# CE MARKING OF MEDICAL DEVICES

LNE G MED

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# Table of Contents

# 1. Introduction to the guide

The National Metrology and Testing Laboratory (LNE) is a widely-recognized European Notified Body with lots of experience in the European regulations. As a Notified Body, LNE evaluates and certifies a wide range of business and consumer products to be sold in Europe. LNE wanted to focus its expertise on the certification of medical devices within its subsidiary, LNE/G-MED. This subsidiary focuses on the medical device market to help manufacturers market their devices in Europe.

This guide is for medical device and in vitro medical device manufacturers who may call on LNE/G-MED to receive the necessary certificates for CE Marking to put their products on the European market. This guide is no substitute for the regulations or the official guidance documents.

To comply with the provisions of the Directives, manufacturers must develop a strategy. The Directives governing medical devices are not guidelines, but rather laws that must be followed. While the Directives may seem straightforward, the reality is that implementing the requirements is usually much more difficult than initially perceived. As a result, it is important to develop a strategy for implementing the Directives' requirements. With this Guide, LNE/G-MED will explain the requirements in the Directives, giving the manufacturer the ability to create a strategy unique to their device that will help usher their device into Europe.

Even though complying with the directives could be difficult, the directives also offer the manufacturer choices. Manufacturers face an optimization problem as they must reflect the interests and realities of their business. This guide, we hope, will help to determine the solution that is best suited to the manufacturer and make the best possible route for the manufacturer, along with LNE/G-MED to put its products on the European market. To do so, this guide aggregates the main content of the guidance documents for each issue addressed and discusses the links with the most relevant European standards.

LNE/G-MED is available to manufacturers to discuss any questions raised by their specific situation. Through Regulatory and Technical Assistance, LNE/G-MED helps to formulate a strategy that is best suited to the manufacturer.

# 2. The Regulatory Scheme for Medical Devices in Europe

## 2.1 Context

By the **"Single Act"** in December 1985, the Member States of the European Economic Community (EEC) created an area with no internal borders to allow the free movement of people, goods, and services. Practically, this meant the removal of technical barriers to trade. These had their origin in the national technical rules and regulations which showed specific differences from one country to another.
For medical devices these internal borders were especially onerous because each country maintained its own safety laws.
They could not be removed by substituting these national regulations harmonized Community rules guaranteeing a high level of protection for the user and the consumer safety and health.
However, the **"New Approach"** harmonized many technical barriers, allowing for freer medical device trade within the EEC.

Some major objectives and principles of the "New Approach" are:

- Freedom of movement for CE-marked devices throughout the European Economic Area;[1]
- CE marking is mandatory for marketing medical devices in Europe, except for devices intended for clinical investigations, "custom-made" devices[2], or IVDs for performance evaluation;
- CE marked devices conform to all the "Essential Requirements" as defined in the relevant directives.
- The procedures for determining compliance with the Essential Requirements. These procedures include when a manufacturer would use a third party, or a notified body. Notified bodies issue certificates that are valid for marketing a device across the European Economic Area, regardless of which Member State the notified body comes from.
- Implementing the Directives requires transposing them into national law after they are published in the Official Journal of the European Community. The EU Directives are addressed to the Member States, so the Member States incorporate the Directives' provisions into their laws and regulations without making changes to the provisions.

The Directives cover the definitions of the various types of medical devices, who is responsible for marketing medical devices, and coordinating with Notified Bodies and other actors in the regulatory process. In this framework, the three principal directives adopted that relate to medical devices are:

- Active Implantable Medical Device Directive (90/385/EEC of 20 June 1990), modifying directive 93/42/EEC, modified by directive 93/68/EEC, modified by regulation 1882/2003, modified by directive 2007/47/EC;
- Medical Device Directive (93/42/EEC of 14 June 1993), modified by Directive 2007/47/EC of 5 September 2007, modified by directive 2001/104/EC, modified by regulation 1882/2003, modified by directive 2007/47/EC; and
- In Vitro Medical Device Directive (98/79/EC of 27 October 1998), rectified by the corrigendum of 25.5.2000, modified by regulation 1882/2003 and regulation 596/2009.

Other directives that apply to more specific medical devices also apply.

[1] The European Economic Area (EEA) consists of the member states of the European Union, Norway, Iceland and Liechtenstein which are member states of the European Free Trade Association (EFTA).

[2] 93/42/EEC

Their relations with the three principal directives are defined in their text:

- Medical Devices Incorporating a Human Blood Derivative or Human Plasma (2000/70/EC of 16 November 2000);
- Breast Implants (2003/12/EC of 3 February 2003);
- Medical Devices Using Substances of Animal Origin (2003/32/EC of 26 April 2003); and
- Reclassification of Hip, Knee, and Shoulder Joint Replacements in the Framework of Directive 93/42/EEC Relating to Medical Devices (2005/50/EC of 11 August 2005).

### 2.1.1 Particular Case of the Common Technical Specifications

Directive 98/79/EC introduces, for its most critical devices – those mentioned in its Annex II List A and List B, if any – the concept of common technical specifications (CTS). They establish criteria for evaluation and re-evaluation of performance, batch release criteria, reference methods and reference materials. They are prepared by experts from Member States authorities, formally adopted and published in the OJEU. Manufacturers are generally required to comply with the CTS. If, for duly justified reasons, they do not comply with those specifications, they must adopt solutions of an equivalent level.

These texts are available at:
http://ec.europa.eu/health/medical-devices/regulatory-framework/legislation/index_en.htm
http://ec.europa.eu/health/medical-devices/documents/index_en.htm

## 2.2 To which products do the Directives apply?

In all cases, it is fundamental that before a manufacture gets to the Essential Requirements, it must determine and verify which regulation governs their product's market entry. To figure out which devices are covered by which Directives, a manufacturer can look at the first articles of the Directives, which contain the definitions and exclusions.

The Medical Device Directive[1] defines medical device as:

> ...any instrument, apparatus, appliance, software, material, or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:
>
> - diagnosis, prevention, monitoring, treatment or alleviation of disease,
> - diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
> - investigation, replacement or modification of the anatomy or of a physiological process, control of conception,
>
> and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.[2]

[1] 93/42/EEC

[2] 93/42/EEC Art. 1(2)(a).

The In Vitro Diagnostic Medical Device Directive[1] defines in vitro medical device as:

> ...any medical device which is a reagent, regent product, calibrator, control material, kit, instrument, apparatus, equipment, or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information:
>
> - concerning a physiological or pathological state, or
> - concerning a congenital abnormality, or
> - to determine the safety and compatibility with potential recipients, or
> - to monitor therapeutic measures.
>
> Specimen receptacles are considered to be in vitro diagnostic medical devices. 'Specimen receptacles' are those devices, whether vacuum-type or not, specifically intended by their manufacturers for the primary containment and preservation of specimens derived from the human body for the purpose of in vitro diagnostic examination.
>
> Products for general laboratory use are not in vitro diagnostic medical devices unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination.[2]

Further details on the interpretations of these definitions are detailed in the following MEDDEV guides
(cf §2.3):

- MEDDEV 2.1/1
- MEDDEV 2.1/2
- MEDDEV 2.14/1
- MEDDEV 2.14/2

Other devices that are not considered medical devices are:

- Medicinal products covered by Directive 2001/83/CE;
- Cosmetic products covered by Directive 76/768/EEC;
- Human blood and human blood products, human plasma or blood cells of human origin or to devices which incorporate at the time of placing on the market such blood products, plasma, or cells;
- Human transplants, tissues, cells, or products incorporating or derived from human tissues or cells;
- Animal origin transplants, tissues, or cells unless a device is manufactured using animal tissues rendered non-viable or non-viable products derived from animal tissues.

For the record, based on 14 years of experience, **the regulatory recast** that began in 2012 confirmed the extension of the medical device regulations of medical devices to certain products without direct medical purpose. These are products for esthetic purposes whose use may represent health hazards: non-corrective contact lenses, implants for augmentation, fixation or sculpting of body parts, skin fillers, liposuction devices, and lasers.

Regarding the field of diagnostic medical devices in vitro, software has been confirmed as part of the scope of the draft, together with, for example, products intended to screen for predisposition to a medical condition or disease.[3]

[1] 98/79/EC
[2] 98/79/EC Art. 1(2)(b).

[3] Editor's note: this data may change during the year 2012.

## 2.3 What can a manufacturer do when the regulatory texts don't answer his or her questions – Where to find interpretations?

Despite the drafter's best intentions, the reality of regulations and legislations is that sometimes they need to be clarified to be understood and applied in a consistent manner. To help readers, the European Commission develops guides and interpretive texts for the Directives to clarify some points. These guides are drafted by experts from different Member States, although it should be noted that they aren't legal texts as such. But these guides provide significant help in interpreting, applying, and avoiding mistakes with the Directives.

These texts, the MEDDEV guides, are interpretive documents or consensus statements that do not have a regulatory status. Therefore, the basis of a decision or action remains the Directives themselves and their implementation into national law of the Member States. However, their use represents an important aid for interpreting and applying the Directives and avoiding mistakes with very damaging consequences

These guides can be found on the European Commission's website,[1] and others on NBOG's website.[2]

Finally, it is worth mentioning the important guide to the European Commission intended to explain the concepts of the "New Approach." This guide, the Blue Guide, covers the placing all CE marked products on the European market and is not limited to medical devices.[3]

The experts from LNE/G-MED are able to help to analyze the contents of these different guides.

## 2.4 Who is responsible for placing medical devices on the market?

The directives define placing on the market as:

> ...the first making available in return for payment or free of charge of a device other than a device intended for clinical investigation, with a view to distribution and/or use on the Community market, regardless of whether it is new or fully refurbished.

An interpretive document from the European Commission is available on this point at: http://ec.europa.eu/health/medical-devices/files/guide-stds-directives/placing_on_the_market_en.pdf.

Putting into service is:

> ...the stage at which a device has been made available to the final user as being ready for use on the Community market for the first time for its intended purpose.

[1] http://ec.europa.eu/health/medical-devices/regulatory-framework/index_en.htm.
http://ec.europa.eu/health/medical-devices/documents/consensus-statements/index_en.htm
http://ec.europa.eu/health/medical-devices/documents/interpretative-documents/index_en.htm

[2] http://nbog.eu/index.html

[3] http://ec.europa.eu/enterprise/policies/single-market-goods/files/blue-guide/guidepublic_en.pdf

### 2.4.1 Manufacturer

The manufacturer takes the responsibility for placing the medical device on the market. The Directives define a manufacturer as:

> The natural or legal person with responsibility for the design, manufacture, packaging and labelling of a device before it is placed on the market under his own name, regardless of whether these operations are carried out by that person himself or on his behalf by a third party.
>
> The obligations of this directive to be met by manufacturers also apply to the natural or legal person who assembles, packages, processes, fully refurbishes and/or labels one or more ready-made products and/or assigns to them their intended purpose as devices with a view to their being placed on the market under his own name. This subparagraph does not apply to the person who, while not a manufacturer within the meaning of the first subparagraph, assembles or adapts devices already on the market to their intended purpose for an individual patient.

If a manufacturer has no registered offices in Europe, it must appoint an authorized representative in one of the Member States. The manufacturer could then instruct the authorized representative to take over some of the conformity assessment procedures. So, the authorized representative would seek the help of a notified body at the manufacturer's request.

In the context of fulfilling its statutory responsibilities, the manufacturer must pay particular attention to its relations with the subcontractors involved in the design and manufacturer of the product, as well as potential distributors. A proxy must be appointed if the headquarters of the manufacturer is not the territory of the European Economic Space or Switzerland.[1]

### 2.4.2 Other Parties

Sometimes, in specific situations, other parties are also responsible for putting a device on the market along with the manufacturer. These parties are:

**Authorized Representative** of the manufacturer is a legal person established in the EEC who acts as the face of the manufacturer to the Competent Authorities. More information about the Authorized Representative, its role, and its responsibilities can be found in MEDDEV 2.5/10.
**Subcontractors or suppliers** of the manufacturer who may be involved when establishing the conformity of the device. Information about the control of the suppliers and subcontractors may be found in the NBOG Best Practice Guide 2010-1.
**Distributors** can also be involved when:

- It is the European-based importer for a non-European manufacturer; and
- The distributor can be intermediary for transmitting post-market surveillance information

While it may seem confusing, LNE/G-MED is here to help discern which parties must be involved in a device's certification. To establish which parties must be involved in your device's certification, contact LNE/G-MED to speak with a project manager or one of our regulatory experts.

[1] See guide "MEDDEV 2.5/10" (cf 2.3)

## 2.5 Role of Notified Bodies

As a third party officially nominated by their respective national authorities, notified bodies issue statutory certificates that manufacturers need to get their products on the market. As a result, notified bodies are key to performing the conformity assessments that the Directives establish.

The main task of the notified body is to provide conformity assessment services according to the Directives, taking into account all of the guides, interpretive material, and standards. These activities include:

- Confirmation of the classification of medical device by the manufacturer taking into account the classification rules defined in the guidelines;
- And depending on the class,
- The compliance of the medical device (testing, release of manufactured products, ...);
- The compliance of the manufacturer's quality system (on-site audit);
- Assessment of the technical documentation of the medical device, whether systematically, for the products most at risk, or on a sampling basis for medium-risk products; and
- Assessment of critical subcontractors.

The purpose of the quality system audits is to verify that the manufacturer defines, documents, and implements a coherent set of policies, procedures and practices to control and manage its business. The quality system must comply with applicable regulatory requirements. Examination of technical documentation and testing are intended to verify compliance of the medical device to all essential requirements.

A favorable assessment of the quality system and / or technical documentation allows the notified body to issue CE certificates. These certificates are necessary for the manufacturer to issue a declaration of conformity prior to placing the device on the market. This is the manufacturer's responsibility, that after verifying that all requirements are met and, where applicable, that all the notified body's necessary assessments lead to a CE certificate.

LNE / G-MED is actively involved in the European Commission-sponsored group of Notified Bodies, NB-MED. NB-MED meets twice each year in Brussels, Belgium, with European Commission and major professional European medical device manufacturers' organizations' representatives. During these meetings, practical issues that can lead to differences of interpretation or action are identified and openly discussed. These discussions result in consensus statements and recommendations that are written and prepared by task forces and overseen by the Group of Notified Bodies Recommendations (NBRG).

LNE / G-MED is also a member of the Professional Association Team NB.[2] As such, it was one of the five notified bodies responsible for drafting the Code of Conduct (CoC). The CoC intends to contribute to improving the implementation of the certification of medical devices under the CE marking by specifying criteria or jurisdictional elements relating to methods of assessment.

[2] http://www.team-nb.org/.

# 3. What should a manufacturer do before contacting LNE/G-MED or another Notified Body?

The process outlined in the Directives allows a manufacturer to enter the European market in accordance with Directives 90/385/EEC, 93/42/EEC and 98/79/EC (see § 2.1.) goes through several stages and involves some choices. Unsuitable choices can lead to extended delays or increased costs required to obtain certificates and possibly lead to deadlock.

**Defining the best approach is of strategic importance.**

The main steps are:

1. Identifying the "Manufacturer" and, where applicable, its agent, its subcontractors and distributors;
2. Characterizing the products;
3. Determining applicable Directives;
4. Determining product classes for Directives 93/42/EEC and 98/79/EC;
5. Selecting the most appropriate procedures to determine compliance - "Methods of proof"
6. Collecting necessary data for the chosen procedures or, in particular for meeting the demands of certain "horizontal" provisions (risk analysis, clinical evaluation, performance evaluation (IVD) etc.); and
7. Consulting LNE / G-MED once the appropriate procedure is decided.

These milestones are the subject of the sub-chapters below.

## 3.1 Who is the "Manufacturer" of the Product?

The definition referenced in § 2.4 of this guide enables a company, on the basis of its activity and methods of marketing the product, to define whether it will be considered the product manufacturer.

It should be noted that if an authorized representative is required, then the manufacturer may instruct his authorized representative established in the EEA, engaging some of the procedures laid down in Directives, including Annexes III (EC type examination), IV (EC verification ) VII (EC Declaration of Conformity) and VIII (Devices for special purposes) of Directive 93/42/EEC or Annex III (EC Declaration of Conformity), V (EC type examination), VI (EC verification), VIII (Statement for devices intended for performance evaluation) of Directive 98/79/EC.

## 3.2 Characterizing the Product

Characterizing the product is fundamental because it speaks to which European Directive to use and the classes of the devices if they are medical devices according to Directive 93/42/EEC.

When the manufacturer establishes that the product meets the definition of an active implantable medical device (see 90/385/EEC), or a medical device (see 93/42/EEC), or a, in vitro diagnostic medical device (see 98/79/EC), or an accessory, it should respond to certain specific and detailed questions, including:

- What is the manufacturer's intended use for the device in question, which will be included in the documents accompanying the device (sales literature, catalog, label, user guide, etc.)?
- Does the device depend on a source of energy other than that directly generated by the human body or gravity for its operation?
- Is a drug related to the use of the device? If so, how?
- Does the device incorporate products of animal origin?
- And any others.

## 3.3 Determining the Applicable Directives

By applying Article 1 of Directives 90/385/EEC, 93/42/EEC, and 2000/79/EC, manufacturers can determine which Directives apply to which products. It is also necessary at this stage if another, broader, directive applies (EURATOM, EMC, machinery etc.). Difficulties may arise for certain borderline products, like "protective equipment" (see Directive 89/686/EEC), cosmetics (Directive 76/768/EEC), and especially drugs (see Directive 2001/83/EC and further guidance).

The guide "MEDDEV 2.4 / 1 rev 9" (see § 2.3) and the manual "Borderline and Classification" (see § 3.4) provide guidelines for determining the boundary between medical devices and other products.

## 3.4 What is the Class of the Medical Device?

### 3.4.1 Case of Directive 93/42/EEC – Medical Devices

The devices relating to Directive 93/42/EEC are broken up into four classes based on risk: I, IIa, IIb, and III.
Medical devices are classified according to the rules contained in Annex IX to this Directive. Parts I and II of this Annex provide definitions and methods for applying the classification rules. It is imperative to review the 18 rules of Part III of Annex IX, as it is common that many of these rules are applicable to the same product. In these cases the device's class is the highest class. These rules are based on the following criteria:

- Duration of use;
- Invasive or not, and type of invasiveness;
- If the device is re-usable;
- Therapeutic or diagnostic;
- If the device depends on a source of energy; and
- The part of the body in contact with the device.

In the MDD, There are five major classification groups:

- Rule 1 to 4 : Non-Invasive Devices, but these rules may cover devices in contact with wounds or biological fluids;
- Rule 5 : Devices that are invasive via a body orifice, which includes permanent artificial openings;
- Rules 6 to 7 : Devices that are invasive via surgery;
- Rule 8 : Long-term implantable and invasive devices;
- Rules 9 to 12 : Additional rules for active devices; and
- Rules 13 to 18 : Special rules intended for special categories of device, like contact lens solution.

### 3.4.2 Case of Directive 98/79/CEE – In Vitro Diagnostic Devices

Although we are not talking about class, in vitro diagnostic medical devices are divided into 2 groups: IVDs that fall within Lists A (safety) and B (diagnosis) of Annex II and those that are not on these lists. The guides MEDDEV 2.1 / 3 rev 3 (see § 2.3), MEDDEV 2.1 / 6, MEDDEV 2.17 / 1 rev 2 and the manual Borderline and Classification (see § 2.3) provide guidelines for determining class of medical devices.

## 3.5 Choice of the Conformity Evaluation Procedures

The conformity evaluation procedures are designed to evaluate compliance with the essential requirements of the directives. They are the main obligations of the manufacturer for the placing medical devices on the market in the EEA. Once a device gains compliance according to the procedures, the manufacturer may affix the CE marking on the device in question and put it on the market.

The choice of the procedure, which is the manufacturer, must be performed as described in:

- Article 9 of Directive 90/385/EEC as amended by Article 21.3.2 of Directive 93/42/EEC for active implantable medical devices (AIMD);
- Article 11 of Directive 93/42/EEC for other devices (MD), depending on the class to which the device in question, a class which was previously determined as described in section 3.4. of this guide; and
- Article 9 of Directive 98/79/EC for medical devices for in vitro diagnosis according to reagent grade (or related item) to see why, Annex II of the Directive.

Choosing the procedure best suited to the manufacturer's needs can be guided by the following criteria:

- The operation of the business for the organization to ensure the required quality (quality system); and
- How to design and manufacture of medical device taking into account the share of outsourced processes.

For each of the three directives, the evaluation procedure is a combination of the following modules, taking into account the device's class:

| Modules | Directive | | |
|---|---|---|---|
| | 90/385/EEC (AIMD) | 93/42/EEC (MDD) | 98/79/EEC (IVDD) |
| CE Declaration of Conformity Full Quality Assurance System<br>• Design examination included or not included<br>• Production Quality Assurance included or not included | Annex II | Annex II | Annex IV |
| CE Type Examination | Annex III | Annex III | Annex V |
| CE Verification | Annex IV | Annex IV | Annex VI |
| CE Declaration of Conformity – Production Quality Assurance | Annex V | Annex V | Annex VII |
| CE Declaration of Conformity – Product Quality Assurance | NA | Annex VI | NA |
| CE Declaration of Conformity | NA | Annex VII | Annex III |

The Directives state which procedures are possible with each class. Flow charts showing the procedures are included in Appendices A and B. Essentially, the conformity assessments have two aspects:

- Evaluating the design of the medical device to determine if it meets the requirements of the Directives; and
- Assessing the ability of the manufacturer to mass produce conforming devices and to fulfill its regulatory obligations.

The manufacturer has the obligation to respect the regulatory process it chose prior to placing the device on the market and it must be able to demonstrate its approach. Also, depending on the class (or similar for IVD), it may also be required to verify compliance of this process by a third party: the notified body (see § 2.5).

Depending on the class (or similar for IVD) of the device, the choice of different possible procedures (methods of proof), the association consists of various modules. And these procedures are shown in figures in Appendices A and B.

The only procedure that doesn't require a Notified body is the "CE Declaration of Conformity." This procedure can only be used for Class I devices that are not sterile or that do not have a measuring function. Even in these cases, the Notified Body only assesses the points related to securing and maintaining sterile conditions or metrology.

# 4. Deciphering the Role of the Notified Body

Assessments, by LNE / G-MED are required and performed through the different types of evidence as described below.

**Note:** More detailed information on the contents of different dossiers can be obtained from the Certification Project Managers at LNE / G-MED.

## 4.1 Design: Examination of the Medical Devices' Design Conformity with the Essential Requirements

**The design examination** can be, according to the manufacturer's choice given the device's class, either:

- The responsibility of the manufacturer as part of the Declaration of Conformity (for example, Annex VII to the MDD or Annex III of 98/79/CE); or
- By the Notified Body according to the Product Design Examination or the Type Examination.

### 4.1.1 Design Examination

This is part of the "approval of the complete system of quality assurance" module. LNE / G-MED review the design from a file provided by the manufacturer. The design dossier must contain, in particular, data on the following:

- General description of the medical device;
- Design data: characteristics, safety and device performance;
- Data on the product realization;
- Information provided by the manufacturer;
- Risk Management (EN ISO 14971); and
- Compliance with the essential requirements

This information provides evidence of product conformity, such as reports of pre-clinical and clinical validation, quality system-approved procedures, and records related to the design of the device.
This module will result in a Certificate of design examination with a 5-year validity period according to the Directive. LNE/G-MED will also provide a design report review. The manufacturer must inform LNE / G-MED of any plan for substantial changes of the products covered.

### 4.1.2 EC Type Examination

LNE/G-MED will certify that a representative sample of the device's production meets the Essential Requirements. To do so, LNE/G-MED will examine and evaluate the design, manufacturing, and product performance documentation. It will also conduct inspections and tests necessary to ensure the device complies with the Essential Requirements. The Directives allow LNE/G-MED to issue an EC Type Examination certificate for 5 years, and LNE/G-MED will provide an EC Type Examination report. The manufacturer must inform LNE/G-MED of any plan for any substantial changes to the products that the certificate covers.

## 4.2 Evaluating the Manufacturer's Quality Management System

The manufacturer also chooses the route for the Notified Body, depending on the device's class, to assess its quality system of manufacturing and regulatory compliance:

- Under the manufacturer's direct responsibility as part of the "Declaration of Conformity" (for example, Annex VII in Directive 93/42/CEE or Annex III in Directive 98/79/CE);
- By the Notified Body as part of the "Complete Quality Assurance System," "Production Quality Assurance System," or "Product Quality Assurance System assessments;" or
- By the Notified Body as part of the EC Verification, done on a unitary or sampling basis.

### 4.2.1 Complete Quality Assurance System

In the Complete Quality Assurance System, LNE/G-MED will evaluate the manufacturer's quality system for the products that will be covered under the certificate, and it will ensure the system is continuously applied. Depending on the classes, point 4 of Annex II, "Design Review," may not apply. According to the class of the device, the part described in point 4 of Annex II "Design Review" does not apply. LNE/G-MED will perform all the audits annually as part of the certification cycle, and the manufacturer must inform LNE/G-MED of any substantial changes for the device or the covered products.

### 4.2.2 Production Quality Assurance

This module involves the approval and monitoring by LNE / G-MED, the quality assurance system for manufacture and final inspection of the products. LNE/G-MED will approve and monitor the manufacturer's quality management system for the manufacture and final inspection of the product. To do so, LNE/G-MED will evaluate the manufacturer's quality management system for the products and ensure the system is applied continuously. LNE/G-MED will also perform any necessary audit. The manufacturer must inform LNE/G-MED of any substantial changes to the approved system or the product coverage.

### 4.2.3 Product Quality Assurance

LNE/G-MED will approve and monitor the manufacturer's quality management system for the final inspection of the products. To do so, LNE/G-MED will evaluate the manufacturer's quality management system for the products and ensure the system is applied continuously. LNE/G-MED will also perform any necessary audit annually as part of the certification cycle. The manufacturer must inform LNE/G-MED of any substantial changes to the approved quality system or the product scope.

## 4.3 Evaluating the Conformity of Each Lot of the Product

### 4.3.1 EC Verification

LNE/G-MED will make examinations and tests by checking every product or statistical control of a homogenous sample of each bath (batch sampling) to ensure the device complies with the Essential Requirements. LNE/G-MED will then issue a certificate.

## 4.4 Verification of Manufactured Products (The Only Assessment Procedure Under the IVDD)

For IVDs that are in Annex II, List A of the IVDD, this procedure is mandatory. The manufacturer will give LNE/G-MED the relevant batch reports immediately after the examinations and tests are performed. The manufacturer will also provide to LNE/G-MED the samples of the batches it produced. If LNE/G-MED detects any abnormalities in the samples that reveal a non-compliance with the Essential Requirements, LNE/G-MED must notify the manufacturer within an agreed-upon timeframe. The manufacturer cannot market the affected lots.

## 4.5 Case of Devices Incorporating a Medicinal Product

Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product, the Notified Body must, in addition, consult one of the Competent Authority for drugs appointed by the Member States or the European Medicines agency (EMA). This consultation consists of an assessment of the aspects linked to quality and safety of the combined devices, as well as the risk/benefits profile as part of an evaluation of EC type or design examination. The evaluation of the usefulness of the drug substance is the responsibility of the Notified Body.

More information can be provided by the MEDDEV Guidance 2. 1/3 rev 3.[1]

[1] http://ec.europa.eu/health/medical-devices/files/meddev/2_1_3_rev_3-12_2009_en.pdf

# 5. Demonstrating the Conformity to the European Regulatory Scheme: Some Key Principles

## 5.1 Demonstrating Product Conformity to the Essential Requirements

### 5.1.1 Essential Requirements

All the directives refer to the "Essential Requirements" as the technical conditions to which medical devices must comply in order to be put on the market. Annex I of these directives describe the Essential Requirements. Article three of Directive 93/42/EEC states, for instance, "The devices must meet the essential requirements set out in Annex I which apply to them, taking account of the intended purpose of the devices concerned."

Part I of Annex I describes the general requirements applicable to any medical device, including the risk management and clinical evaluation. Part II of this annex sets out the essential requirements, which are grouped according to the following themes:

| MD & AIMD | IVDD |
|---|---|
| • Chemical, physical, and biological properties;<br>• Infection and microbial contamination;<br>• Construction and environmental properties;<br>• Devices with a measuring function;<br>• Protection against radiation;<br>• Requirements for medical devices connected to or equipped with an energy source;<br>• Information supplied by the manufacturer | Same Essential Requirements as MD/AIMD, also includes rrequirements for self-testing devices for self-testing |

### 5.1.2 Risk Management

Included in the Essential Requirements is the concept that a manufacturer should eliminate or reduce risks as far as possible while designing and manufacturing the device. Manufacturers catalog these risks and the actions they take to eliminate and minimize these risks in a Risk Management File, part of the technical documentation for the device. The EN ISO 14971 standard is the European Harmonized Standard for risk management.

### 5.1.3 Clinical Evaluation

The clinical evaluation is the process that the manufacturer applies to identify, select, appraise, and critically analyze the clinical data to meet the applicable essential requirements of the MDD and the AIMDD. Clinical evaluations are not used for IVDs. There are four MEDDEVS that manufacturers can use to guide them in collecting the data and reporting on their clinical evaluations:

- MEDDEV 2.7/1 rev. 3 – Clinical Evaluation: Guide for manufacturers and notified bodies
- MEDDEV 2.7/4 – Guidelines on Clinical Investigations: a guide for manufacturers and notified bodies
- MEDDEV 2.12/2 rev. 2 – Post Market Clinical Follow Up Studies

#### 5.1.4 European Harmonized Standards

Because of the general nature of the essential requirements, as they apply to all medical devices, and the difficulty of guaranteeing a common approach from all manufacturers and Notified Bodies, the "New Approach" attributes a particular role and significance to standards. Where the European essential requirements provide the goals for proving a medical device's safe and effective performance, the harmonized standards provide methods for reaching those goals. Their application is not mandatory for placing on the market in the EEA, however the compliance with all European Harmonized Standards is a presumption of conformity with the essential requirements.

The bodies responsible for developing and ratifying these standards at the European level are CEN and CENELEC. Their national equivalents for France are AFNOR and UTE.

#### 5.1.5 Common Technical Specifications

Specifically, Directive 98/79/EC introduces (exclusively) for the most critical devices – those mentioned in Annex II List A and, if necessary, List B – the concept of "Common Technical Specifications." These specifications establish appropriate performance evaluation and re-evaluation criteria, batch release criteria, reference methods, and reference materials.

Experts of Member States Authorities set up these Common Technical Specifications, which were officially adopted and published in the OJEU of 3 February 2009.

Manufacturers are, as a general rule, required to comply with the CTS. If, for a duly justified reason they don't comply with those specifications, they must adopt solutions of an equivalent level.

### 5.2 Demonstrating Conformity of the Quality System

The European directives require the manufacturer to implement a quality management system for some classes of MD or IVDMD. The objectives and structure of the QMS are described within the corresponding annexes (see § 3 and 4).

EN ISO 13485 (Medical devices - Quality management systems - Requirements for regulatory purposes) is the European Harmonized standard on this matter. Specific attention should be paid to the European foreword of this standard. Indeed, Annexes ZA, ZB and ZC of EN ISO 13485:2012 show the comparison between the chapters of the standard and the requirements of the annexes of the Directives.

More information about what a QMS is expected to be may be found in the following guidance documents: NBOG BPG 2010-1 and NBOG BPG 2010-2 (http://nbog.eu/2.html).

# 6. Maintaining CE Marking

This chapter describes the measures taken by the manufacturer, as well as the obligations laid on the manufacturer, for the purpose of maintaining the CE marking for given devices over time.

Every device placed on the European market must conform to the essential requirements. Indeed, the concepts of **placing on the market and putting into service** refer to each individual product and not to a type of device.

This means that in this regard, two objectives must be met:

Objective 1: Controlling changes in the model.
**When the design of a model is changed, or when its manufacture is changed**, the change must not have the effect of removing its conformity with the essential requirements.

Objective 2: Each copy must be the same as the model.
**Each copy** of a model whose design has been approved by a Notified Body through application of one of the measurement procedures laid down in the directives or, where applicable, whose design has been declared in conformity by the manufacturer himself, must be made in such a way that it remains identical to the model.

**For this reason, the directives contain provisions that are intended to ensure the permanent maintenance of this conformity.**

## 6.1 Full quality assurance system

### 6.1.1 If the examination of the design of the product has been done

Changes to the approved design must receive further approval from the Notified Body which issued the EC design-examination certificate wherever the changes could affect conformity with the essential requirements of the directive or with the conditions prescribed for use of the product.

In addition, for diagnostic in vitro medical devices listed in annex II, list A, the manufacturer shall inform,

> ...immediately the Notified Body if it has obtained information about changes to the pathogen and markers of infections to be tested, in particular as a consequence of biological complexity and variability. In this connection, the manufacturer shall inform the Notified Body whether any such a change is likely to affect the performance of the concerned device.[1]

The manufacturer is responsible for declaring design changes to the Notified Body when these changes meet the conditions referred to above.

[1] Directive 98/79/EC annex IV, point 4.5

It may be said that if one or other of the following circumstances were to arise, but not limited to, a declaration should be made:

- Change in the "intended purpose" (indication or use intended by the manufacturer);
- Change in design having an impact on the results of the risk analysis or on the clinical data;
- Change in design having an impact on the declared performances;
- Substantial change in the instructions for use.

#### 6.1.2 General cases

The manufacturer must inform the Notified Body that approved the quality system of any plan for substantial changes to the quality system or the product range covered.

In addition, to check that the manufacturer applies his approved quality system permanently to all products placed on the market which are supposed to have originated in this system, the directives stipulate that surveillance audits shall be performed. LNE/G-MED performs this surveillance annually.

In addition, the Notified Body may pay unannounced visits to the manufacturer. At the time of such visits, the Notified Body may, where necessary, carry out or ask for tests in order to check that the quality system is working properly.

### 6.2. Production quality assurance

The content of § 6.1.2 above applies here, though its bearing is limited to the nature of the quality system initially approved (i.e. without taking control of design into account).

### 6.3. Product quality assurance

The content of § 6.1.2 above applies here unchanged, though its bearing is limited to the nature of the quality system initially approved.

### 6.4. EC type-examination

Changes to the approved product must receive further approval from the Notified Body that issued the EC type-examination certificate wherever the changes could affect conformity with the essential requirements of the directive or with the conditions prescribed for use of the product.

As in the case of EC type-examination, the applicant, who here may be the manufacturer's representative, is responsible for declaration.

The extent of change in a product which may require such a declaration is not specified in the directives, but in this regard the conclusions of paragraph § 6.1.1 of this guide may be applied.

In addition, for diagnostic in vitro medical devices listed in annex II, list A or list B, the manufacturer shall inform the Notified Body on changes of pathogen agent and infection markers, as stipulated in the paragraph § 6.1.1 of this guide.

## 6.5 EC verification

**Note:** This procedure must not be confused with the "verification of manufactured products" specific to certain in vitro diagnostic devices.

In this procedure, the Notified Body intervenes either for each copy placed on the market (unit verification), or for each batch released (statistical verification). The question of the maintenance, during the time, of CE marking conditions does not occur in this case.

**However, for devices placed on the market in a sterile condition**, the conditions for maintaining CE marking as described in § 6.2 of this guide apply for aspects regarding the securing and maintenance of sterility.

## 6.6 EC declaration of conformity

Here, the obligations the manufacturer has consist of keeping up-to-date technical documentation which is made available to the national authorities for inspection for a period five years at least after the manufacture of the last product marketed.

**However, as before, for devices placed on the market in a sterile condition**, the conditions for maintaining CE marking as described in § 6.2 of this guide apply for aspects regarding the securing and maintenance of sterility.

## 6.7. Verification of manufactured products

In the case of in vitro diagnostic medical devices covered by annex II, list A, the manufacturer shall forward to the Notified Body the relevant reports on the tests carried out on each batch of manufactured devices. Furthermore, the manufacturer shall make the samples of manufactured devices or batches of devices available to the Notified Body in accordance with pre-agreed conditions and modalities.

The manufacturer may place the devices on the market, unless the Notified Body communicates to the manufacturer within the agreed time-frame but not later than 30 days after reception of the samples, any other decision, including in particular any condition of validity of delivered certificates.

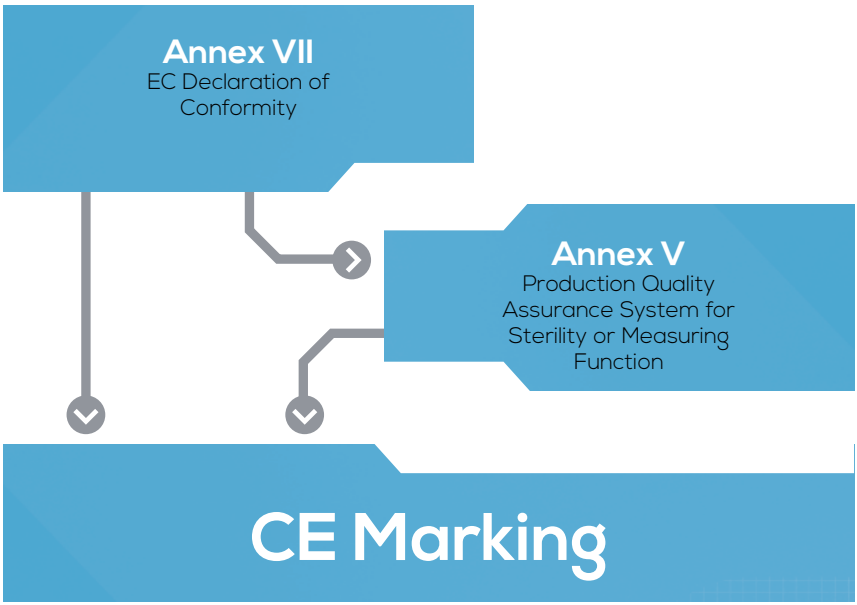
# 7. Conclusion

Marketing medical devices in Europe requires CE Marking and following the applicable regulations and standards for the devices. Forming a deep understanding the regulations is key to forming the regulatory strategy for the device's entry into the European market. This Guide, along with the expertise at LNE/G-MED, gives manufacturers this deep understanding of the regulations for creating an effective strategy. LNE/G-MED, as a Notified Body, enjoys a front-row seat to the European medical devices regulatory scheme and can help to open the European market for medical device manufacturers. Manufacturers can use this expertise and experience for their benefit by choosing LNE/G-MED as their Notified Body.

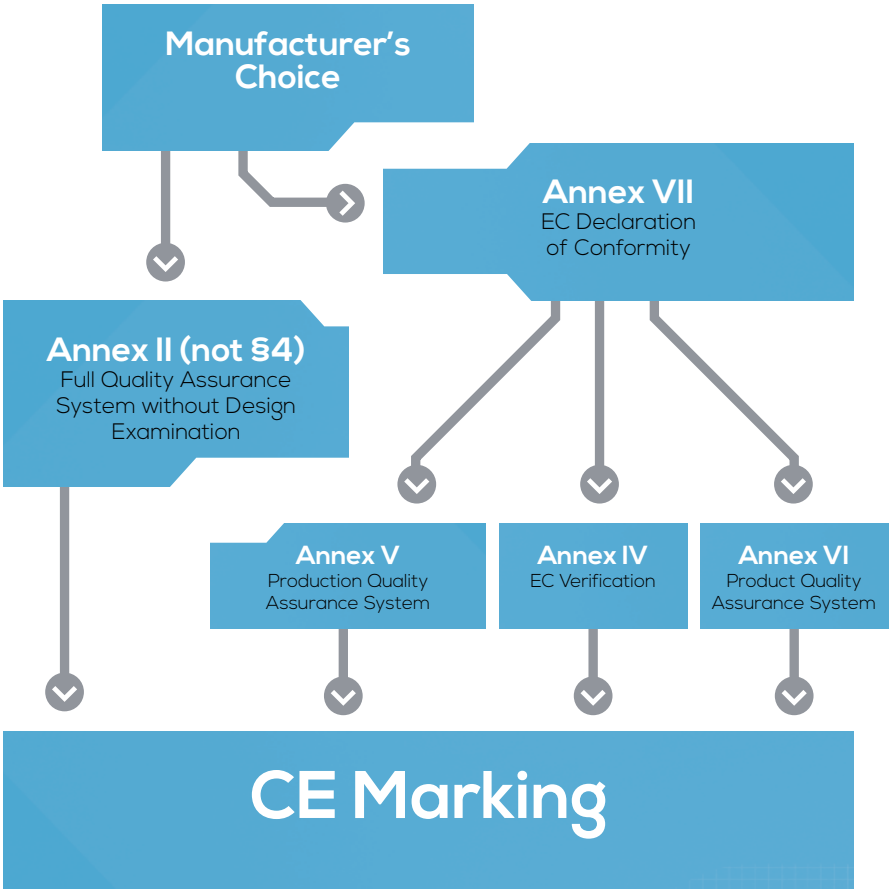
# Annexes

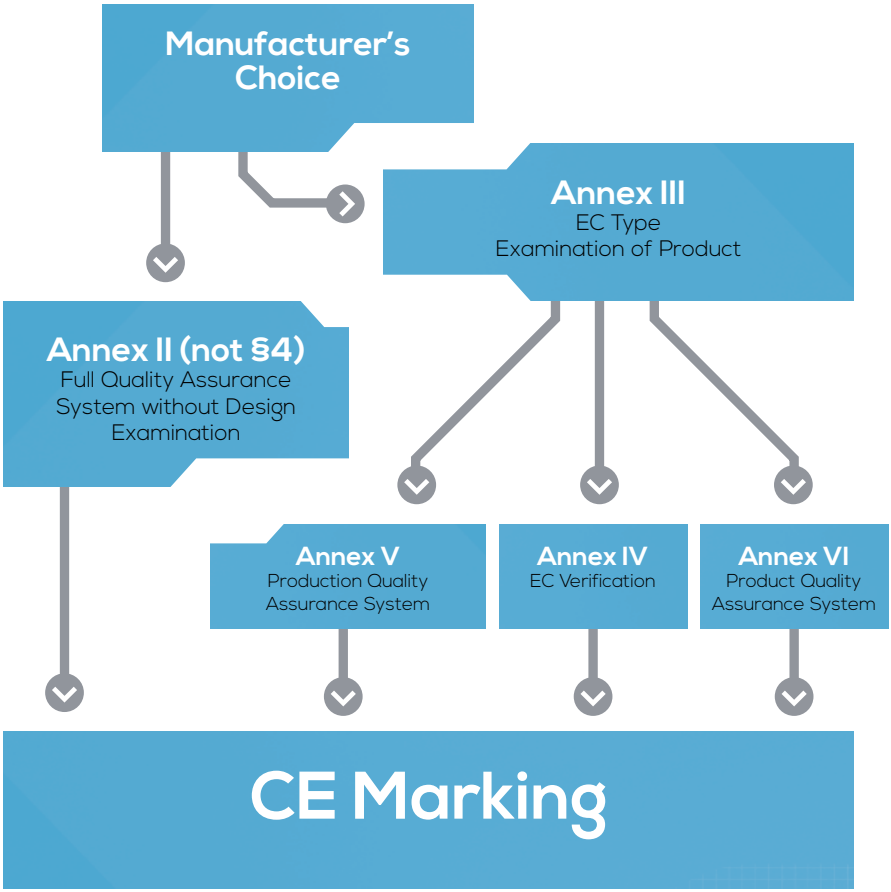
## Annex A: Conformity Assessment Routes for Medical Devices under Directives 93/42/EEC (MDD) and 90/385/EEC (AIMDD)

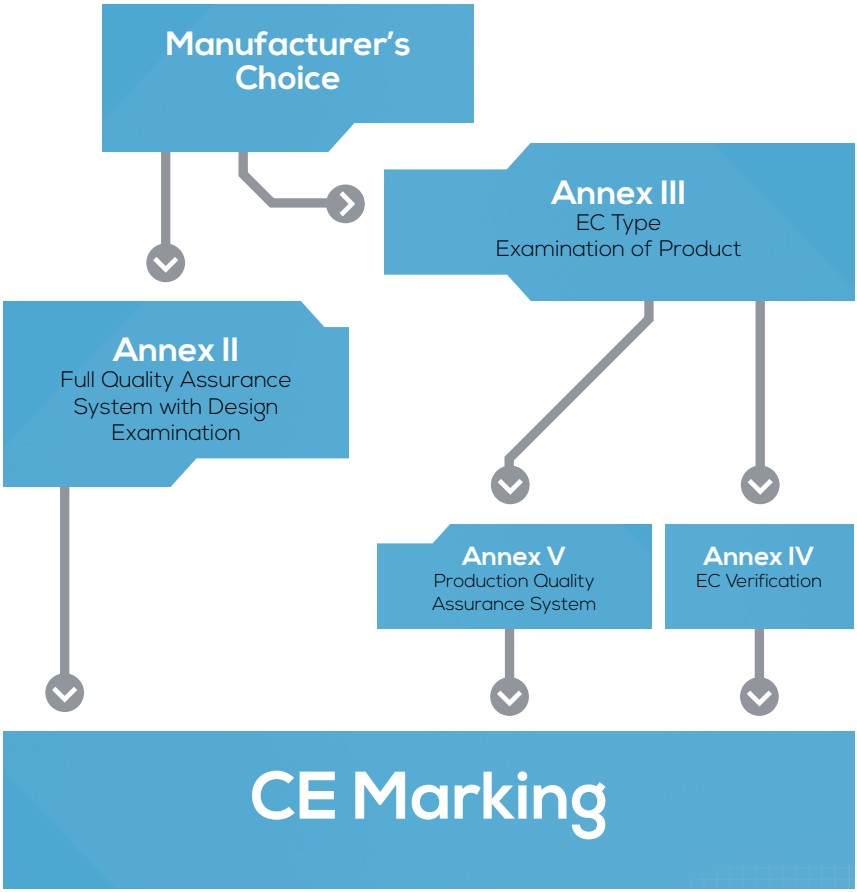
### Class I Medical Devices

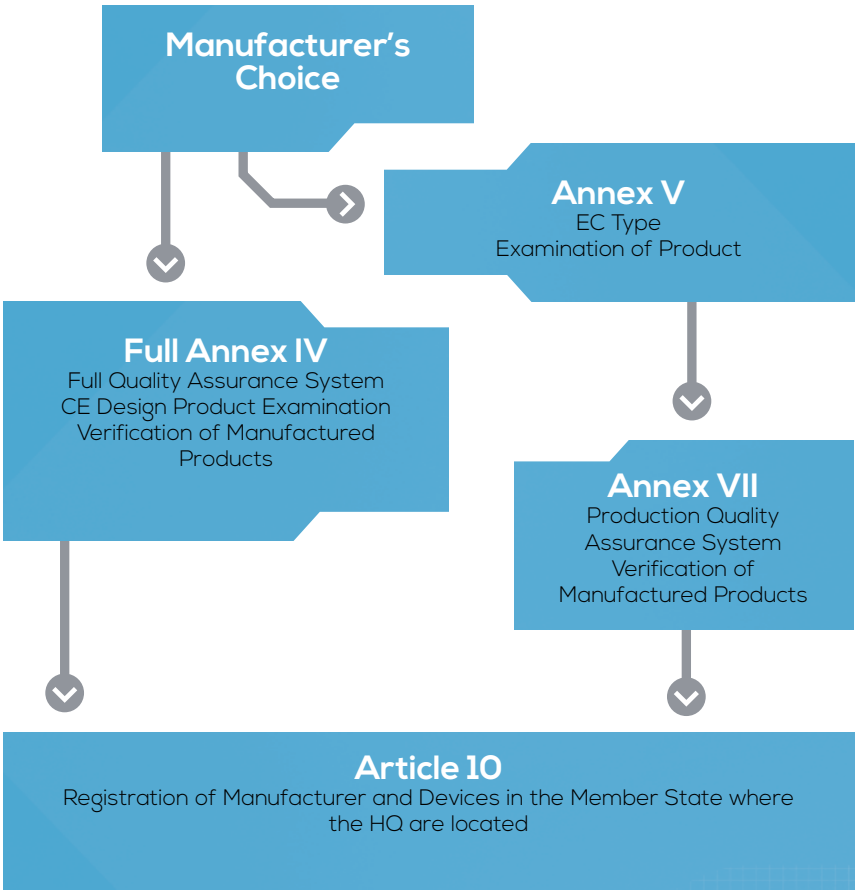


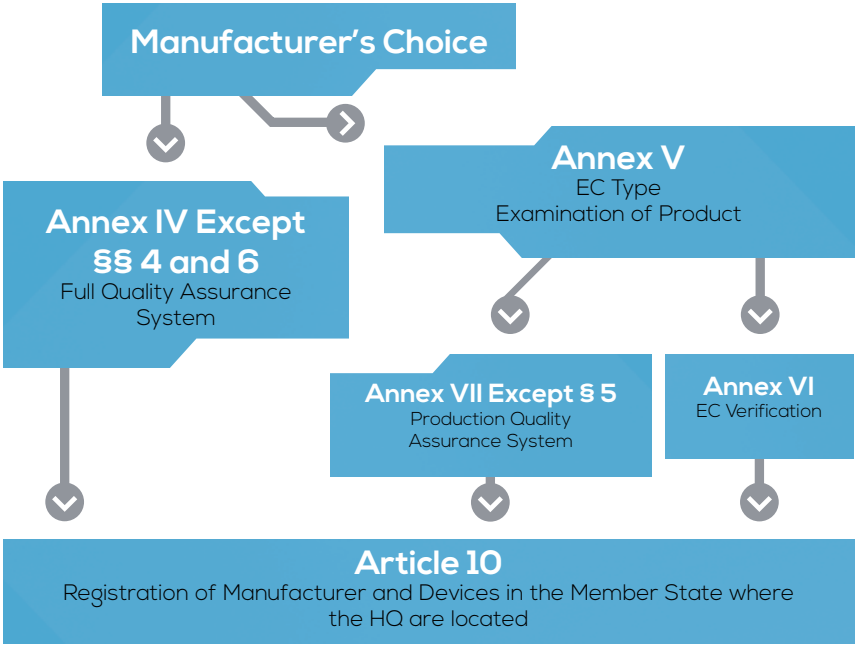
## Class IIa Medical Devices

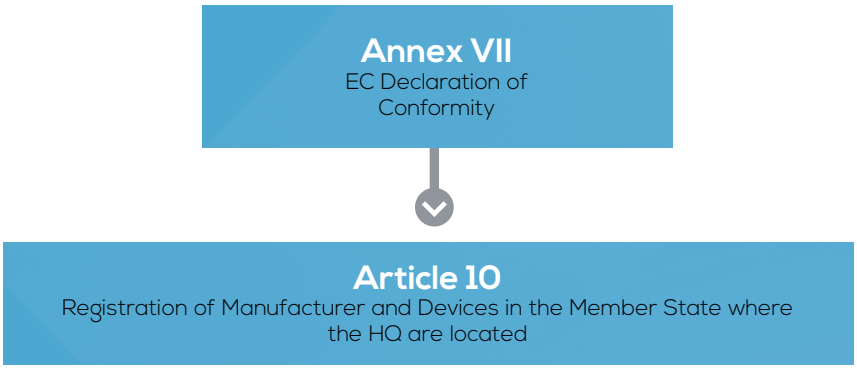










# Our services

## TESTING & CALIBRATION

- Electrical safety and EMC testing
- Climate-mechanical test (accelerated aging, transportation simulations...)
- Physicochemical testing
- On-site or in-laboratory measurements

## CERTIFICATION

Voluntary or Regulatory Certification

- LNE/G-MED, Notified Body CE 0459
- Management and issuing of NF Marks in the medical field
- Access to international markets: Canada, Brazil, Japan, Taiwan, Australia, New Zealand

## RESEARCH & TRANSFER

Serving the Safety and Health Industry

- Reference standard development
- Development of new methods
- Stakeholder in the normative field

## TRAINING & INFORMATION

- On-site or intra-company training courses (regulatory requirements, CE marking, risk management)
- Technical seminars (MD Forum, IVD Seminar, MRI compatibility seminar)

## TECHNICAL ASSISTANCE

- Technical/regulatory assistance
- Prototype Specification Drafting
- Benchmark Development
- Performance Validation

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