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GUIDE

Pathway of medical devices in France

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Preface

Regardless of its missions (assessment of health technologies, definition of good professional practices, certification, etc.) and the audiences it addresses (public authorities, healthcare professionals, manufacturers, etc.), Haute Autorité de santé (HAS) [the French National Authority for Health] is at the service of citizens, users of the health system and patients. Ultimately, all actions undertaken by HAS are guided by the usefulness for those who receive care.

The CNEDiMTS is therefore particularly committed to ensuring that patients and people with disabilities can benefit as quickly as possible from clinical and technological advances in Medical Devices.

In its task of assessing the relevance of reimbursement of a Medical Device (MD) by the community, the CNEDiMTS focuses on promoting access of patients and healthcare professionals to useful and safe innovation.

In fact, the CNEDiMTS feels it is important that manufacturers, researchers and healthcare professionals working on a project know the pathway of MDs in France. While the CE marking of an MD allows its free circulation in Europe, the devices reimbursed by the community are specific to each member state.

By raising awareness of medical device pathway in France among stakeholders, the CNEDiMTS wishes to be part of this constructive dynamic to ensure rapid access to incremental advances in the field of medical devices and to innovative medical devices.

If all of the different steps in the MD pathway are known from the start of clinical development of the MD, time and resources will be saved for the benefit of all, and especially patients and people with disabilities. That is the objective of this document.

Happy reading

I. Adenot

Chair, CNEDiMTS

Introduction

Facilitating access to medical devices (MDs) aimed primarily at improving quality of life for patients or people with disabilities is a major concern for HAS. In this context, HAS has implemented support measures for manufacturers, such as early dialogues and pre-submission meetings. This guide, which aims to help manufacturers improve their application submissions, is also part of these measures.

In fact, a lack of clarity regarding the pathway to be followed in France to make an MD available to patients is a complaint that is sometimes expressed.

The continuous evolution of the industry means information needs to be updated regularly, and so this is the fourth update of the MD practical guide by HAS. This update comes at a time when European Regulation 2017/745 (1), implemented on 26 May 2017, was meant to have become mandatory on 26 May 2020. In order to prioritize the battle against the COVID-19 pandemic, the European Parliament and Council adopted an amendment¹ delaying its date of application by a year, until 26 May 2021.

This European regulation replaces the directives on MDs [Directive 93/42/EEC (2)] and AIMDs (active implantable medical devices) [Directive 90/385/EEC (3)]. It should be noted that Regulation (EU) 2017/745 states the clinical requirements that manufacturers need to meet to obtain CE marking: demonstration of conformity with general safety and performance requirements includes a clinical assessment.

This guide does not cover in vitro diagnostic MDs (IVDMDs), which are governed by Regulation (EU) 2017/746.

All requirements concerning clinical assessments, those of the European regulation and those for an application for reimbursement by the national solidarity scheme, should be taken into consideration from the beginning of clinical development to save time and resources and to provide all the necessary items for the successive assessments of the medical device.

This guide follows the chronological pathway of an MD development:

- ➔ assessment for marketing;
- ➔ assessment for reimbursement and pricing principles in France;
- ➔ a focus on the challenges of clinical development with its key concepts prior to the application for reimbursement;
- ➔ clinical follow-up after marketing and after reimbursement.

This guide aims to describe the market access conditions as defined in Regulation (EU) 2017/745. However, this guide only covers the parts of the regulation explaining the continuum of assessment in the life cycle of an MD and is not a guide for application of Regulation (EU) 2017/745.

¹ Regulation (EU) 2020/561 delaying the date of application of regulation (EU) 2017/745

1. Marketing

Before undertaking development of a product, it is important to precisely determine its status, based on the available regulatory definitions (e.g. cosmetic, medicinal product, medical device (MD)², tissues or cells of animal origin, etc.). This status will determine the regulations with which the product must comply.

Regulation (EU) 2017/745 (1), which definitively replaces directives 93/42/EEC (2) and 90/385/EEC (3) in 2021, defines a medical device 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:

- ➔ diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- ➔ diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,
- ➔ investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,
- ➔ providing information by means of *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.”

This definition highlights the significant heterogeneity in the MD sector, including products as diverse as, for example, dressings, prescription glasses, cardiac pacemakers or medical imaging devices.

In addition to MDs, the scope of application of the regulation covers their accessories and products without a medical purpose, namely for aesthetic purposes, listed in Annex XVI of the regulation.

Note:

Application of Regulation (EU) 2017/745 became mandatory on 26 May 2021, on which date Directives 93/42/EEC and 90/385/EEC were repealed with the exception of a few provisions.

Certificates issued under Directives 93/42/EEC and 90/385/EEC by a notified body will remain valid until their expiration date, at most 5 years after issue and no later than 27 May 2024. The devices may continue to be marketed or used until 27 May 2025.

² To simplify reading of this guide, the term MD includes active implantable medical devices (AIMD)

1.1. CE marking

To be marketed in the European Union, an MD must **comply with the general safety and performance requirements** applicable to it. These requirements depend on different criteria, including the intended use of the MD and its risk class. They are stated in Annex I of Regulation (EU) 2017/745 for MDs and active implantable MDs (AIMDs). *In vitro* diagnostic MDs (IVDMDs) are covered by Regulation (EU) 2017/746 (4); elements specific to this regulation will not be covered in this guide.

It is up to a **notified body**³ (NB) **chosen by the manufacturer** to carry out the assessment⁴ of this conformity (except for certain class I MDs, where this responsibility falls on the manufacturer). Once conformity has been demonstrated, manufacturers may establish the EU declaration of conformity and affix the CE marking of conformity.

MDs can be marketed only if the **CE marking has previously been affixed under the responsibility of the manufacturer**⁵ (does not apply to MDs for clinical investigations or “custom-made” MDs) and the manufacturer has drawn up the EU declaration of conformity⁶.

[The list of notified bodies in accordance with regulation \(EU\) 2017/745](#) on MDs is available on the European Commission website (5).

Note:

Each EU country has one or more competent authorities for the safety of health products. In France, the French National Agency for Medicines and Health Products (ANSM) is in charge of device market surveillance and is responsible for designation and monitoring of the notified bodies within its territory. Multiple NBs may be designated in the same country; these NBs may have specific areas of competence.

A manufacturer is free to choose the NB that it wishes, provided that the MD to be assessed falls within the area of competence of the body.

1.1.1. Device risk class

Determining the risk class of an MD is essential. It will determine the steps to take to obtain CE marking, in particular the choice of assessment procedure and the clinical requirements necessary.

MDs are divided into four classes: class I, class IIa, class IIb and class III⁷ based on their **level of risk** (Table 1).

³ Articles 35 to 50 of European Regulation 2017/745

⁴ Articles 52 to 55 of European Regulation 2017/745

⁵ Articles 20 to 56 of European Regulation 2017/745

⁶ Article 19 of European Regulation 2017/745

⁷ Classification rules set out in annex VIII of European Regulation 2017/745.

Table 1. Classification of medical devices based on risk⁸

Class	Risk level
Class I	Low level of risk
Class IIa	Medium level of risk
Class IIb	High potential of risk
Class III	Very high potential of risk

The rules for determining the class of the MD are listed in Annex VIII of Regulation (EU) 2017/745 and, in particular, take into account the duration of use, the invasive or non-invasive nature and the type of invasiveness, the possibility (or not) of reuse, the therapeutic or diagnostic aim, and the part of the body concerned.

Non-sterile class I MDs or those without a measuring function are self-certified by the manufacturer. For other devices, the intervention of a notified body is mandatory for the CE certification process.

Classification rules

The number of rules and classification criteria was expanded (22 rules and 80 criteria instead of 18 rules and 56 criteria). For example, software is the subject of a classification rule, based on its estimated level of risk.

1.1.2. Device identification

The identification and traceability of MDs are reinforced through the creation of a Unique Device Identification system (UDI system). Each MD will have a unique identifier, if applicable, for each packaging. The UDI is composed of:

- ➔ a unique UDI device identifier (UDI-DI) specific to a device model
- ➔ a UDI production identifier (UDI-PI) specific to a medical device production unit

Note:

The affixing of UDI carriers on the label and on all higher packaging levels, will come into effect on different dates, based on the risk class:

- Implantable and class III MDs: 26 May 2021
- Classes IIa and IIb: 26 May 2023
- Class I: 26 May 2025
- For reusable MDs, the UDI support must be affixed on the device itself.

Manufacturers are responsible for the initial introduction and updating of identification data and other data elements concerning the device in the UDI database⁹.

⁸ Article 51 of European Regulation 2017/745

⁹ Annex III, Part C - Article 5.2 of European Regulation 2017/745

1.1.3. Choice of the assessment procedure

The assessment procedures to obtain CE marking vary **based on the risk class and characteristics specific to** certain devices. These procedures include both an audit of the manufacturer's quality management system (QMS) (except for some class I devices) and an inspection of technical documentation (TD) of the devices by the NB (see Figure 1).

Two QMS assessment methods (QMS1 and QMS2) are possible. Article 52 of Regulation (EU) 2017/745 specifies these procedures in detail.

	I	I*	IIa	IIb	IIb [‡]	III
Technical Documentation (TD)	Annexes II and III					
TD assessment	NA		Annexes IX (chap.2) on at least one MD in the same category	Annexes IX (chap.2) on all MDs in the same category		
QMS 1 or QMS 2	NA	Annexes IX (certain sections)	Annexes IX (chap.1 and 3) on at least one MD in the same category			
	NA	Annexes XI (part A)	Annexes XI (sections 10 or 18)	Annexes X and XI		

This figure covers medical device classes I to III, other than custom-made devices or devices used in investigations.
QMS: Quality management system.
I*: Sterile class I medical device, with a measuring function or reusable surgical MD.
IIb[‡]: Class IIb device not on the list of article 52.4 of Regulation EC 2017/745.
NA: not applicable

Figure 1. Procedures for assessment of conformity based on the class of medical device

For MDs that are not the subject of harmonised standards or for which the existing standards are insufficient or in case of public health concern, the European Commission may define common specifications for these devices. These specifications will be able to define supplemental requirements in terms of safety, performance, technical documentation, clinical assessment, post-marketing clinical follow-up (PMCF) or clinical investigations¹⁰.

Note:

The quality management system includes **clinical assessment and post-marketing clinical follow-up** (PMCF). A clinical assessment plan must be established prior to the clinical assessment (see Annex XIV-1a of Regulation (EU) 2017/745).

¹⁰ Article 9 of European Regulation 2017/745

1.1.4. Clinical requirements for CE marking

Regulation (EU) 2017/745 reinforces the requirements for clinical assessment. In particular, it includes the **phase of collection of clinical data** already available in the literature, as well as the **implementation of any clinical investigations** (also called clinical trials) that may be necessary. In a limited number of situations, it is possible to appeal to the notion of “equivalence”¹¹.

Clinical assessment

The manufacturer is responsible for planning, performing and documenting a clinical assessment. It **specifies and justifies the level of clinical evidence necessary** to demonstrate conformity with the safety and performance requirements of the regulation, which depend on the characteristics of the device and its intended purpose.

The clinical assessment of the MD must follow a defined procedure methodologically based on **critical assessment of the relevant scientific literature, the results of all available clinical investigations** as well as the consideration of alternative treatment options currently available.

Regulation (EU) 2017/745 requires the manufacturer to have a **post-marketing surveillance plan** so that knowledge about the MD can be updated throughout its life cycle. This surveillance plan must in particular include a **post-marketing clinical follow-up (PMCF)** which is a continuous process that updates the clinical assessment through which the manufacturer proactively collects and assesses clinical data (already mandatory since March 2010).

For some MDs (see below), it will be necessary to conduct a clinical investigation to obtain CE marking.

Clinical investigation

Regulation (EU) 2017/745 specifies that, in the case of implantable devices and class III devices, **clinical investigations (CIs) must be conducted, unless the three following criteria are met:**

- ➔ the device has been designed by modifying a device already marketed by the same manufacturer;
- ➔ equivalence with this device has been demonstrated and approved by the NB;
- ➔ the clinical assessment of the currently marketed device is sufficient to demonstrate conformity of the modified device with the relevant safety and performance requirements.

Additional exceptions:

The manufacturer of an MD demonstrated to be **equivalent** to an already marketed device **not manufactured by them**, may also rely on the 3 criteria mentioned above in order not to perform a clinical investigation, provided that the following conditions are also met:

- the two manufacturers have a contract in place that explicitly allows the manufacturer of the second device full access to the technical documentation on an ongoing basis, and
- the original clinical assessment has been performed in compliance with the requirements of this Regulation, and the manufacturer of the second device provides clear evidence thereof to the notified body.

¹¹ Article 61 of European Regulation 2017/745

Note: While clinical investigations implemented to obtain CE marking are primarily conducted to demonstrate the performance and safety of a device, expected clinical investigations for reimbursement and pricing must also answer the question of the role of the device in the available arsenal in France (therapeutic, diagnostic or compensation for disability). To save time, it is therefore important for a manufacturer to anticipate in their clinical development programme, before marketing, expectations for:

- obtaining CE marking;
- access to reimbursement, if applicable.

Notion of equivalence

It is important to properly understand the notion of **device equivalent** to another device. Two devices are considered equivalent if it is possible to simultaneously verify¹²:

- ➔ **clinical** equivalence (intended purpose, site in the body, population, etc.);
- ➔ **technical** equivalence (specifications, properties, set-up, etc.);
- ➔ **biological** equivalence (biocompatibility, tissues, materials, etc.).

The characteristics listed above must be similar to the extent that there would be no clinically significant difference in the safety and clinical performance of the device. Considerations of equivalence are based on proper scientific justification. It must be clearly demonstrated that manufacturers have sufficient access to the data relating to devices that they consider equivalent in order to justify their claims of equivalence.

Note:

Requirements related to clinical investigations are specified via Article 62 and Annex XV. Other than the exceptions listed above, implantable MDs and class III MDs must undergo clinical investigations in order to obtain CE marking.

Obligations concerning equivalence of MDs are reinforced.

For all class III devices and for class IIb devices intended to administer/eliminate a medicinal product into or from the body, the manufacturer may, before carrying out their clinical assessment and/or clinical investigation, consult a group of European experts.

Summary of device characteristics

The information to be included in the summary of device characteristics (SDC) is specified in Article R.5211-66-1 of the French Public Health Code (elements of identification, of use, of description and of clinical assessment of the MD).

The same obligation features in Article 32 of Regulation (EU) 2017/745.

Article 32 of Regulation (EU) 2017/745 establishes that manufacturers produce a summary of safety and clinical performance (SSCP) for implantable devices and for class III devices. The SSCP will be

¹² Annex XIV-A-3 of European regulation 2017/745

validated by the NB. It is intended for the user/patient of the device and will be made available to the public via Eudamed.

Note:

In the regulation, the SSCP is a component of the technical dossier sent to the NB. It will be intended to be communicated to the public by Eudamed (European Database on Medical Devices); thus, it will be written so as to be comprehensible by patients.

1.2. ANSM missions

The French National Agency for Medicines and Health Products (ANSM) performs an assessment of the benefits and risks related to the use of the medical devices, in particular. It monitors the risk related to these products and performs reassessments of the benefits and risks. It is involved in certain steps prior to and after the CE marking, but does not directly take part in the review of the CE marking application (which falls within the scope of expertise of the notified bodies).

1.2.1. Clinical studies

The ANSM is involved during the clinical studies phase in France through the assessment and authorisation of research involving human subjects.

Regulation (EU) 2017/745 will bring the rules into line with the rules that will come into effect in application of the European regulation on clinical trials of medicinal products (6).

1.2.2. Notified bodies

The ANSM, as a designating authority, is in charge of **assessing, designating and monitoring** notified bodies (NB) in France. To date, only the Group for Assessment of Medical Devices (G-Med) of the French National Laboratory for Metrology and Testing in the Medical Health Field (LNE/G-Med) is a notified body in France for regulation (EU) 2017/745. For more information [the list of notified bodies in accordance with regulation \(EU\) 2017/745](#) on MDs is available on the European Commission website (5). A manufacturer is free to choose the NB that it wishes from this list, irrespective of the Member State in which the MD will ultimately be marketed.

1.2.3. Market surveillance

The ANSM is the competent authority responsible for market surveillance for medical devices. To this effect, it can, in particular, monitor technical documentation, carry out inspections (announced and spot) and pronounce sanitary policy measures for compliance or prohibition of marketing.

More information is available on the [ANSM website](#).

Medical devices (other than custom-made MDs) placed on the market are subject to prior registration on the EUDAMED database, as scheduled by regulation (EU) 2017/745.

The registration procedure schedules that:

- ➔ manufacturers, authorisation holders and importers must register in the Eudamed system if they are not already registered. This information will then be updated in accordance with the provisions scheduled by regulation (EU) 2017/745.
- ➔ the manufacturer allocates an UDI-DI to the device and transmits it to the UDI database. The manufacturer registers the information stipulated by the regulation in Eudamed - or verifies it if it has already done so - and ensures this information is subsequently kept up to date.

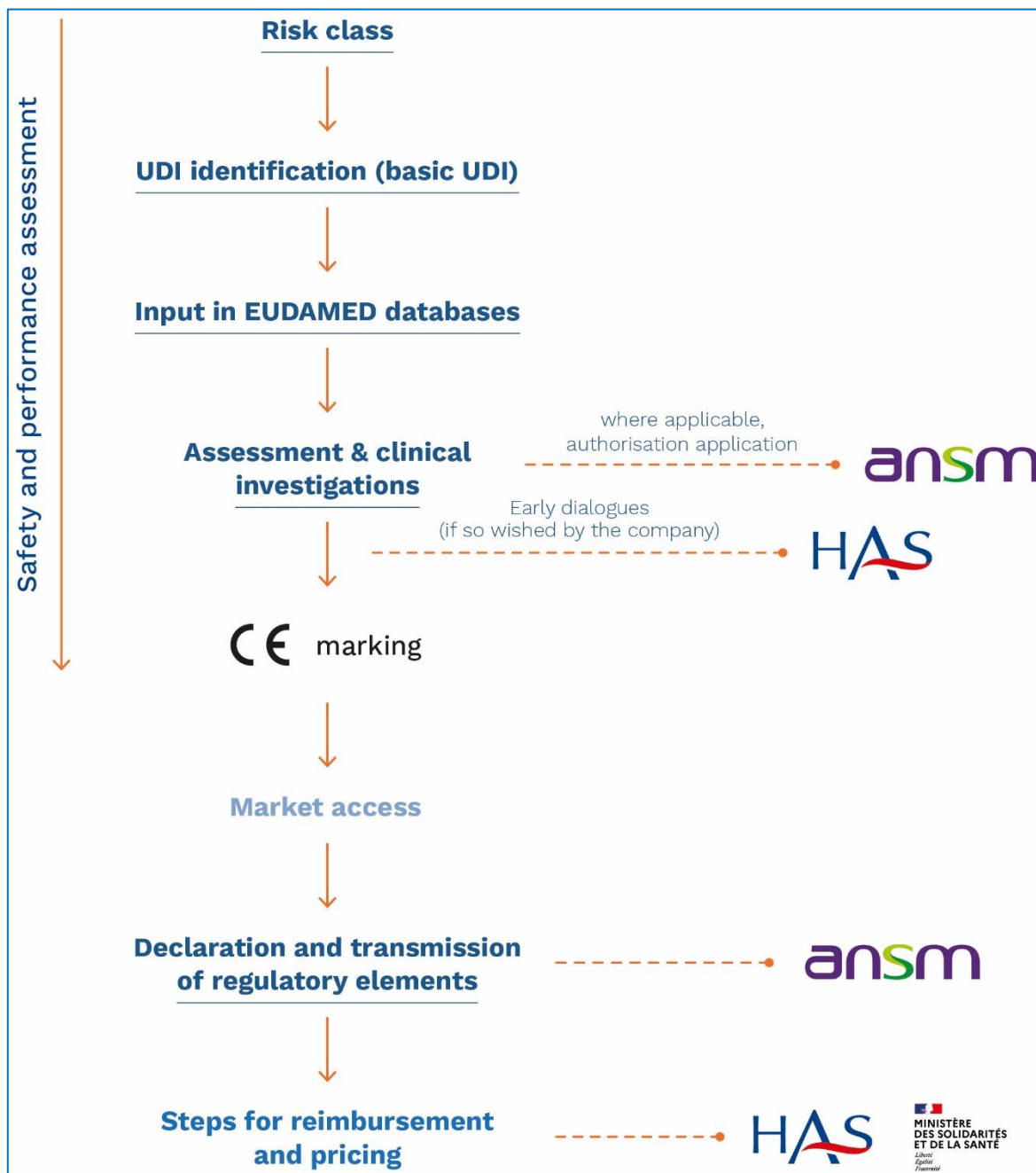


Figure 2. Simplified steps to market access*

*The modifications scheduled by regulation (EU) 2017/745 will be implemented progressively and their application became compulsory from 26 May 2021.

2. Steps for reimbursement and pricing in France

2.1. Introduction

After obtaining CE marking, the MD can be marketed on the European market. This step does not imply its automatic reimbursement by the national solidarity scheme of a member state, in this case France. To this end, additional procedures must be implemented with each member state.

For reimbursement by the national solidarity scheme, data related to the clinical benefit and role in the therapeutic strategy are expected.

The reimbursement methods determine the assessment circuit for reimbursement.

Information provided about the application for reimbursement and pricing described apply to MDs, AIMDs and IVDMDs.

2.2. Different reimbursement arrangements

There are different reimbursement arrangements for medical devices and they depend, among other factors, on the conditions of use of the device.

In a private practice setting, MDs for individual use at the patient's home (outside of any context of hospitalisation) may be reimbursed through their inclusion in the LPPR, while those related to a procedure performed by a healthcare professional are included in the tariff of the procedure. When used for or during the performance of a professional procedure, MDs used outside of any context of hospitalisation are not subject to individualised pricing; they are valued through the procedure. The latter is included in the joint classification of medical procedures (CCAM).

MDs used at healthcare organisations are primarily reimbursed through diagnosis related groups (DRGs), except for certain MDs reimbursed outside of DRGs (they are in this case included in the list of products and services reimbursed in addition to hospital service, more commonly known as the "[additional list](#)"¹³).

¹³ Article L162-22-7.

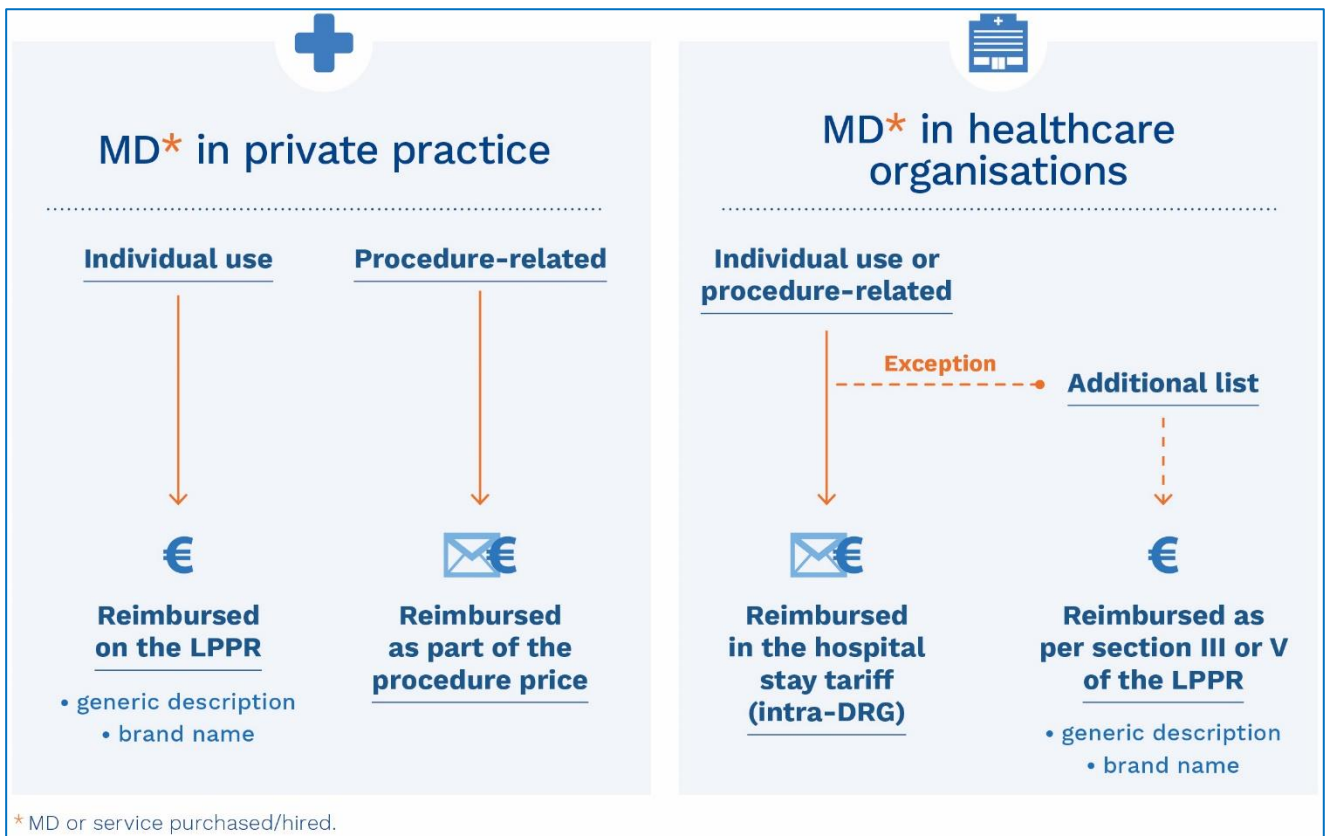


Figure 3. Reimbursement arrangements for medical devices: private practice/healthcare organisation

2.2.1. Reimbursement by Diagnosis-Related Group (DRG)

This reimbursement arrangement only involves healthcare organisations. Since 2005, the latter have been financed within the framework “*Tarifification à l’activité*” (T2A), a fee-for-service pricing system in which expenditures on most MDs are directly integrated into hospital service. Thus, in 2017, MDs such as lens implants and osteosynthesis implants were included in the cost of diagnosis-related groups (DRGs).

For most MDs, no specific assessment is carried out for reimbursement of devices via DRGs. It is up to the Health Care Organisation Medical Committees (CMEs) of public healthcare organisations or organisation medical conferences of private healthcare organisations to create the list of sterile devices that the organisation plans to use¹⁴. The tariff for the MD is then negotiated directly with each purchaser or hospital purchasing group.

“Positive” intra-DRG list

Nevertheless, HAS is asked to perform a specific assessment of certain categories of MDs. The law of 2011, reinforcing the safety of medicines and health products, also introduced the possibility of inclusion of certain homogeneous categories of MDs on a positive list by the Minister of Health. This provision determines not only the reimbursement for these products, but also their purchase, supply and use by all healthcare organisations.

¹⁴ Article R6111-10 of the French Public Health Code

In application of this provision, two decrees from the Minister of Health¹⁵ have been published. They concern 9 MD categories.

Table 2. Homogeneous categories of health products submitted to the positive list by decree¹⁶

Terms	Method of inclusion
Intracranial stents used in angioplasty of atheromatous stenosis	Brand name
Conventional implantable cardiac defibrillators: with endocardial lead (single-, dual-, and triple-chamber)	Generic description
Implantable cardiac defibrillators: without endocardial lead (single-, dual-, and triple-chamber)	Brand name
Biological surgical heart valves	Brand name
Implantable devices for the treatment of pelvic organ prolapse by the vaginal route	Brand name
Implantable devices for the treatment of urinary incontinence by the vaginal route	Brand name
Devices for the treatment of pelvic organ prolapse by the abdominal route	Brand name
Intracranial flow diverter stents	Brand name
Thrombectomy devices	Brand name

If the device belongs to one of these categories, manufacturers (or their representatives) or distributors must submit an application for inclusion on this intra-DRG list to the National Committee for the Evaluation of Medical Devices and Health Technologies (CNEDiMTS). These MDs must then meet, considering their invasiveness or the risks they may pose to human health, at least one of the following requirements¹⁷:

- ➔ validation of their clinical effectiveness,
- ➔ definition of particular technical specifications,
- ➔ assessment of their efficiency compared with available therapeutic alternatives.

This inclusion is given for a fixed term, which is renewable, and may be subject to conditions of prescription and use or subject to the completion, by the manufacturers (or their authorised representative) or distributors, of additional studies requested on the products concerned.¹⁷

¹⁵ Order of 29 January 2016 amending the 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

¹⁶ Order of 29 January 2016 amending the 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

¹⁷ Article L165-11 of the French Social Security Code

2.2.2. Reimbursement through the LPPR

The LPPR¹⁸ is the list of products and services qualifying for reimbursement by the French national health insurance scheme. It allows reimbursement of MDs for individual use in a private practice setting or of some devices, reimbursed outside of DRGs, in healthcare organisations (see the box below about the “additional” list).

This list **relates to the medical device itself** (e.g. a hearing aid) and also the service necessary for its proper use (e.g. service of a hearing aid specialist to adjust and set the hearing aid for a patient). This complementarity between the device and the service is one of the characteristics of the LPPR.

It is divided into five parts:

- ➔ **Section I:** MDs for treatments at home, living aids, dietary products and dressings;
- ➔ **Section II:** Orthotics and prostheses;
- ➔ **Section III:** Implantable medical devices, implants and tissue grafts of human origin;
- ➔ **Section IV:** Vehicles for physically-handicapped people;
- ➔ **Section V:** Invasive medical devices not eligible under Section III of the LPPR.

Creation of section V:

Until 2015, the LPPR was reserved for MDs used in a private practice setting (sections I, II and IV) and for MDs implanted or present in the body for more than 30 days (section III).

In 2015, Section V of the LPPR was created (see Decree of 4 May 2017 published in the official journal of 6 May 2017) to allow the inclusion on the LPPR of invasive devices not eligible under Section III that meet the following two criteria:

- **invasive nature:** those that partially or fully penetrate the interior of the body, either through an orifice of the body or through the surface of the body;
- **placement criteria:** those that can only be used by a physician.

The purpose of Section V is to be able to reimburse certain invasive devices used as part of a procedure performed by a physician and not meeting the criteria of Section III.

If the manufacturer (or their representative) or the distributor of an MD for individual use wants it to be reimbursed by the national Health Insurance, they must submit an application for inclusion of their MD on the LPPR. Inclusion can either be under the **generic description** of all or part of the product in question, or under a **brand name**. It is up to the manufacturer or distributor to initiate the application for reimbursement.

Manufacturers or distributors **are required to declare to the ANSM** all products or services that they market and include on the LPPR, specifying the corresponding inclusion code. They are also required to report any modification affecting the code of a product or of a service previously declared^{19,20}.

¹⁸ Article L165-1 of the French Social Security Code

¹⁹ Article L165-5 of the French Social Security Code

²⁰ Article 11 of Law no. 2008-337 of 15 April 2008

Inclusion as a generic description is the general rule

This inclusion arrangement identifies a type of product according to its indications and its technical specifications, without mentioning brand name or company name. If a product or service is compliant with the description and minimal technical specifications of an already existing generic description included on the LPPR, it is sufficient for the manufacturer, or the distributor:

- [to request an individual code](#) identifying their products reimbursed according to a generic description of the LPPR^{21,22}.
- and to submit the declaration of inclusion under the corresponding code to the ANSM.

This inclusion is the responsibility of the manufacturer or distributor. The manufacturer will indicate the code issued on the labelling of its product.

Note:

Since June 2019, manufacturers (or their representative) or distributors have been required to obtain an individual code identifying their products reimbursed according to a generic description of the LPPR^{23,24}. [The procedure put in place to obtain an individual code](#) can be consulted on the Ministry of Solidarity and Health website.

Enhanced generic description

Since 2015, 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 scheme²⁵. In 2020, this provision has not yet been used.

Inclusion possible under a brand name or trade name

In some cases, inclusion under a generic description is not possible. The alternative is then inclusion under brand name or trade name. This is the case, in particular²⁶:

- ➔ for a product of an innovative nature (according to Article R.165-3 of the French Social Security Code;
- ➔ for a unique product and/or one which does not allow a generic description to be drawn up;
- ➔ to ensure follow-up of a device when required by the impact on the French national health insurance scheme expenditures, by public health needs or by the monitoring of minimal technical specifications.

In other cases, inclusion on the LPPR is carried out under a generic description which is the default inclusion choice.

²¹: Decree No. 2019-571 of 11 June 2019.

²² Order of 26 August 2019 amending the decree of 24 June

²³: Decree No. 2019-571 of 11 June 2019.

²⁴ Order of 26 August 2019 amending the decree of 24 June

²⁵ Decree 2015-1649 of 11 December 2015

²⁶ Framework Agreement of 16 December 2011 between the CEPS and the professional organisations affected by the products and services included on the LPPR

Inclusion under brand name requires the electronic submission of a reimbursement application dossier to the Ministry of Health (via the [MedimedDM](#) submission platform) and simultaneous sending of an electronic copy of the dossier to the CNEDiMTS (via the [Sésame](#) submission platform).

The CNEDiMTS assesses the request made in the application dossier submitted by the manufacturer (or its representative) or distributor. In the event of a favourable opinion for reimbursement, the MD reimbursement tariff is then negotiated between the Committee for the Pricing of Healthcare Products (CEPS) and the manufacturer or the distributor.

It is the Minister of Health who issues the decision for inclusion on the LPPR after the CNEDiMTS and the CEPS have given their opinion. Inclusions or refusals to include MDs in a therapeutic indication that has been the subject of an opinion by the CNEDiMTS are examined by the Ministry with regard to the following elements:

- ➔ the expected use of the MD in the therapeutic indication considered;
- ➔ the actual clinical benefit (ACB)
- ➔ the clinical added value (CAV)

The maximum inclusion duration is 5 years. The applicant must submit an application for renewal of inclusion 6 months before the expiration date for reimbursement on the LPPR.

Inclusion under a brand name is intended to be temporary²⁷ and the CNEDiMTS may ask for reimbursement under a brand name to be replaced by reimbursement in the form of a generic description. In particular, this may be the case in situations for which several MDs from the same class have been the subject of inclusion under a MD brand name, without any clinical added value compared to the others and in the absence of any specific public health issues that could justify their long-term inclusion under a brand name. Exceptions from the principle of inclusion on the LPPR are possible, in particular for certain custom-made devices or in the case of certain patients with rare diseases or chronic conditions.

“Additional” list in healthcare organisations:

The principle of the *tarification* T2A involves flat-rate pricing for care. The expenditures for most MDs are thus directly integrated into the hospital services (DRGs). As an exception, and in order to support and disseminate innovation in healthcare organisations, some MDs likely to introduce a heterogeneity in the cost of hospitalisation due to their variable prescription within the same DRG, or in the cost of the MD in relation to the hospital services tariff, may be reimbursed in addition to the hospital services tariff. These devices are then included on a list, called the “additional list” (see article L162-22-7 of the Social Security Code).

Inclusion on the additional list is a decision of the Minister of Health after the CNEDiMTS has given its opinion. To be included on this list, the products must also be included on the LPPR in Section III or V.

²⁷ Article R165-3 of the French Social Security Code “(...) At any time, inclusion using a generic description can be substituted for inclusion of one or more products using the brand or trade name by decree of the Minister of Social Security and the Minister of Health after the National Committee for the Evaluation of Medical Devices and Health Technologies (CNEDiMTS) has given its opinion”

[The information leaflet](#) published on the Ministry of Solidarity and Health website specifies that “*Inclusion of or refusal to include MDs on the additional list in a therapeutic indication that has been the subject of an opinion by the CNEDiMTS will be examined by the Ministry with regard to the following elements:*”

- *the expected use of the MD in the therapeutic indication considered;*
- *the actual clinical benefit (ACB);*
- *the clinical added value (CAV);*
- *estimated frequency of placement within homogeneous patient groups (HPGs);*
- *estimated cost of the device(s) considering associated MDs in relation to the tariff of the hospitalisation service;*
- *application of the principle of equal treatment with regard to existing comparators in the indication involved.*”

For each of these criteria, this note specifies the arguments that may be taken into account in favour of or against inclusion on the additional list.

The figure below summarises the general process for inclusion of an MD on the LPPR.

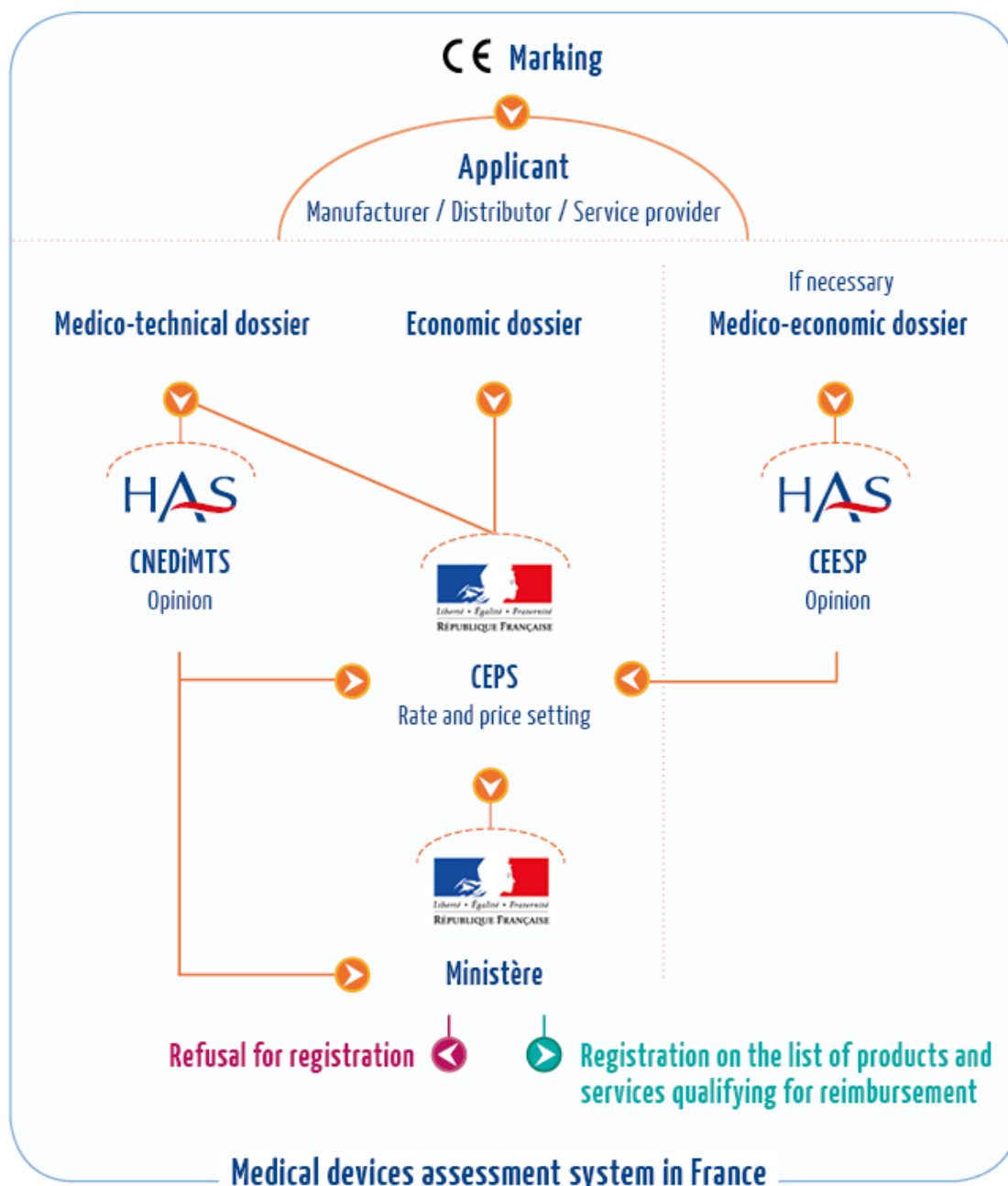


Figure 4. Inclusion of a medical device on the LPPR

2.2.3. Reimbursement as part of a professional procedure

A “professional procedure” is a category of health technologies that involves any clinical or technical action performed by a healthcare professional with the aim of diagnosis, prevention, treatment or rehabilitation²⁸. Based on the situations, the professional procedure may involve the use of MDs for individual or collective use or also medicinal products.

²⁸ Doctor / surgeon, medical biologist, dental surgeon, midwife, physiotherapist, nurse etc.

Some MDs for individual use, used for or during a procedure by healthcare professionals and whose action is not carried out beyond the medical procedure, are reimbursed through these professional procedures.

When no procedure on the CCAM corresponds to the action using the MD, the CNEDiMTS on its own initiative proceeds with the assessment of the procedure at the same time as the assessment of the device.

2.2.4. Specific procedures to promote rapid access to innovative MDs

Various exceptional reimbursement arrangements exist to support early access to innovative health technologies or organisations.

Forfait Innovation (Innovation Funding)

The national Innovation Funding mechanism allows exceptional and temporary reimbursement with the aim of facilitating access to innovative technologies. This procedure is open to a broad range of health products: MDs, IVDs and professional procedures.

Principle:

Innovation Funding allows the exceptional and temporary reimbursement of an innovative MD, IVD or procedure subject to the performance of a study to provide missing clinical or medico-economic data (7). This exceptional reimbursement is a decision made, after receiving the opinion of HAS, by the Ministers of Health and Social Security and is the subject of publication of a specific decree. As it is an exceptional reimbursement, its implementation implies the selection of the technologies likely to benefit from it.

At the time of submission of the application, candidate technologies must have early data establishing that the MD or procedure is liable to provide a substantial benefit to health or reduce health spending but that this data is not yet adequate to claim public coverage in accordance with common law.

The objective of Innovation Funding is therefore to promote the implementation of a decisive clinical study that will later allow the reimbursement of the technology according to the “pay to see” principle (contrary to common law: “see to pay”). This exceptional funding is therefore dependent on the performance of a clinical study or a cost minimisation study aimed at confirming the value of the technology.

Determination of the flat fee takes into account the duration of the study as well as the time necessary for the assessment and pricing of the product.

The Ministry of Health monitors the progress of the study.

Eligibility criteria are based on the innovative nature of the technology and on the relevance of the clinical or medico-economic study proposed. Compliance with these criteria is assessed by the HAS Board and the Ministry of Health.

Two important points should be emphasised:

- ➔ the proposed study protocol, which is necessarily comparative, is an integral part of the application dossier;
- ➔ the applicant for Innovation Funding is also the sponsor of the study.

Note:

The application may be submitted before obtaining CE marking.

The proposed study may be a study conducted exclusively in France or an international study. In the case of an international study, coverage as part of the Innovation Funding mechanism will concern only those patients treated at French study sites.

Further information about the Innovation Funding, in particular [eligibility criteria](#) (8) and [application submission procedures](#) (to HAS and the Ministry of Health) (9) and [applications for early dialogues](#) (10), can be found on the HAS website (www.has-sante.fr).

Innovation funding – Examination procedure

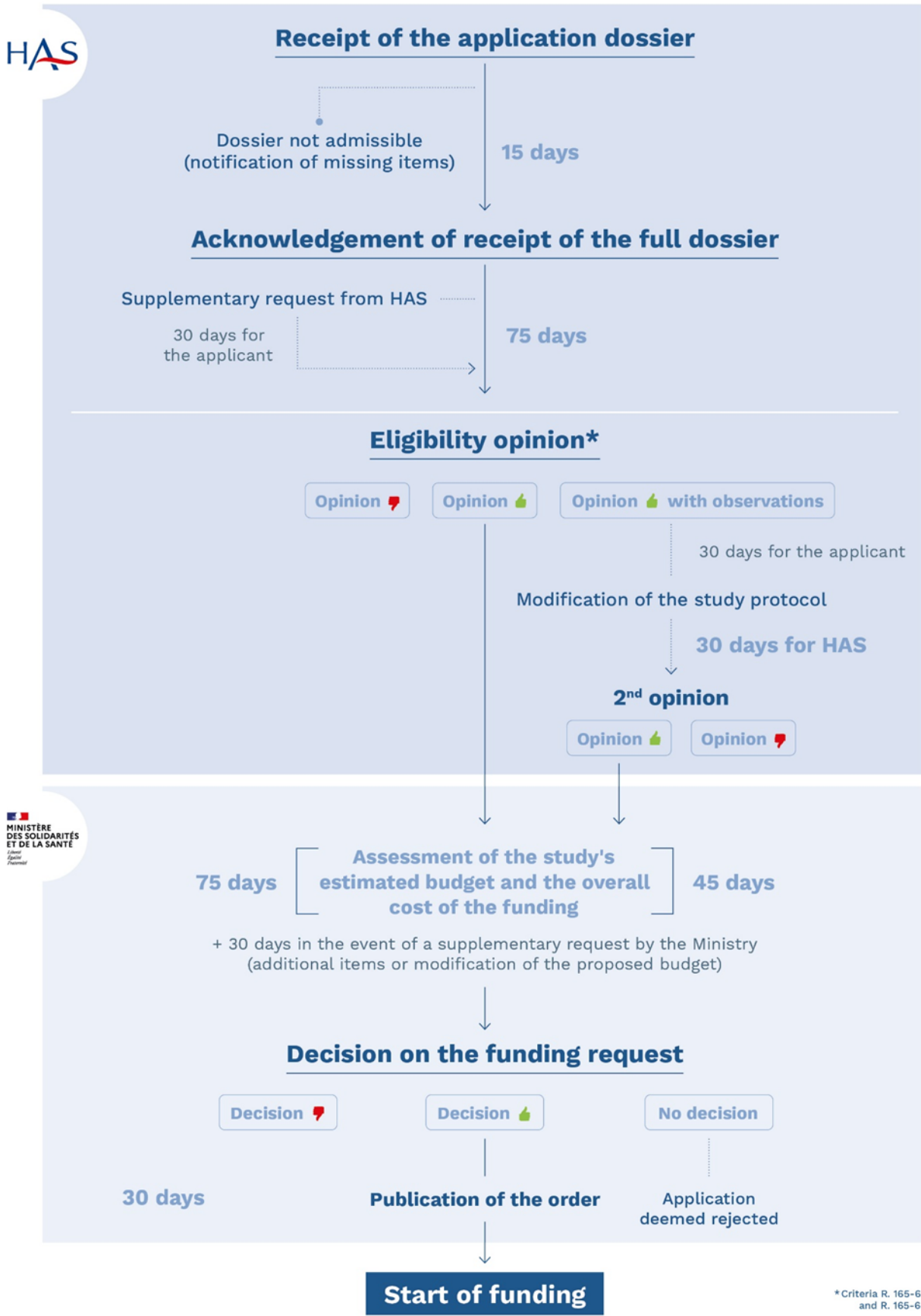


Figure 5. Innovation Funding application procedure

Temporary coverage under Article L165-1-5 of the French Social Security Code (CSS)

Principle:

Temporary coverage is a scheme for reimbursing health products presumed to be innovative and which have a therapeutic purpose or are intended to compensate for disability, and fall within the scope of the LPPR. It means they can be reimbursed for one year, pending conventional reimbursement via the LPPR (11).

To be eligible, the products and services must meet the conditions set out in the [decree of 23 February 2021](#). The CNEDiMTS returns an opinion on the 5 eligibility criteria used to assess the potential of the technology, for each medical indication covered by the medical device:

- used for the treatment of a serious or rare disease or compensate for disability;
- without relevant comparator, in other words used for a partially met or unmet medical need;
- likely to provide a significant improvement to the state of health of the patient or in the compensation of their disability;
- likely to be innovative, especially since it is novel in a way other than a simple technical upgrade with regard to health technologies used in the claimed indication;
- likely, in light of the results of clinical studies, to present relevant clinical efficacy and a substantial effect, and for which the adverse effects are acceptable.

Three prerequisites must be met for a product to be eligible for temporary coverage:

- it must have CE marking if it is a medical device;
- the product must not already be reimbursed as part of hospitalisation services;
- and the manufacturer must undertake to submit a request for inclusion on the list of products and services qualifying for reimbursement (LPPR) for the medical device within 12 months of the application for temporary coverage.

This reimbursement is decided on by order of the Ministers for Health and Social Security, following the opinion of the CNEDiMTS, returned within 45 days following submission of the complete application dossier, indicating whether the application meets the eligibility conditions for each indication considered.

After the CNEDiMTS has issued an opinion, when reimbursement is granted, the amount of the compensation is set by the Ministries and notified to the company according to the process and to strict deadlines, as referred to in [article R.165-91 of the French Social Security Code](#).

In addition to the exemptions possible for medical devices described in the previous chapter, **several trials are currently under way to test new care organisations and/or new mechanisms for remuneration of stakeholders.**

These are not clinical trials but organisational trials. Consequently, if they involve the use of a medical device:

- ➔ the device must first have obtained CE marking;

- the trial will not allow the collection of clinical data, which will be required for reimbursement, in accordance with common law, of the medical device on the LPPR list.

The following examples can thus be cited:

“Article 51” trials of the French Social Security Financing Act for 2018

This mechanism, introduced in April 2018, aims to trial new health organisations in order to promote cooperation between regional or national players. The objective is to be able to help improve the patient care pathway, the efficiency of the healthcare system or the relevance of health product prescriptions, with exemptions from certain common law organisational or financing rules during these trials.

[Further information on “Article 51” trials](http://www.solidarites-sante.gouv.fr) can be found on the Ministry of Solidarity and Health website (www.solidarites-sante.gouv.fr).

ETAPES programme (telemedicine trials to improve the care pathway)

The ETAPES project, renewed for a period of 4 years²⁹ (over the period 2018-2022) is a trial designed to encourage and provide financial support for the national roll-out of remote monitoring projects for patients with:

- diabetes,
- chronic kidney disease,
- chronic respiratory disease,
- chronic heart disease,
- implantable cardiac prostheses for therapeutic purposes.

The aim of this programme is to help coordinate the players involved in remote monitoring around the patient in order to carry out remote medical monitoring, provide the technical solution, or provide therapeutic support for the patient. For each disease concerned, specifications define the eligible patients, in particular, as well as the terms and conditions of treatment and remuneration for healthcare professionals and technical solution providers.

[Further information on the “ETAPES” programme](http://www.solidarites-sante.gouv.fr) can be found on the Ministry of Solidarity and Health website (www.solidarites-sante.gouv.fr).

2.3. Medico-Technical Assessment by the CNEDiMTS

The medical-technical assessment conducted by the CNEDiMTS **only** concerns devices within the scope of the LPPR and devices on the so-called “intra-DRG” positive list.

Note:

The expected clinical investigations for reimbursement must answer the question of the role of the device in the therapeutic strategy and allow its added value to be determined compared to the available arsenal in France.

²⁹ Article 54 of the French Social Security Financing Act for 2018

2.4. Medical Device and Health Technology Evaluation Committee (CNEDiMTS)

The CNEDiMTS is the HAS committee which assesses MDs and health technologies in view of their reimbursement by the national Health Insurance and their proper use, including those funded as part of hospital services (12).

The following are members of the CNEDiMTS:

- ➔ A chairperson with voting rights chosen from among the HAS board members,
- ➔ 21 full members with voting rights: 19 with scientific or technical skills in the field of health products and services (physicians, nurses, occupational therapists, pharmacists, etc.) and 2 members chosen from members of a patient and user association; and 7 substitute members.
- ➔ 7 members in an advisory role (representatives from the of the Ministry of Health, the ANSM and the 2 main French national health insurance funds).

The following may also contribute to the Committee's work, with an advisory vote, if necessary:

- ➔ the Biomedicines Agency representative, when the Committee examines the inclusion, renewal or modification of inclusion of tissues or cells from the human body;
- ➔ the military health service representative, when the Committee examines the inclusion, renewal or modification of inclusion of custom-made orthotics and prosthetics, orthopaedic shoes or vehicles for people with physical disabilities.

Where required, the Committee consults a representative from the national testing laboratory (LNE) or the study and research centre for prosthetics/orthotics for people with disabilities (CERAH).

It may also consult any qualified person or expert that it deems useful.

Within HAS, the Medical Device Assessment Department (SED) supports the CNEDiMTS in its missions and ensures the internal expertise of all topics examined.

Each dossier or topic addressed by the SED is discussed and voted on at a CNEDiMTS meeting. Opinions and recommendations are thus based on the principle of collegiality.

Four types of activity are carried out:

- ➔ assessment of MD reimbursement application dossiers (under brand name or on intra-DRG list) with delivery of opinion;
- ➔ assessment of homogeneous categories of products, in particular generic descriptions;
- ➔ assessment of health technologies (not medicinal products);
- ➔ assessment of temporary coverage application dossiers (stipulated in article L165-1-5 of the French Social Security Code (CSS)).

2.4.1. Medico-technical opinion

The medico-technical assessment is prepared by the SED for the members of the CNEDiMTS on application of the manufacturer. This application can be of different types. It may correspond to inclusion of an MD on the LPPR or, when the MD has already been included once, a modification of the conditions of inclusion or a renewal of the inclusion of the device.

A [guide for submission of an application](#) to the CNEDiMETS is available on the HAS website (13). For each type of application (inclusion, modification and renewal), it details the elements to be provided to enable the examination of the dossier and its review by the CNEDiMETS. The submission applications for the assessment of devices by HAS is fully computerised via the [Sésame submission platform](#) (14).

In the cases of initial applications for inclusion or of applications for renewal of inclusion, the Committee's opinion relates in particular to the assessment of the actual clinical benefit (ACB) and, if the latter is sufficient, to the assessment of the clinical added value (CAV).

The medical device assessment principles established by the CNEDiMETS have been published and are available on the HAS website (15).

Considering that patients have specific knowledge about their disease, HAS has developed the following [ways to involve patients in the medico-technical assessment](#)(16):

- ➔ the opportunity given to patient associations to submit a “patient contribution” on an MD (in the context of submission of an application dossier for inclusion under brand name);
- ➔ stakeholder hearings.

Application for inclusion on the LPPR

Assessment of actual clinical benefit

The actual clinical benefit (ACB) is a clinical service. It is assessed in each of the indications of the product or service and, if applicable, by population group. The assessment of the ACB is based on two criteria defined in Article R.165-2 of the French Social Security Code³⁰:

- ➔ the benefit of the product with regard to its therapeutic or diagnostic effect or its effect in compensating for disability, as well as its adverse effects or risks related to its use and its role in the therapeutic strategy considering other available therapies;
- ➔ its expected public health benefit, in particular its impact on the health of the population, in terms of mortality, morbidity and quality of life, its ability to meet a therapeutic need with regard to the severity of the condition or disability, its impact on the healthcare system and on public health policies or programmes.

The ACB is assessed, where appropriate, according to the technical specifications and the specific conditions of prescription and use on which inclusion depends.

Products or services whose expected clinical benefit is insufficient are not included for reimbursement. The decision is taken by the Minister of Health.

Assessment of clinical added value

When the ACB is sufficient to justify inclusion for reimbursement, the CNEDiMETS must also deliver an opinion on “the assessment of the clinical added value (CAV) compared to a comparable product, procedure or service or to a group of comparable procedures, products or services, precisely designated, considered as standard according to the current data of science and subject or not to reimbursement³¹”.

This evaluation leads us to consider the CAV as major (I), high (II), moderate (III), minor (IV) or to note its absence (V). It is conducted for each therapeutic, diagnostic or disability compensation indication in

³⁰ Article R165-2 of the French Social Security Code

³¹ Article R165-11 of the French Social Security Code

which the Committee deems the inclusion justified. The CAV level is one of the criteria used by the CEPS to determine the tariff for a device.

Note:

In the case of a medico-technical assessment of an MD included on the “intra-DRG” list, the CAV is not assessed, since the tariffs are not negotiated with the CEPS.

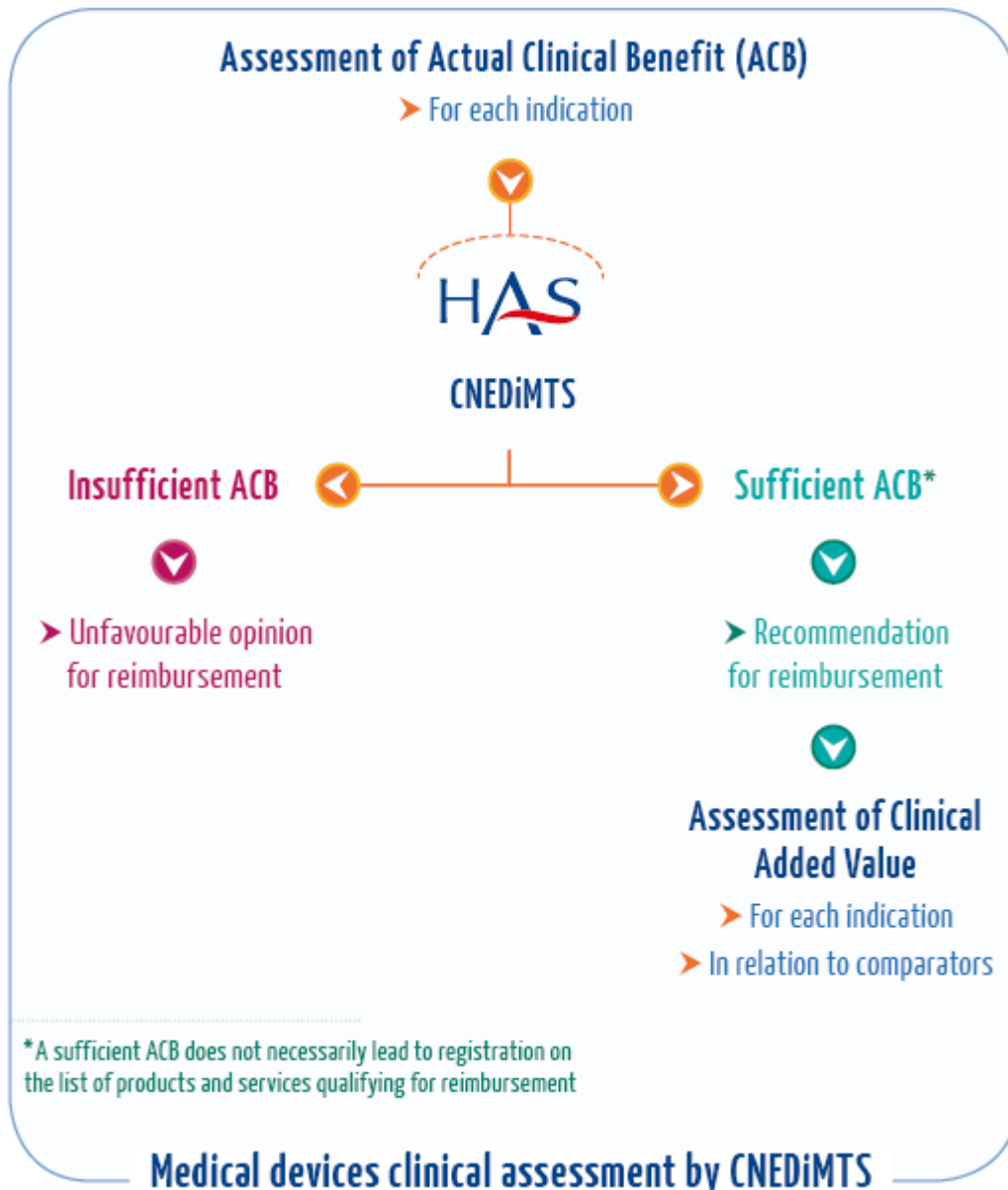


Figure 6. Assessment of clinical added value by the CNEDiMTS when the actual clinical benefit is sufficient

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 light. For an application for inclusion of an MD from a category of products not yet assessed, the CAV is granted in relation to the existing therapeutic or diagnostic strategy or strategy for compensation of a disability.

In its opinion, the Committee may also specify the additional studies necessary for assessment of the actual clinical benefit, or clinical added value, which should be submitted at the time of renewal of inclusion.

Inclusion of a product included under the brand name is granted for a maximum of 5 years. Its ACB and CAV are then re-assessed periodically. Inclusion of the product can only be renewed if the product or service has a sufficient actual clinical benefit to justify continuing its reimbursement.

In the case of a renewal of inclusion, the actual clinical benefit (ACB) is determined by re-assessment of the criteria that led to the assessment of the ACB determined at the previous assessment, taking into account new data available (new clinical studies, new international guidelines, other products and services included since, data from the post-inclusion study requested if applicable, etc.). The ACB is assessed in each of the indications initially submitted for reimbursement.

When the ACB is sufficient to justify renewal of inclusion, the assessment of the clinical added value (CAV) compared to the comparator, considered standard according to current data, is carried out.

In the case of generic descriptions, the assessment carried out by the CNEDiMTS concerns the same assessment criteria as those mentioned above and makes it possible, if necessary, to propose an update of the minimum technical specifications, funding indications and methods of use of the device categories assessed.

2.5. Medico-Economic Assessment by the CEESP

The medico-economic assessment only involves certain applications for inclusion on the LPPR.

2.5.1. Commission for Economic and Public Health Evaluation (CEESP)

To ensure the sustainability of the health system largely based on collective management of health care expenditures, choices about the allocation of resources must be made. [The Commission for Economic and Public Health Evaluation \(CEESP\)](#) at HAS was created to ensure that the **measurement of the benefit for society of a strategy or a product** is taken into account in decisions about strategies or products, and in particular decisions about their price (17).

The **measurement of the benefit, for society, of a new strategy or a product, compared to the existing strategy or product**, is established by comparison of the resources used (costs) with the results obtained, which allows the efficiency to be assessed. This analysis makes it possible to adequately articulate public health objectives and the resources that are dedicated to it.

The CEESP takes a stance and develops opinions and recommendations based on a number of scientifically established grounds and elements. The efficiency opinions of the CEESP are intended for the CEPS. These additional assessments are conducted in parallel with those of the two medical-technical committees of HAS, i.e., the Transparency Committee (CT) for medicinal products and the CNEDiMTS for medical devices. The CEESP is ultimately responsible for the scientific validity, methodology and ethical quality of the work of HAS in matters of economic assessment and assessment of public health actions and programmes ([see 2019 activity report](#)) (18).

2.5.2. Efficiency opinion

A medico-economic assessment is required when an MD claims a CAV of I to III and is likely to have a significant impact on French national health insurance scheme expenditures^{32,33}.

The impact on French national health insurance scheme expenditures is qualified as significant³⁴:

- when the manufacturer claims, for their product, an impact on the organisation of care, professional practices or patient care conditions;
- in the absence of such claim, when the annual revenue from the product, all indications combined, is greater than or equal to EUR 20 million incl. tax (the second full year of marketing).

The HAS Board ensures application of the terms of the decree and does not require an economic assessment when a conventional low-cost procedure is planned or when the product patent is in the public domain ([see 2019 activity report](#)).

For the medico-economic assessment, the manufacturer must submit an economic assessment application presenting the context of the application, the data used as well as an explanation of the structuring choices of the assessment, the modelling parameters and the results obtained, according to [the methodological guidelines established by HAS](#) (19).

The assessment application must be submitted to the CEESP at the same time as the assessment application is submitted to the CNEDiMTS (article R.161-71-3 of the French Social Security Code). A note detailing the electronic submission amendments via the SESAME platform, as well as format templates for the presentation report and the technical report are available on the HAS website.

The CEESP then delivers an opinion about the foreseeable or observed efficiency of reimbursement of the health product or technology by the French health insurance scheme.

The opinion is based on:

- the comparative analysis, between the different relevant therapeutic alternatives;
- the ratio between the costs incurred and the expected or observed benefits for health;
- the quality of life of the people involved.

Additional information about the content of the efficiency opinion and its appendices are available in the HAS document "[efficiency opinion format](#)" available on the HAS website (www.has-sante.fr).

2.5.2.1. Conclusion of the CEESP

The conclusion of the Committee relates in particular to the methodological conformity of the medico-economic model submitted (assessed with regard to the determining factors mentioned above and further explained in the methodological guide). In case of methodological non-conformity, the CEESP rules on the nonconforming nature of the study due to major reservations and considers the results of

³² Decree no. 2012-1116 of 2 October 2012 on the medico-economic missions of the Haute Autorité de santé

³³ Decision no. 2013.0111/DC/SEESP of 18 September 2013 of the HAS Board on the significant impact on Health Insurance expenditures triggering the medico-economic assessment of products claiming a, IACB or IECB level I, II or III

³⁴ https://www.has-sante.fr/upload/docs/application/pdf/2019-02/definition_de_l'impact_significatif_sur_les_depenses_de_l'assurance_maladie_declenchant_evaluation_medico-economique_des_prod.pdf

the study submitted to be unusable. Thus, no quantitative results are included in its conclusion and it is specified that the efficiency cannot be assessed.

When the study method is considered acceptable, the CEESP specifies:

- ➔ the incremental cost-effectiveness ratio (ICER) of the product or average net profit to interpret the result;
- ➔ the nature of any methodological reservations;
- ➔ the assessment of the level of uncertainty characterising the results and the main sources of uncertainty;
- ➔ elements allowing assessment of the impact of a price variation on the ICER.

Note:

To help public decision-making and to negotiate prices, the CEESP may be required to comment on the high nature of the ICER. However, at this stage, no reference value has been defined to consider an ICER “too” high.

The final efficiency opinion issued by the CEESP is primarily intended for the CEPS for negotiation of pricing. It is made public on the HAS website (www.has-sante.fr).

Methodological guides aimed at manufacturers have been drafted by HAS (20)(21). They aim to explain the reference framework for economic assessment by presenting the principles and methods used to carry out and analyse these assessments.

2.6. HAS support

Before submitting a dossier, communication between applicants and HAS departments is recommended. This communication can take place in various ways depending on the state of progress of the dossier.

2.6.1. Early dialogues

For medical devices in clinical development – including before obtaining CE marking – the HAS Assessment and Access to Innovation Division (DEAI, previously DEMESP) has implemented the opportunity for [early dialogues \(ED\)](#) (10).

The company or developer can request an ED focused on questions related to the clinical development of the health product in question or a joint ED also covering questions related to conducting a medico-economic study, if an assessment of the product’s efficiency is planned.

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

No member of the HAS committees concerned (CNEDiMTS or CEESP) participate in these dialogues.

The answers provided by the HAS departments to companies or developers during these EDs are in no way an assessment and do not prejudice the conclusions that may result from the assessment by the Committees involved, namely the CNEDiMTS and, where applicable, the CEESP (if submitting an economic assessment dossier).

ED for products in clinical development

The objective of these early dialogues organised by the SED is to provide answers to questions posed by companies or developers with respect to how they may conduct clinical studies in order to be able to supply data meeting health technology assessment requirements with a view to reimbursement and pricing.

The implementation of such a dialogue is only useful for products that are in clinical development:

- once the protocol plan is established;
- before starting the clinical study.

This type of dialogue can be organised with a view to discussing the relevance of a clinical study protocol, aimed at generating the data required to obtain reimbursement:

- under a brand name on the LPPR, for an application that will be submitted after the study,
- via Innovation Funding, to finalise the study protocol that will be submitted in the application dossier.

No member of the CNEDiMTS participate in these meetings.

The answers provided by the SED do not commit the Committee as regards the opinions it may deliver when assessing the dossier submitted by the manufacturer.

For these EDs, refer to the document dedicated to medical devices: "[Early dialogue with HAS for a medical device in clinical development - MD methods for submission and proceedings](#)" available on the HAS website (www.has-sante.fr).

ED before submitting a medico-economic study

To promote the conformity of economic studies submitted with HAS guidelines, the manufacturer is offered the opportunity to request an early dialogue with HAS. This dialogue allows the manufacturer to present to HAS the main methodological choices it is leaning towards to structure its economic study, and to share methodological questions raised.

No member of the CEESP participates in these meetings.

The answers provided by HAS do not commit the Committee as regards the opinions it may deliver when assessing the dossier submitted by the manufacturer.

For these EDs, refer to the document: "[ED economic dossier](#)" available on the HAS website (www.has-sante.fr).

2.6.2. Pre-submission meeting

Manufacturers or service providers and home equipment distributors who want to receive clarification about the technical and regulatory aspects necessary for creation of the medico-technical dossier, can request a pre-submission meeting (22).

These meetings are arranged by HAS (on request) prior to the submission of a dossier for inclusion in the LPPR.

Meetings of this type cannot result in advice being given about the company's strategy. They are optional, non-binding, confidential and free of charge.

A distinction should be drawn between these meetings and the early dialogues designed to give an insight into the methodological elements regarding the device development.

2.7. Pricing of medical devices included on the LPPR

2.7.1. The French Healthcare Products Pricing Committee

The French Healthcare Products Pricing Committee (CEPS), **an inter-ministerial body**, placed under the joint authority of the Ministries of Health and Economics, is primarily tasked by law with setting the prices of medicinal products and tariffs of medical devices for individual use and services reimbursed by compulsory Health Insurance (23).

The decisions of the CEPS are made in a collegial manner, in accordance with the guidance it receives publicly from the ministers, and under the supervision of the administrative judge. The prices or tariffs are preferably set by means of **agreements** concluded with the companies marketing the products or, for some MDs, with the representative professional organisations of these companies.

The CEPS also contributes, through its proposals, to defining economic policy for health products.

The CEPS is tasked with proposing the reimbursement tariffs of products and services included on the LPPR and, if appropriate, their price. It may, in setting these tariffs and prices, conclude agreements with the manufacturers and/or distributors involved regarding sale volumes, proper use clauses or the conducting of a post-inclusion study.

2.7.2. Setting the “*tarif de responsabilité*” and price

A new framework agreement is in the process of being negotiated between the CEPS and the professional organisations concerned by the products and services listed in the LPPR.

Tarif de responsabilité (TR): The *tarif de responsabilité* is the tariff on which French social security reimbursement is based.

Prix limite de vente (PLV) [Sale price limit]: This is the maximum price that the public can be charged for a product.

The difference between the PLV and the TR is thus the responsibility of the patient or falls under the private insurance system.

In most cases, the TR and the PLV are identical, so there is no amount to be paid by patients who have no supplemental health insurance.

The determination of tariffs primarily takes into account³⁵:

- ➔ the CAV;
- ➔ if applicable, the results of the medico-economic assessment of tariffs of comparable products or services;

³⁵ Articles L.165-2 and R.165-14 of the French Social Security Code

- ➔ planned or observed sale volumes;
- ➔ planned or observed amounts reimbursed by the compulsory French national health insurance scheme;
- ➔ anticipated and actual conditions of use.

For inclusions in generic description form, a TR and a PLV are set in the LPPR for each product category and are applicable to all MDs meeting the generic description.

Note:

During its lifetime - and particularly when a competitor arrives - the MD may have its pricing conditions reviewed at the initiative of the CEPS.

More information on price and tariff regulation can be found in the CEPS activity report.

The pricing of procedures included on the joint classification of medical procedures (CCAM) is not negotiated with the CEPS but with the National Association of Health Insurance Funds (UNCAM).

The figure below shows the main steps of reimbursement and pricing applications.

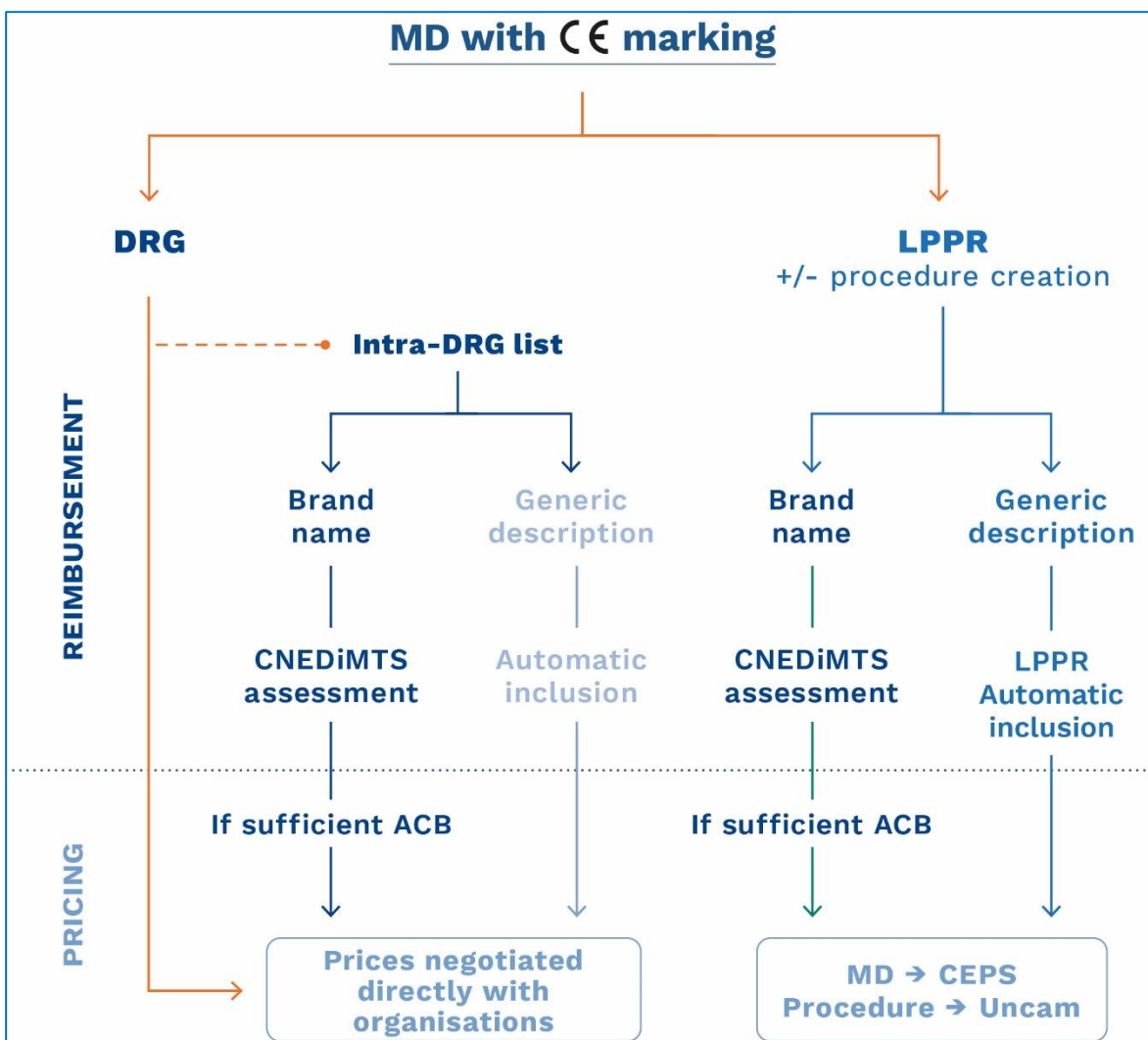


Figure 7. Simplified pathway of steps to take for reimbursement and pricing

3. Clinical development challenges

3.1. Key stages in clinical development

Clinical development and optimisation of prototypes are crucial stages for a new MD.

These stages must be prepared as early as possible. Anticipating these stages enables relevant clinical studies to be proposed that demonstrate the benefit of this new MD and will eventually optimise its use. Conducting a quality clinical study is an opportunity to show the interest of the new MD both with respect to patients and to obtain reimbursement. To improve the readability of the guide, the decision was made to group sick people and people with disabilities under a single term, patient.

It is important **to identify from the outset, through systematic research, the clinical data that is already available** and the studies in progress **within the domain of the new MD** or the reference strategy in question as well as any recommendations.

- ➔ **The preclinical phase** includes not only the technological development but also the implementation of *in vitro* tests and sometimes animal experiments.
- ➔ **The clinical phases** include feasibility and development studies (safety and performance), as well as studies demonstrating the clinical benefit. The implementation of a protocolised collection of clinical data from the first patient is an asset for the distribution of a new technology. The existence of a protocol and the quality of this collection are determining factors.

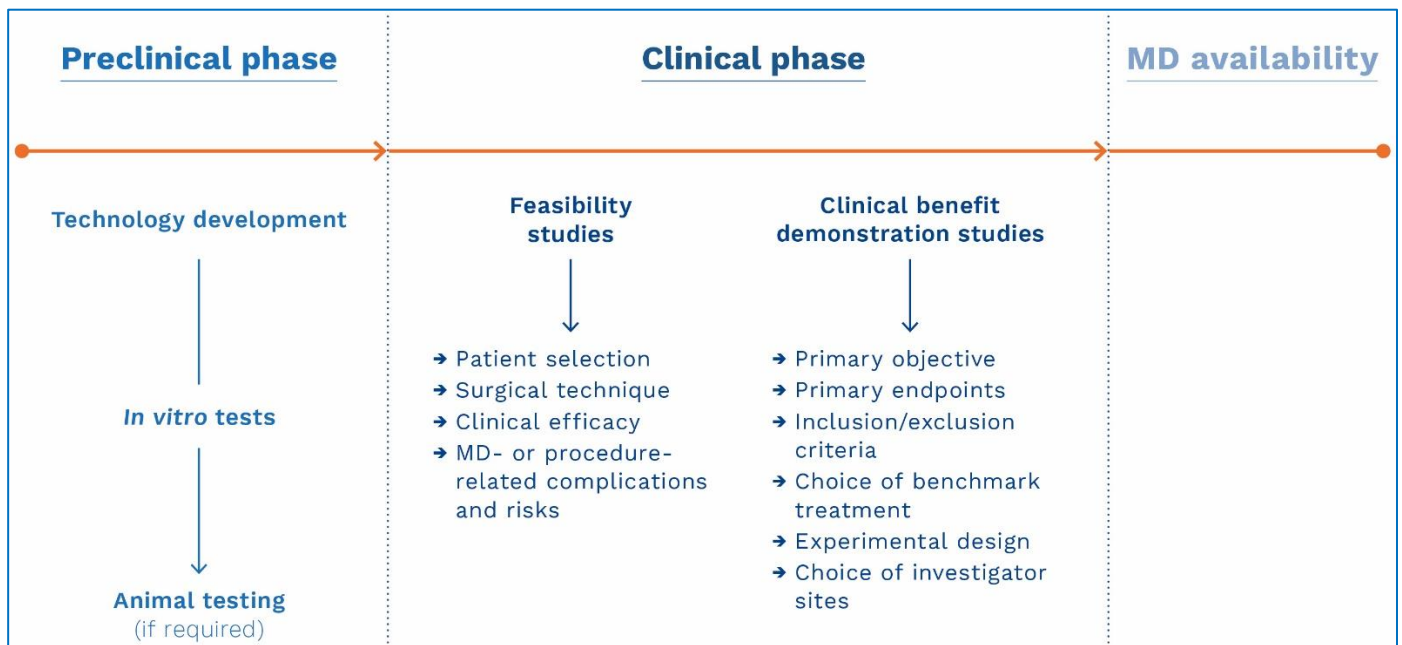


Figure 8. Key stages in clinical development

Throughout the clinical development of an MD, some specific characteristics must be taken into account, namely:

- the product status based, for example, on whether or not it is combined with a medicinal product;
- the life cycle which can be very short due to rapid technical progress;
- the lifetime, which depends on the obsolescence of the MD or, if applicable, the duration of implantation;
- the technical performance (to be separated from the clinical benefit);
- the clinical benefit, which can depend not only on the MD itself, but also on the performance of the medical team (operator-dependent nature, learning curve) and the technical facilities;
- the target population affected by the MD, which may sometimes be small.

3.2. Feasibility studies

Depending on the type of MD, they are proposed immediately following the pre-clinical phase or in parallel with industrial development. Generally, the methodologically appropriate type of study at this stage is a non-comparative prospective study.

The results of feasibility studies may, in particular, provide elements to:

- determine the effect size that will be used to design future studies
- estimate the number of patients necessary for future studies;

Depending on the context, one or more studies are necessary to answer different questions, in particular:

- the type of patients who will benefit from the new MD;
- the development of the surgical technique, in particular implantation;
- the clinical efficacy;
- the complications and risks associated with the MD and the implantation technique.

3.2.1. Selecting patients who will benefit from a new MD

This stage makes it possible to specify the clinical forms of the condition in which the new device would bring about the expected therapeutic efficacy in the patients.

It must also specify the characteristics of the patients (age, sex, acceptable comorbidities) **which would have the least possible effect on the result, in order to select a sufficiently homogeneous group of patients for future studies.**

However, even at this early stage of development, a choice must be made, which is often delicate, between a very narrow selection of patients that could optimise the amplitude of the observed effect, and a wider selection that would optimise recruitment conditions and the possibility of generalising the study results.

3.2.2. Development of the surgical technique, in particular implantation

One or more studies are necessary to develop the implantation technique of a new MD and **to describe the different surgical steps, the technical facilities and the personnel** necessary for the success of the procedure.

At the end of this stage, actual specifications are established to standardise the technique as best possible. They include the description of the procedure and necessary resources. They facilitate implementation of the next stage for demonstration of clinical benefit.

3.2.3. Complications and risks

Two types of adverse events may be reported:

- ➔ those linked directly to the MD;
- ➔ those that are related to the implantation or surgical technique.

At this stage, the objective of the studies is to identify the main complications. This estimate is essential for establishing the future benefit/risk ratio.

3.3. Studies to demonstrate the clinical benefit

The design of the studies essential to demonstrating the clinical benefit of the new MD **must be based on the different feasibility and development studies.**

Depending on the stakes, the studies selected can be superiority, equivalence or non-inferiority studies.

The type of trial with the best level of evidence to demonstrate the clinical superiority of a new MD over the reference strategy is a randomised, controlled trial. This type of trial, when it can be carried out and when it is well designed, optimally enhances a new MD. The randomised, controlled trial can also be used to show equivalence or non-inferiority of the MD.

The randomised, controlled trial, in addition to having to fulfil standard methodological criteria, must also be clinically relevant.

When drawing up the study protocol, particular attention must be paid to a certain number of points, presented below.

These various points must be systematically addressed, and the **questions must be asked when developing any trial to demonstrate the clinical benefit of a new MD.** This **systematic approach** allows the creation of a trial that will best show the interest of the new MD.

It is possible that this trial, depending on the **specific characteristics of the MD**, cannot be controlled and randomised. In this case, the people conducting the project can use other experimental plans suitable to the context.

In all cases, this strategy must make it possible to clearly explain and justify alignment between the methodological choices made and the expected level of demonstration to show a benefit of the device assessed.

Note:

In most cases, a randomised controlled trial can be performed. **However, in some very specific situations, this type of study is not applicable and the use of another experimental plan should be justified.** [A guide presenting the methodological choices for clinical development of MDs](#) has been made available by HAS to guide the persons conducting the project on the HAS website.

3.3.1. Primary objective

The primary objective must obligatorily be defined before the study protocol is drawn up. It must be unique. Its wording provides elements essential to the indication that the MD will ultimately have on the market.

The difficulty is choosing the right objective for the clinical demonstration of the new MD. In fact, the entire trial is built around the **wording of this primary objective** which must be clear, precise and based on relevant and valid clinical criteria.

The following elements are specified in the wording of the objective:

- ➔ the treatment tested;
- ➔ the control treatment, which ideally corresponds to the reference strategy;
- ➔ the type of trial: superiority, equivalence, non-inferiority;
- ➔ the patients concerned.

For example, “to demonstrate that the aortic endoprosthesis reduces perioperative mortality compared with open surgery in patients suffering from an unruptured aortic aneurysm”.

The primary objective of a study may be the demonstration of improvement in the patient’s quality-of-life if the product studied has demonstrated its efficacy.

3.3.2. Primary endpoint

Identification of a single primary endpoint is suggested in accordance with the primary objective of the study. It must be defined before the protocol is drawn up ([see Guide on Methodology for the Clinical Development of Medical Devices](#)) and allow quantification of the therapeutic effect of the new MD in relation to the control treatment (24).

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.

Endpoints of studies supporting applications for inclusion on the LPPR must also be suitable for the type of technology considered and be consistent with the claims of the manufacturer.

Examples of endpoints that can be used in the various studies:

- ➔ mortality reduction in the short, medium or long term;
- ➔ reduction or improvement in morbidity: pain, scarring, decreased relapses, pain reduction, etc.);
- ➔ compensation for a disability (degree of dependence and autonomy, resumption of lifestyle, mobility, socio-professional insertion, etc.);
- ➔ reduction in complications or adverse events from the surgical technique or procedure: number of hospitalisations, duration of hospitalisation, infections, haemorrhages, repeat procedures;
- ➔ improvement in the patient’s quality of life;

- impact on the organisation of care: reduction in duration of hospitalisation, decrease in consumption of healthcare products or decrease in number of procedures, decreased use of medical transport...

The aspect of quality-of-life of patients or people with disabilities is essential.

Quality-of-life can be a very relevant endpoint for some technologies, in particular those that involve patient adherence to the use of the product. This type of criterion must be taken into account as often as possible in studies supporting applications.

The principles concerning primary endpoints are detailed in the document "[Assessment principles established by the CNEDiMTS to determine the reimbursement eligibility of MDs for individual use](#)" (15).

Note:

A specific methodological guide on the consideration of organisational impacts in the evaluation of health technologies by HAS is in the process of being developed. The objective of this work, the roadmap of which can be consulted on the [HAS website](#), is to set out benchmarks on the best way to take into account the assessment of organisational impacts, in addition to the medical and economic assessment, in particular for MD dossiers submitted by manufacturers.

3.3.3. Eligibility criteria: inclusion and non-inclusion criteria

Ideally, the study population must correspond to the patients for whom this new MD is intended in **standard practice**. The eligibility criteria are based not only on a precise description of **clinical forms of the condition** but also on the **characteristics of patients** to be included: age, sex and comorbidities.

The patients included in the trial must be sufficiently homogeneous so as not to increase variability, which could have too great an effect on the result of the trial. Studies already carried out should assist in the description of the inclusion and non-inclusion criteria of the trial.

The eligibility criteria must correspond to the same indications as the reference strategy and the patients likely to participate in the trial must be able to be included in all of the treatment groups to be compared.

It is important to anticipate the feasibility of the study considering the size of the target population and the calculated sample size necessary to demonstrate the clinical benefit; the clinical forms of the condition must be sufficiently common to allow recruitment of patients within a realistic time frame.

3.3.4. Choice of comparator

The comparator is derived from the reference strategy according to the current scientific data. It is defined for a **given indication and may or not be reimbursed**.

The nature of this comparator can vary greatly:

- a product (medical device or medicinal product or another healthcare product);
- and/or a procedure or a group of procedures;
- and/or a service.

The reference strategy is based on reliable **data from the literature**. In the absence of valid scientific evidence, the reference strategy is defined as that used in practice according to expert opinion. This reference strategy should be that which, in the absence of the new MD, is supposed to give the **best results** in patients affected by the illness or the disability in question.

The last important point involves specifying the **role of the comparator in the therapeutic strategy or compensation for disability**. This specification serves to reinforce the value of correctly conducting this trial to ensure demonstration of the potential clinical benefit of the new MD in the care of patients with the condition in question.

The choice to conduct a superiority, equivalence or non-inferiority study takes into consideration both the existence of a reference strategy and the supposed contribution of the new MD in terms of efficacy compared with the reference strategy.

3.3.5. Choice of investigator sites

Trials are preferably **multicentre**. The objective is dual; to facilitate:

- ➔ patient recruitment to ensure the shortest possible inclusion period;
- ➔ extrapolation of the study results. In fact, the different teams participating in the trial will be more representative of a certain variability in medical practice.

The teams likely to participate in a multicentre trial must master the implantation technique or the surgical procedure. When drawing up the study protocol, actual **specifications** are proposed for the **eligibility** of teams that can participate in the trial. The specifications include standardisation of the implantation technique, the experience of the medical team, the required technical facilities and the quality control of medical data.

In the case of practice of procedures and prescription of certain MDs which require a specific framework for public health reasons or which are likely to involve unjustified expenditures, rules established by decree by the Minister of Health, after receiving the opinion of HAS, may be applied. These rules concern in particular the **training** and **qualification** of professionals and the technical conditions for implementation. The use of these MDs and the practice of these procedures may be limited **to certain healthcare organisations for a given period**³⁶.

3.3.5.1. Calculation of the sample size

The theoretical estimate of the number of patients to be included is essential. The population sample size depends on two variables:

- ➔ the expected significance of the therapeutic effect;
- ➔ the prevalence of the event being researched.

The greater the therapeutic effect, the fewer patients are needed to demonstrate that a difference is great. On the other hand, if rare events are being researched, numbers will be large.

Depending on specific characteristics of the MD, patient recruitment may sometimes be limited. In this case, it may be beneficial to implement **international multicentre studies** and emphasise the support role of assessment agencies.

³⁶ Article L1151-1 of the French Public Health Code

3.3.6. Management of protocol deviations and missing data

Bias in follow-up may appear during the course of the study. This can translate into a difference in the level of study “drop-outs”, namely with treatment discontinuations, patients lost to follow-up or use of concomitant treatments.

Study “drop-outs” can be related to adverse events or a lack of therapeutic efficacy. This may result in a disappearance of the effect related to the treatment, or conversely, the appearance of a false difference.

The experimental plan must be designed to minimise the number of patients lost to follow-up or who withdraw from treatment. The manufacturer, in cooperation with the investigators, should implement all possible means to limit these biases.

3.3.7. Data quality

The protocol must report the methods that will be used to limit the number of patients lost to follow-up and missing data. Quality control of data is essential. It should be described with precision for both the investigator sites and the database used.

3.3.8. Methodological specificities for the assessment of connected medical devices (CMDs)

CMDs have common specific features related, in particular to their very high speed of technological evolution, their interaction with other devices/objects/platforms or the existence of expert systems to process the information. These specific features need to be taken into account in the methodological choices to be implemented for the clinical development of these MDs.

[A guide designed to help companies manufacturing or operating a CMD](#) to anticipate the clinical requirements demanded by the CNEDiMTS to determine their usefulness with a view to their reimbursement by national solidarity is available on the HAS website (25).

3.4. Clinical development strategy

It is essential to have a **strategic and anticipatory vision** from the design of the clinical development plan. This means anticipating, from the outset, the aspects that will add value to the MD until it is made available to the patient.

This approach enables the project leader **to save time** by avoiding, for example, having to start a new study, in addition to the study conducted for CE marking at the time of the MD’s arrival on the market, in order to meet HAS requirements on clinical benefit data from a therapeutic strategy or disability compensation point of view.

If, for example, reimbursement of the MD is planned in France, it would then be appropriate, before implementing clinical research to obtain CE marking, to take into account the clinical requirements that will be required by the CNEDiMTS in order to anticipate them. **The studies obtained could then be useful throughout the MD pathway.**

For devices with embedded functions based on artificial intelligence such as automatic learning processes, a descriptive list has been added to the guide for submission of applications to the CNEDiMTS to specify the type of information expected (11).

4. Post-marketing surveillance and clinical follow-up

Once CE marking has been obtained, surveillance and medical device vigilance must be put in place in order to continuously assess the risks associated with the use of the MD. At the same time, once access to reimbursement is obtained, a post-inclusion study may be requested in some cases in order to obtain new data about the **clinical performance** with a view to renewal of inclusion.

4.1. Surveillance and medical device vigilance

4.1.1. Medical device vigilance

Medical device vigilance concerns all medical devices after their marketing, whether or not they have CE marking, apart from those subject to clinical investigations³⁷.

Medical device vigilance aims to avoid serious incidents and risks of serious incidents jeopardising medical devices (re)occurring, by taking appropriate preventive and/or corrective measures (26).

Regulation (EU) 2017/745 modifies the rules of medical device vigilance³⁷.

4.1.1.1. Case-by-case medical device vigilance

Operators must notify the ANSM of the following elements:

- ➔ any serious incident (except those involved in trend reports);
- ➔ any corrective safety measure taken with regard to a device on the market in the European Union;
- ➔ the report will be made upon establishment of imputability and, in any event, within the time frames specified below:

Once the Vigilance module in Eudamed becomes operational, operators will be able to submit this report via Eudamed. From May 2022, the use of Eudamed to submit these reports will be compulsory.

It should be noted that healthcare professionals or users may report any adverse events to the national health authorities on the signalement-sante.gouv.fr website, including adverse reactions, incidents or risks of incidents related to health products.

Table 3. Maximum time frame for medical device vigilance before reporting to ANSM

	Serious incident	Death or unanticipated serious deterioration in a person's state of health	Serious public health threat
Maximum time frame for reporting after learning of the incident or threat	15 days	10 days	2 days

Except in an emergency, corrective measures must be reported to the ANSM before they are implemented.

³⁷ Chapter VII of European Regulation 2017/745

Serious incident:

Any incident that directly or indirectly led, might have led or might lead to any of the following:

- the death of a patient, user or any other person;
- the temporary or permanent serious deterioration of a patient's, user's or any other person's state of health;
- a serious public health threat.

Serious public health threat:

An event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness that may require prompt corrective measures, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time.

These definitions are from Regulation (EU) 2017/745.

Other types of incidents lead to optional reporting to the ANSM⁴⁴, but should be the subject of a trend report in accordance with Article 88 of Regulation (EU) 2017/745.

4.1.1.2. Assessment by ANSM

Assessment of incidents by the ANSM is carried out in 3 stages. After recording and sorting upon receipt of incident reports, the assessment is organised according to 4 procedures, 3 of which are defined by the criticality (the fourth procedure, independent of criticality, concerns global assessments). Incidents can be considered minor, major or critical. The methods and the procedure time frames given by the ANSM will depend on this classification. A global assessment may also be implemented for known incidents of a high frequency; they are then collected and statistically analysed.

Medical device vigilance contact person:

The French Public Health Code, via Article R.5212-13, specifies that all manufacturers of medical devices, or their representatives, must designate a medical device vigilance contact person and report their name to the ANSM.

4.1.1.3. Periodic summary report and trend report

When similar serious incidents relate to the same device or type of device, the cause of which has been determined or for which a corrective safety measure has been applied, or when incidents are common and well documented, the manufacturer may periodically send summary reports instead of individual serious incident reports³⁸.

Manufacturers must report, in a trend report via Eudamed, any statistically significant increase in frequency or severity of incidents that are not serious or which are expected undesirable side effects that may affect the benefit/risk ratio and may pose risks to the health and safety of patients

³⁸ Articles 86 to 87 of European Regulation 2017/745

4.1.2. Post-marketing surveillance

4.1.2.1. By manufacturers

For each device, manufacturers design, establish, document, apply, maintain and update a post-marketing surveillance system based on the risk class and type of device³⁹. This system is an integral part of the quality management system implemented by the manufacturer⁴⁰.

This surveillance system enables the active and systematic collection, recording and analysis of relevant data on the quality, performance and safety of a device throughout its lifetime, in order to draw necessary conclusions and to define and apply any preventive or corrective measures and to monitor them.⁴⁰

Documents relating to post-marketing surveillance make up Annex III of Regulation (EU) 2017/745, which is necessary to obtaining CE marking. It includes, in particular:

- ➔ The post-marketing surveillance plan on which the surveillance system is based and which aims to specify the methods and procedures that will be followed to proactively collect and assess clinical data.
 - This surveillance plan must include as a minimum a certain number of elements, including the plan for collection of clinical data to confirm the benefit/risk ratio of the PMCF (previously mentioned in this guide).
- ➔ The periodic safety update report (PSUR) (classes IIa, IIb, III) and the surveillance report (class I) which summarise the results and conclusions of the analysis of the surveillance data, stating the justification for any preventive or corrective measures taken and describing them
 - Post-marketing surveillance report: the report is updated when necessary and made available to the competent authority upon request.
 - Periodic safety update report (PSUR): established for each device and where relevant for each category or group of devices:
 - IIa: must be updated when necessary and at least every two years;
 - IIb and III: must be updated annually.
 - For class III devices, manufacturers submit the PSUR to the NB involved in the assessment. For other devices, the PSUR is made available to the NB involved.

Changes brought by the regulation:

The main changes concern the application for a PSUR or a surveillance report, which are included before development, in the surveillance plan.

4.1.2.2. By ANSM

The ANSM monitors the marketing conditions of MDs and ensures compliance of devices declared by the manufacturer with the regulations (27). It organises, on its own initiative or when requested by the Ministry of Health, implementation of permanent actions, one-time surveys and theme-based programmes.

³⁹ Articles 83 to 86 of European Regulation 2017/745

⁴⁰ Article 83 of European Regulation 2017/745

These market monitoring and assessment operations are not intended to determine the performance of devices, which is the responsibility of the manufacturer, but to demonstrate a possible nonconformity compared to the performance reported and/or compared to the state-of-the-art.

They may correspond to:

- one-time assessments of a single device;
- assessments focusing on an entire category of devices marketed in France.

For each of these assessments, two types of procedures can be used:

- dossier analysis (technical documentation, bibliography, etc.);
- technical analysis performed at the ANSM laboratories or at expert laboratories.

These operations may lead to requests for compliance, recommendations or restrictions of use, or withdrawal from the market.

These operations may also lead to the conclusion that there is no objection to the marketing. This conclusion of the conformity verification must not be presented as an endorsement or a validation of the medical device for commercial or promotional purposes.

Moreover, the ANSM performs surveillance of devices with specific risk and innovative devices. This activity is based on data sent by the manufacturers in the sector, and on innovation watch.

At national level, the ANSM also monitors:

- advertising: verification of compliance of advertising with the regulations in effect;
- observance of technical specifications.

4.2. Post-inclusion studies

Applications for a [post-inclusion study](#) may be requested when the device is included on the LPPR or following certain reviews of generic descriptions (28). In general, these requests for supplemental studies are the subject of a contractual clause between the CEPS and the company.

Post-inclusion studies on MDs aim to answer, for the French population, certain questions that still persist about these products, with a view to their renewal of inclusion or an anticipated re-assessment. These questions are generally of two types:

- the efficacy and safety of use of the device in the target population are not clearly demonstrated: in fact, it is not uncommon for additional clinical data to be necessary to confirm the efficacy and safety of use of the device in question;
- the transferability of the results of clinical studies to routine practice is not totally guaranteed: these problems of transferability may occur due to multiple factors (interactions with patient environment, different methods of use compared to those followed in the trials, heterogeneous experience of teams, suboptimal compliance, target population different from that included in the trials, etc.).

Thus, the main objectives of post-inclusion studies on medical devices are to provide “real-life” data. They are usually observational and may be performed on databases. The CNEDiMTS indicates the primary endpoint of the post-inclusion study and, if necessary, its secondary endpoints, in its opinion.

The Framework Agreement of 16 December 2011 between the CEPS and the professional organisations concerned specifies the implementation of these studies based on the method of reimbursement of the product or service (generic description, brand name). This Framework Agreement is in the process of being updated, but it is currently used as a guide in relations between the CEPS and companies or their professional organisations.

The objective of the studies, the obligation to establish a scientific committee, as well as the time frames in which the studies must be conducted and their results obtained are defined in the LPPR inclusion agreement for the product.

The draft study protocol is discussed at a tripartite meeting (CEPS, HAS, manufacturer) then submitted in its finalised version to the CNEDIMTS within 2 months so that it can return its opinion relative to the capacity of the study to answer the questions formulated by the CNEDIMTS in its opinion. Ultimately, it is the manufacturer's responsibility to conduct the study with the protocol it deems to be appropriate.

The results of conventional studies, including interim results when the agreement so provides, are submitted to the CEPS and to the CNEDiMITS during the application for renewal of inclusion of the MD in question. On the other hand, if they are of a nature that may alter the conclusions of the Committee, these results must be communicated without delay.

The decree of 25 August 2020 ⁴¹ specifies that the assessment of the actual clinical benefit for a renewal of inclusion can take into account "uncertainty consecutive to the absence - observed at the time of the new assessment - of essential additional information or studies demanded in a previous opinion issued by the Committee".

Note:

For any further questions, a [Frequently Asked Questions \(FAQ\)](#) – CNEDiMITS section can be found on the HAS website (www.has-sante.fr).

⁴¹ Decree No. 2020-1090 of 25 August 2020 relating to various measures relative to the reimbursement of health products

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Abbreviations and acronyms

ACB	Actual clinical benefit
AIMD	Active implantable medical device
ANSM	Agence Nationale de Sécurité du Médicament et des Produits de Santé (French National Agency for Medicines and Health Products)
CAV	Clinical Added Value
CCAM	<i>Classification commune des actes médicaux</i> (Joint classification of medical procedures)
CEESP	<i>Commission évaluation économique et santé publique</i> (Commission for Economic and Public Health Evaluation)
CEPS	<i>Comité économique des produits de santé</i> (French Healthcare Products Pricing Committee)
CI	Clinical investigation
CME	Health Care Organisation Medical Committee
CNEDIMTS	<i>Commission nationale d'évaluation des dispositifs médicaux et technologies de santé</i> (Medical Device and Health Technology Evaluation Committee)
CSP	<i>Code de la santé publique</i> (French Public Health Code)
CSS	Code de la sécurité sociale (French Social Security Code)
CT	Transparency Committee
DEAI, previously	<i>Direction de l'évaluation et de l'accès à l'innovation</i> (Assessment and Access to Innovation Division), previously <i>Direction de l'évaluation médicale, économique et de santé publique</i> (Medical, Economic and Public Health Evaluation Division)
DEMESP	
DRG	Diagnosis-related group
IVDMD	In vitro diagnostic medical device
IMD	Implantable medical device
ED	Early dialogues
EU	European Union
EUDAMED	European Database on Medical Devices
HAS	<i>Haute Autorité de santé</i> (French National Authority for Health)
ICER	Incremental Cost-Effectiveness Ratio
LNE/G-Med	<i>Laboratoire national de métrologie et d'essai dans le domaine médical santé</i> (National metrology and testing laboratory in medicine and health)
LPPR	<i>Liste des produits et prestations remboursables</i> (List of products and services qualifying for reimbursement)

MD	Medical Device
NB	Notified body
PMCF	Post-marketing clinical follow-up
PLV	<i>Prix limite de vente</i> (Sale price limit)
PSUR	Periodic Safety Update Report
SDC	Summary of device characteristics
SEAP	<i>Service évaluation des actes professionnels</i> (Diagnostic and Therapeutic Procedure Evaluation Department)
SED	<i>Service évaluation des dispositifs</i> (Medical Device Evaluation Department)
SSCP	Summary of Safety and Clinical Performance
TR	Tarif de responsabilité
QMS	Quality management system
UDI	Unique Device Identifier
UDI system	Unique Device Identification system
UDI-DI	UDI device identifier
UDI-PI	UDI production identifier
UNCAM	<i>Union nationale des caisses d'assurance maladie</i> (French Association of Health Insurance Funds)

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