** www.legifrance.gouv.fr/jo_pdf.do?id=JORFTEXT000021017634

Decree No. 2015-1649 of 11 December 2015 concerning the terms and conditions for the inclusion of certain products and services in the list provided for in Article L. 165-1 of the French Social Security Code.
www.legifrance.gouv.fr/eli/decret/2015/12/11/AFSS1514541D/jo/texte

Article R. 165-2 of the French Social Security Code
www.legifrance.gouv.fr/affichCodeArticle.do?cidTexte=LEGITEXT000006073189&idArticle=LEGIARTI000006747700&dateTexte=&categorieLien=cid

Article R. 165-11-3 of the French Social Security Code
www.legifrance.gouv.fr/affichCodeArticle.do;jsessionid=DD9EC56159002070EE063E456DED95CB.tplgfr42s_1?idArticle=LEGIARTI000034630339&cidTexte=LEGITEXT000006073189&dateTexte=20171113

Order of 28 November 2013 laying down for 2013 the homogeneous healthcare product categories mentioned in Articles L. 165-11 and R. 165-49 of the French Social Security Code.
www.legifrance.gouv.fr/jo_pdf.do?id=JORFTEXT000028266835&oldAction=rechExpTexteJorf

Order of 14 December 2015 fixing the new inclusion periods applicable to the generic descriptions figuring in the list of products and services qualifying for reimbursement as per Article L. 165-1 of the French Social Security Code.
www.legifrance.gouv.fr/eli/arrete/2015/12/14/AFSS1529250A/jo

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. Official Journal of the European Union 1990.
http://eur-lex.europa.eu/legal-content/FR/TXT/?uri=celex%3A31990L0385

Council Directive 93/42/EEC of 14 June 1993 concerning medical devices Official Journal of the European Union 1993.
http://eur-lex.europa.eu/legal-content/FR/ALL/?uri=celex:31993L0042

Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 concerning medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. http://eur-lex.europa.eu/legal-content/FR/TXT/PDF/?uri=CELEX:32017R0745&rid=4

Regulation of the CNEDiMTS. Adopted on 13 March 2019.
www.has-sante.fr/portail/jcms/c_420290/fr/reglement-interieur-cnedimts

Composition de la CNEDiMTS. www.has-sante.fr/jcms/c_419486/fr/commission-nationale-d-evaluation-des-dispositifs-medicaux-et-des-technologies-de-sante

► Documentary references

MEDDEVs guidance documents. https://ec.europa.eu/growth/sectors/medical-devices/current-directives/guidance_fr [consulted on 11/15/2019].
MEDDEVs are guidance documents to assist stakeholders in implementing European directives relating to medical devices. Their purpose is to guide the various parties (manufacturers, competent authorities, Notified Bodies, etc.) in the uniform application of the provisions of Directives 90/385/EEC, 93/42/EEC and 98/79/EC within the European Union.

Practical guide to medical device assessment in France, HAS updated 2017 (2009 and 2013).
The purpose of this guide is to help companies better understand the rules of medical devices marketing and reimbursement. At the same time it presents the key stages in clinical development, with a focus on clinical monitoring.
www.has-sante.fr/portail/jcms/c_891379/fr/parcours-du-dispositif-medical-guide-pratique

Guide for submission of a dossier to the Medical Device and Health Technology Evaluation Committee (CNEDiMTS), HAS May 2015.
The purpose of this guide is to assist applicants in compiling an application dossier for inclusion/amendment of the inclusion conditions/inclusion renewal of a product or service under a brand name in the LPPR.
www.has-sante.fr/portail/jcms/c_419016/fr/guide-lppr-pour-le-depot-de-dossier-mise-a-jour-novembre-2016

Guide for submission of a dossier to the Medical Device and Health Technology Evaluation Committee (CNEDiMTS). Connected medical devices, HAS November 2017 (in French).
The objective of this guide is to help companies manufacturing or operating CMDs to anticipate, in their development strategy, the clinical requirements demanded by the CNEDiMTS to determine their usefulness with a view to their reimbursement by national solidarity.
www.has-sante.fr/portail/upload/docs/application/pdf/2017-11/guide_2017_dispositifs_medicaux_connectes_novembre_2017.pdf

Methodological specificities for the clinical assessment of a connected medical device (CMD). Guide preparation report concerning clinical assessment specificities with a view to access to reimbursement, HAS January 2019 (in French).
This document incorporates an analysis of the literature, data from other assessment agencies, CMD dossiers already assessed by the CNEDiMTS, study regimens identified on the basis of clinical trial data, consultation of the various stakeholders, as well as the position of a multidisciplinary working group mobilised around this theme.
www.has-sante.fr/portail/upload/docs/application/pdf/2019-02/rapport_methodologiques_devaluation_clinique_dun_dmc.pdf

Guide to the specific features of clinical evaluation of a connected medical device (CMD) in view of its application for reimbursement, HAS January 2019.
The objective of this guide is to help companies manufacturing or operating CMDs to include clinical trials for determining their usefulness in view of their reimbursement by national solidarity in their development strategy.
www.has-sante.fr/upload/docs/application/pdf/2019-04/guide_to_the_specific_feactures_of_clinical_evaluation_of_connected_medical_device_cmd_in_viewof_its_application_for_reimbur.pdf

Methodological choices for the clinical development of medical devices, HAS October 2013.
The purpose of this guide is to provide an update on the methods that can be used to assess the clinical benefit of a new MD or a new health technology and to describe possible study designs for assessing clinical quality.
www.has-sante.fr/portail/jcms/c_1696374/fr/guide-methodologique-pour-le-developpement-clinique-des-dispositifs-medicaux

Choices in methods for economic evaluation, HAS October 2012.
This guide presents the principles and methods adopted by HAS to fulfil its mission of medical and economic assessment of health interventions.
www.has-sante.fr/portail/jcms/c_1120708/fr/guide-choix-methodologiques-pour-l-evaluation-economique-a-la-has

Post-inclusion studies on health technologies (medicinal products, medical devices and procedures) – Principles and methods, HAS November 2011 (in French).

The purpose of this guide is to provide practical guidance on the methodological aspects of post-inclusion studies so that HAS can obtain results used when re-listing or performing an early reassessment of the products concerned..

www.has-sante.fr/portail/jcms/c_1191962/fr/les-etudes-post-inscription-sur-les-technologies-de-sante-medicaments-dispositifs-medicaux-et-actes

Early dialogue with HAS about a medical device undergoing clinical development, updated November 2017 (December 2013) (in French).

The purpose of this document is to present the practical procedures for submission and the conduct of early dialogues, arranged at the manufacturer's request.

www.has-sante.fr/portail/jcms/c_2058516/fr/modalites-de-soumission-et-deroulement-des-rencontres-precoces-pour-un-dispositif-medical-actualisation-novembre-2017

Procedure for applying for a pre-submission appointment and sequence of events, HAS update November 2017 (in French).

The purpose of this document is to explain to prospective applicants the technical and regulatory aspects with which they need to be familiar when preparing or finalising their dossier..

www.has-sante.fr/portail/jcms/c_2640062/fr/modalites-de-demande-et-du-deroulement-d-un-rendez-vous-pre-depot-actualisation-novembre-2017

Questionnaire eliciting the point of view of patients and users for the assessment of a medical device (in French). HAS August 2018 (in French).

www.has-sante.fr/portail/jcms/c_2666630/fr/contribution-des-associations-de-patients-et-d-usagers-aux-evaluations-de-medicaments-et-dispositifs-medicaux

Contribution of patients' and users' associations to the assessment of medical devices. Guide for patients' and users' associations". HAS – November 2017.

www.has-sante.fr/portail/upload/docs/application/pdf/2016-11/contribution_asso_patients_guide_v3.pdf

Appendix

The propositions below fall within the scope of the guiding principles of CNEDiMTS's overall strategy for the assessment of MDs and other healthcare products.

Depending on the area under consideration, the guidelines drawn up can be very broad, while others are very specific and relatively detailed in the type of data presented.

These recommendations, listed by medical speciality and MD category, provide the Committee with a basis for discussion each time there is an application for reimbursement. They are not opposable. These guidelines are by nature evolving; they cannot be fixed in time and will therefore, if necessary, be updated over time.

► Cardiology

Reference framework relative to transcatheter aortic valve implantation (TAVI) devices. January 2019
www.has-sante.fr/portail/jcms/c_2901699/fr/bioprotheses-valvulaires-aortiques-implantees-par-voie-transcatheter-tavi-referentiel

Mechanically-assisted circulatory support devices (MCSDs, excluding light devices) – January 2008 (in French)
www.has-sante.fr/portail/jcms/c_659032/fr/evaluation-de-l-assistance-circulatoire-mecanique-hors-dispositifs-legers

In addition to the recommendations that were made when revising this category of MD, the Committee recommends that data representative of the French situation be available when including a new mechanically-assisted circulatory support device; i.e., a prospective study that includes a significant proportion of patients matching the INTERMACS 2 and 3 profile and potentially candidates for transplantation, representative of the French population, aimed at assessing the safety and efficacy of the device in the medium term (6 months).

The Committee can take into account the level of the scientific publications and the requests for comparative studies from other HTAs.

Drug-eluting stents – July 2009
www.has-sante.fr/portail/jcms/c_867966/fr/evaluation-des-endoprotheses-coronaires-a-liberation-de-principe-actif

► Vascular surgery

Bypass prostheses – April 2013
www.has-sante.fr/portail/jcms/c_1528391/fr/evaluation-des-implants-de-pontage

► Dermatology

Primary dressings for the treatment of chronic wounds – December 2013 (in French)
A methodological guide has been drawn up aimed at providing support for the clinical development of dressings. It includes recommendations on clinical studies, the populations concerned, the type of investigators, the judgement criteria, the data on the improvement of care, the comparators, standard care, the associated treatments.
www.has-sante.fr/portail/jcms/c_1713137/fr/choix-methodologiques-pour-le-developpement-clinique-des-pansements

Prevention of bedsores – December 2009 (in French)
www.has-sante.fr/portail/jcms/c_901641/fr/dispositifs-medicaux-d-aide-a-la-prevention-et-d-aide-au-traitement-des-escarres-avis-de-projet-de-nomenclature-cahier-des-charges-techniques-cnedimts-du-22-decembre-2009-1684

► Neurosurgery

Implantable spinal-cord neurostimulators – March 2014
www.has-sante.fr/portail/jcms/c_1351767/fr/evaluation-des-systemes-implantables-de-neurostimulation-medullaire

► Ophthalmology

Tear substitutes

During its recent assessments, the Committee put forward the following recommendations for conducting studies:

- maximum possible blinding (if double-blinding is impossible, then the assessor should be independent);
- duration of treatment and of follow-up should be at least 3 months;
- comparator: physiological saline or reference product;
- primary end-point identified and adapted to the severity of the dry eye.

► ENT-Pulmonology

Home oxygen therapy – April 2012 (in French)

www.has-sante.fr/portail/jcms/c_1265304/fr/evaluation-des-dispositifs-medicaux-et-prestations-associees-pour-l-oxygenotherapie-a-domicile

► Orthopaedics

Cements with or without antibiotics for fixing joint implants – December 2016 (in French)

www.has-sante.fr/portail/jcms/c_2607290/fr/ciments-avec-ou-sans-antibiotiques-pour-la-fixation-des-implants-articulaires

Medical compression/contention for individual use. Used in orthopaedics, rheumatology, traumatology – October 2012

www.has-sante.fr/portail/jcms/c_1318289/fr/dispositifs-de-compression/contention-medicale-a-usage-individuel-utilisation-en-orthopedie/rhumatologie/traumatologie

Elbow joint implants – September 2012

www.has-sante.fr/portail/jcms/c_1311405/fr/evaluation-des-implants-articulaires-de-coude

Shoulder joint implants – March 2014

www.has-sante.fr/portail/jcms/c_1340726/fr/implants-articulaires-d-epaule

Knee joint implants – November 2012 (in French)

www.has-sante.fr/portail/jcms/c_1345397/fr/implants-articulaires-de-genou

Hip joint implants - September 2007

The CNEDiMTS has formulated its expectations in terms of clinical studies for the following categories:

- dual mobility acetabular cups;
- total hip prostheses with acetabular component in highly cross-linked polyethylene;
- modular neck femoral stems.

www.has-sante.fr/portail/jcms/c_674535/fr/evaluation-des-protheses-de-hanche

November 2014

www.has-sante.fr/portail/jcms/c_2006405/fr/evaluation-des-protheses-de-hanche

Spine implants – March 2013

www.has-sante.fr/portail/jcms/c_1517325/fr/evaluation-des-implants-du-rachis-cage-intersomatique-cale-metallique-interepineuse-coussinet-implant-d-appui-sacre

External upper-limb prostheses – June 2010 (in French)

www.has-sante.fr/portail/jcms/c_999782/fr/evaluation-des-protheses-externes-de-membre-superieur

Bone substitutes – May 2013

www.has-sante.fr/portail/jcms/c_1225008/fr/evaluation-des-substituts-osseux

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