UNIVERSITÀ POLITECNICA DELLE MARCHE
FACULTY OF ENGINEERING

Master's degree in biomedical engineering

EUROPEAN CERTIFICATION PROCEDURES FOR MEDICAL DEVICES: TECHNICAL DOCUMENTATION FOR CLASS I MEDICAL DEVICES IN RELATION TO THE NEW EU MEDICAL DEVICE REGULATION 2017/745

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A.A. 2019/2020

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Introduction

The world of medical devices in this last year is facing with the entry into force of new European Union (EU) Medical Devices Regulation 2017/745 (MDR) repealing the actual Medical Device Directive (MDD) 93/42/EEC and the Active Implantable Medical Device Directive (AIMDD) 90/385/EEC.

From 1993 until now, the medical device field is ruled by the actual 93/42/EEC MDD that, over time, has some lacks in the traceability process of medical devices, low clinical evaluation and unclear roles of economic operators. In 2017 the European Commission decided to issue a new medical device Regulation known as a revolution in the medical device area.

The new MDR redefines not only the entire structure based on the number of the articles and chapters but also introduces and clarifies new figures and more clear roles of people that are involved. As a consequence, there is the need to understand and to study the new MDR improvement with respect to the actual and still valid MDD in order to place in the right way the devices on the European market. Therefore, the points of innovation and of dissonance between the new Regulation and Directive 93/42/EEC have been identified with regard to the essential requirements to be met, the classification of devices, the clinical investigations to be conducted, the assessments and management of the possible risks and the steps leading to the conformity assessment, in order to meet all the aspects necessary to obtain the CE marking.

This thesis deals with the role of the technical documentation in the marketing of a medical device. The technical documentation to be drawn up by the manufacturer, under the supervision of a qualified person such as the biomedical engineer, is intended to analyze the physical characteristics, technical, design and risk-related requirements to be met in order to obtain the CE marking from the competent authorities. The provisions to be followed when compiling a technical file relating to a medical device are contained in the Regulation issued by the Council of the European Union.

In order to apply the new Regulation to practical cases, Consultek Group srl gave me the opportunity to study devices, analyzing their physical, technical, design and risk characteristics and the essential requirements to be met, in order to proceed with the preparation of the technical file to be submitted to the supervision of a competent authority. These are devices covered by the definition of Class I medical devices proposed by the Regulation: FIDPAD nasal pad, three-points hyper-extender, anti-bedsore mattress and motorized bed base. In detailed, the entire work is organized in five chapters. The first chapter introduces the world of medical devices starting from the definition of a medical device and analyses the global market to the procedures to be place on the market a device and relative classification. The second chapter specified the current European regulatory framework, an overview

of Directive 93/42/EEC contents and contents regarding the new Regulation and, lastly, a comparison between them. Chapters three and four details the content of the MDR 2017/745 highlighting the strengths and innovations with respect to Directive 93/42/EEC both in the general contents and in the information to be included in the eventual preparation of a technical documentation by the manufacturer. In the last chapter, chapter five, the devices in question were presented to which the technical documentation was drawn up. Initially, it is described their characteristics and then studied the structure of the technical file, the user manual and label, and finally the basic steps and the method used for risk analysis.

Chapter 1

Medical Devices

1.1 Consultek Group

This thesis was carried out in collaboration with Consultek Group srl. The Consultek Group, certified ISO 9001:2015 and ISO 14001:2015, was founded in 2002 by the collaboration of several professionals, experts in different sectors of industry and services, who are periodically trained through continuing educations. The activity of the company is based on the design and provision of consulting and training services in management systems, risk management, health organizational systems and clinical risk, quality, environment and safety at work and CE marking.

In particular, the Consultek Group specializes in several areas:

- Management area: providing support to Organizations in verifying the adequacy and reliability of their organizational and management systems, business accounts and developing strategies for planning and mapping internal processes.
- Auditing area: offering an evaluation of an organization, system, process, project or product.
- Engineering area: offering technical services giving concrete support to Organizations from the design phase, implementation up to the marketing phase of their products, all in compliance with current legislation and regulations.
- Training area: offering a training service to companies on all activities provided in previous areas.

The work carried out in this thesis was concerned with providing consulting assistance to companies operating in medical sectors for the development of medical devices according to the new EU Medical Device Regulation 2017/745, developing the necessary technical documentation.

1.2 Definition of Medical Device

The term "medical devices" refers to a large number of products, such as instruments, apparatus, implants, substances, software and others, intended for use in humans or on humans for the purpose of diagnosis, prevention, control or therapy, attenuation or compensation of injuries or handicaps, but also study, replacement or modification of anatomy or a physiological process, or control of

conception [1]. Therefore, to determine if a product meets the definition of a medical device, it must be defined the intended use and indications for use of the product. Then it is possible to determine if the product meets the definition of a medical device, and so if it performs one of the previous functions that is not pharmacological, immunological or metabolic one. Among the most complex devices there are the active ones. They use sources of energy, that work through the power supply. Other complex devices are the implantable one, that can be short/medium term, for example a resorbable suture wire or permanently, as heart valve or joint prosthesis. Medical devices are not only used in healthcare environments, such as hospital and clinics, but also at home, like thermometers for body temperature measurements.

1.3 Classification of Medical Device

The EU established a classification of medical devices based on potential hazards related to their use but also possible failure considering both the technology used and the health policy. There are four classes of medical devices: Class I, IIa, IIb and III (Figure 1). The risk class determines if a conformity assessment by a notified body is required. A notified body is an organization that has been accredited by an EU Member State to conduct a conformity assessment under the relevant EU Directives and issue CE certificate [2].

As shown in Figure 1, class I medical devices have the lowest risk. In these cases, if the device is class I and it is not a sterile or measuring device (e.g., corrective glasses), the manufacturers can do a self-certificate of it and declare its compliance with the applicable requirement. On the other hand, if it is a sterile (e.g., personal protection kit) or a measuring device (e.g., stethoscope), the manufacturers need a notified body assessment. Then, class IIa medical devices, such as surgical gloves, hearing aids, have low to medium risk. They were designed for a short-term use, precisely less than 30 days. The manufacturers of these devices will have to request an assessment from a notified body before placing the product on the market. Afterwards, class IIb include medical devices such as surgical lasers or defibrillators. They are medium to high-risk devices and are long-term device, patients may use them for a period longer than 30 days. Similarly, the products need a notified body assessment.

To conclude, class III medical devices hold the highest risk and a constant monitoring, carried out by specialized institutions, is needed during their lifetime. Such devices are cardiovascular catheters, aneurysm clips, hip-joint implants, prosthetic heart valves, and others [3] [4].

In class IIa, IIb and III the conformity assessment may include an audit of the technical documentation and quality system inspection.

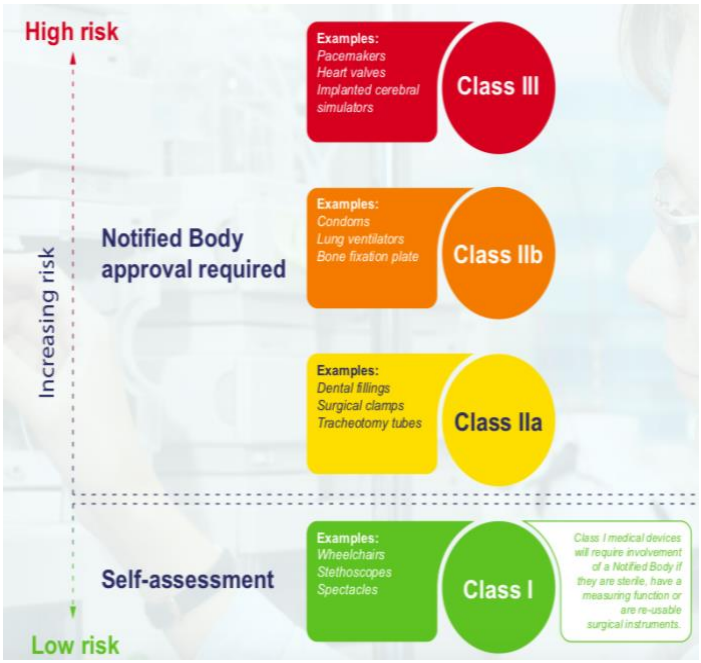


Figure 1: Classification of medical devices [3].

1.4 Social Environment for Medical Device

Since a few years ago the great focus on individual health has led to a continuous product innovation, and the consequent growth for medical technology companies due to increased demand for medical devices [5]. The USA is currently both the largest producer and the consumer of medical devices, with approximately 50% of the world market. It is followed by Japan, the EU, Canada, and Australia, which boast of large and stable markets with medical devices. Whereas the Europe boasts of some 25,000 medical technology companies. Most of them have their headquarters in Germany, the UK, Italy, Switzerland, Spain, and France. 95% of the medical technology industry comprises small and medium sized enterprises. Most of them have less than 50 employees [6].

Figure 2 shows an increased interest of survey participants in Brazilian, Russian, Indian, and Chinese markets. Another attractive market is the Mexican one due to a new and much more efficient regulatory system.

Potential sources of financing health care and the development of medical devices lie in the following funds:

- The European Regional Development Funds, which strengthens cohesion, namely economic, social, and territorial one, by redressing the balance among various regions.
- The European Social Funds, which is the main instrument of the EU for investing in its citizens,

- Horizon 2020.

Thanks to these innovations, constantly by now introduced into the market, more and more human lives are saved. Patients can access new operation not available before, the duration, complexity of these operations and hospitalization times are reduced, also the reduced sizing of products and the improved biocompatibility characteristics make them safer.

In particular, a significant data is the ageing of the population, as the elderly account for almost one third of total health consumption. Figure 3 represents the predict percentage growth in over-65 and over-80 inhabitants in the EU countries. In developed economies, aging population will drive the growth of medical device companies. More than 80% of people aged 65 years or above have at least one chronic disease [7]. Therefore, the worldwide spread of medical devices and the demand from both professional and private users is increasing.

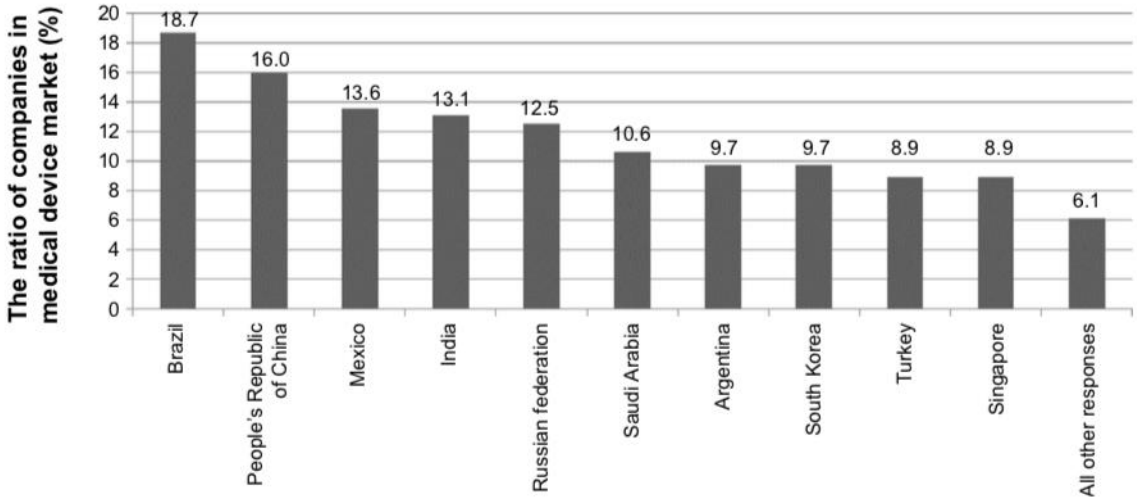


Figure 2: Emerging markets for medical devices [7].

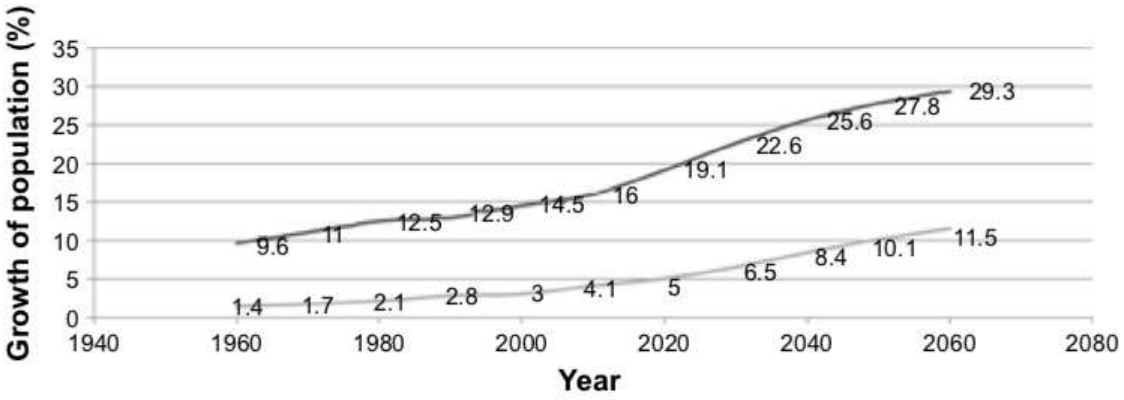


Figure 3: Percentage of growth population over the years. In dark grey the percentage of population aged 65 years and over on 1st January of selected years. In light grey the percentage of population aged 80 years and over on 1st January of selected years [7].

1.5 CE Marking

Medical devices must be CE-marked before they are placed on the market (in Europe) and this marking is indicated on the label and in the instruction for use by means of the CE symbol. The two letter which compose this brand must have the same vertical dimension, which may not be less than 5 mm, although this value may be adjust according to the dimension of the device (Figure 3).

In general, there are three scenarios: firstly, when a product is included in the scope of a directive providing for its application the product must be CE marked, then if the product does not fall within the scope of a directive the product cannot be CE marked and lastly if the product falls within the scope of several directives providing for its application, only one CE marking is needed, which indicate that the product complies with all applicable directives [8].

The CE is neither an initial nor an indication of origin, given the fact that products CE marked may also come from non-European countries. In addition, the CE symbol does not provide any indication about the quality of a product but means that the product meets safety requirements. These requirements, called "essential requirements", are established by European harmonization directives, applied in all 27 member states of the EU and in the member states of the European Economic Area (Norway, Iceland, Liechtenstein).

The CE mark guarantees that the essential requirements are necessary to all devices in the EU countries and, consequently, that the Competent Authorities of each Member State allow the circulation of devices manufactured in other Member States, on the basis of legal certainty as to the equivalence of such products with those which comply with the legislation applicable in their country [9].

Therefore, the challenge of all stakeholders is to allow the development and use of products that guarantee in themselves the requirements of safety and effectiveness and, at the same time, to counter all those practices burdened by ignorance, negligence or forgery.
The Directives demand minimum requirements for the assessment and certification of products and the possibility of obtaining the CE marking. The guarantees must be offered are:

- Information guarantee: a technical documentation of the product must be established. This includes specifications, plans, user manual, technical support service manual, labels and accompanying documentation [9].
- Guarantee of safety: it must be proved that the device complies with its corresponding regulations, according to its classification [9].
- Guarantee of completion of specifications and efficacy: clinical evaluation and, if necessary, clinical research for safety assessment and fulfilment of product specifications.
- Quality assurance: the company must set up a quality assurance system according to ISO 13485:2016, designed to respond to the latest quality management system practices, with the corresponding route that ensures its correct implementation [9].

The CE marking must be carried out by the manufacturer or his stand-in, provided that European, who claims through a declaration of conformity, that his product complies with the safety and health requirements laid down by the relevant directives.
For simpler medical devices, CE marking procedures involve only the manufacturer, while for more complex devices is necessary the intervention of a notified body (Table 1). In particular, certificates issued by the notified body, even when required by the directive, do not replace the CE marking of medical devices, but are an integral part of it.

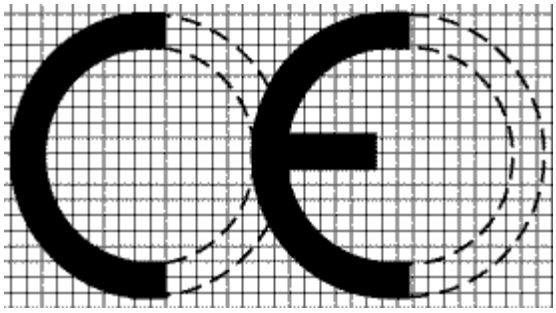


Figure 3: CE mark.

Table 1: List of Notified bodies per country [10].

Country	N° Bodies
Australia	5
Austria	32
Belgium	19
Czech Republic	13
Denmark	22
Finland	15
France	75
Germany	204
Greece	14
Hungary	4
Iceland	2
Ireland	4
Italy	179
Liechtenstein	0
Luxembourg	5
Netherlands	30
Norway	14
Portugal	21
Spain	48
Sweden	44
United Kingdom	206
United States	13

Chapter 2

Medical Devices Directives

The EU Council has issued directives in order to guarantee the proper safety to patients when using medical devices. These directives aim to regulate all the phases of a medical devices, including production, risk assessment and management, essential requirements, clinical investigations, CE marking and post-market and vigilance surveillance. All medical devices placed on the market in the EU must comply with the relevant Directive. The medical device directive covers a wide range of medical devices. In particular, the medical device regulation in the EU is governed by three directives for three different device categories:

- 90/385/EEC on active implantable medical devices, D.Lgs 14 December 1992, n. 507.
- 93/42/EEC on medical devices, D.Lgs 24 February 1997, n.46.
- 98/79/EEC on in vitro diagnostic medical devices, D.Lgs 8 September 2000, n.332.

These Directives are flanked by technical standards. The latter are standards which are suitable for proving the conformity of medical devices with the essential requirements laid down in the directives. Standards are defined "harmonized" when their references are published in the Gazzetta Ufficiale della Comunità Europea (GUCE).

According to Directive 98/34/EEC of 22 June 1998, the word "standard" means a "*technical specification approved by a recognized body to carry out regulatory activities by repeated or continuous application, the observation of which is not mandatory, and belongs to one of the following categories"* [11]. The categories to which the definition refers are: UNI, EN and ISO (Figure 4). UNI is the acronym of the "Ente Nazionale Italiano di Unificazione" and represents an Italian national standard. The initials EN apply to the standards developed by the CEN (Comité Européen de Normalisation) with the aim of standardizing the legislation at European level. Whereas the ISO (International Organization for Standardization) refers to standards with global value that different countries can decide whether to adopt or not.

Therefore, in Italy, the application of one of these standards, will make it recognizable as standard UNI ISO or UNI EN ISO, if this is also adopted in Europe.

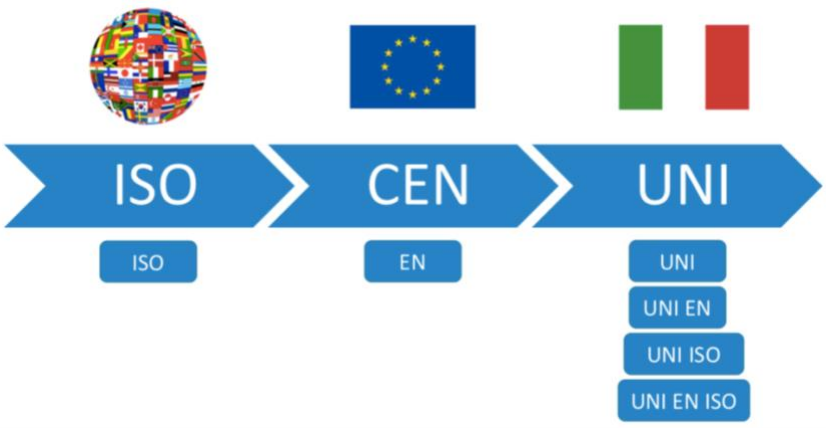


Figure 4: Standardization bodies [12].

Currently, the main technical standards in the medical devices field are:

- ISO 9001:2015 "Quality management systems - Requirements".
- EN ISO 13485:2016 "Medical Devices. Quality Management Systems. Requirements for Regulatory Purposes".
- ISO 14971:2019 "Medical Devices - Application of Risk Management to Medical Devices".
- CEI EN 60601-1 - "Medical Electrical Equipment - Part 1: General requirements for basic safety and essential performance".

The 93/42/EEC and 90/385/EEC Directives and all their relative decrees are replaced by the new EU Medical Device Regulation (MDR) 2017/745, which come into force on 26 May 2017. The aim of MDR is to solve some inherent weaknesses in the previous directives, dealing with the evolution of science and technology in the field of medical devices and introduces several key improvements [13]. Therefore, the manufacturers should prepare for the transition to MDR. Firstly, they must guarantee that the company has understanding of the new legislation and the main changes and do gap assessments to review current products with respect to the new legislation, also taking into account the reclassification of certain product groups[14].

2.1 Overview of 93/42/EEC Medical Device Directive (MDD)

The Directive 93/42/EEC Medical Device Directive (MDD) published on GUCE in June 1993 and transposed with Legislative Decree 46/97, is considered to be the main European directive in the field of medical devices. This Directive aims to ensure the proper functioning of the internal market and a high level of protection for human health and safety. Therefore, MDD contains the requirements to be followed within the EU in the design and implementation of particular categories of medical devices. In addition, it imposes the obligation of CE marking, thus regulating the placing on the market of the devices and allowing them the free circulation in EU countries and Turkey. According to it, medical devices are subjected to a conformity assessment. In particular, devices with a medium-high risk will require the intervention of a notified body for this assessment, designated and monitored by the Member States and operating under the control of the competent authorities, as explained in paragraph 1.3.

It is composed of 23 articles, including a further article, “Article 9 bis”, and 12 annexes. In particular, the Article 1 "*Definitions, scope*" provides the relevant definitions for the classification of the device, the first step in the procedure for marketing a medical device. The categories of devices to which references in the Directive may be applied are listed in Article 2 “*Placing on the market and putting into service*”. Then, Article 9 “Classification” and its Annex IX "*Classification Criteria*" contain the classification rules to be followed in order to match the corresponding class to the device, depending on the risk level. Another important step is to verify the fulfilment of the essential requirements.

The latter are listed in Annex I “*Essential requirements*”, linked with Article 3 “*Essential requirements*” and must be complied with in the order to obtain the CE marking. Subsequently, the conformity assessment of the device mist be carried out and the involved Article is the 11 “*Assessment of conformity*” and Annexes from II to VIII (“*EC declaration of conformity*”, “*EC type - examination*”, “*EC verification*”, “*EC declaration of conformity*”, “*EC declaration of conformity*”, “*EC declaration of conformity*”, “*Statement concerning devices for special purposes*” respectively). Then Article 15 “*Clinical investigations*” and Annex X “*Clinical evaluation*” refer to the assessment and planning principles for the clinical investigations.

2.2 Overview of (EU) Medical Device Regulation 2017/745 (MDR)

Technological progress highlights the need to adapt legislation on medical devices in order to provide an appropriate, robust, transparent and sustainable regulatory framework. For this reason, the MDR is not a simple integration of the previous directives with amendments, but it is precisely a new

certification that provides for much stricter requirements and measures, more in line with the evolution of the medical device market at a global level. First of all, the requirements contained in the MDR are more numerous than the MDD and concern both the product and the quality system. As a consequence, this increase in requirements needs more technical documentation. The MDR aims to ensure a regulatory framework in EU a strengthening of the control companies and post-surveillance market, an improved identification and traceability of devices and to resolve differences in the various national regulatory systems between the EU Member States.

However, device manufacturers can expect higher costs and longer timelines for developing new products, as well as costly new clinical monitoring and evidence generation to recertify many existing products. The top four challenges faced by manufacturers under the new regulation are:

- Changes will be made to the way that medical devices are classified, with requirements being increasingly scrutinized based on risk level.
- Reclassification of devices will require costly certification processes for new products as well as recertification of products already on the market, moving from focus on product approval to the entire product lifecycle, requiring greater clinical evaluation before approval. This will undoubtedly slow device production significantly.
- For medical devices, it requires reassessment of clinical data for devices already on the market. If the data do not meet the new requirements, devices will be required to undergo additional testing to be recertified, increasing the expense of maintaining legacy devices.
- The decrease in availability of notified bodies to review devices, particularly in higher risk classes, will delay product approvals and slow device entry-to-market.
- There will be an increased emphasis on post-market surveillance. This includes proactively monitoring device performance for recertification, annual safety updates for higher-risk class devices, and rapid reporting of safety incidents.

These requirements can better spot potential issues early in the production cycle, protecting patients and reduce manufacturer liability [15].

With regard to the procedure to be followed for the marketing of a medical device, here are the articles and annexes that must be taken into account in the MDR. Firstly, the devices categories to which the references of the Directive may be applied are reported in Article 1 "*Subject matter and scope*", while the relevant definitions for the classification, which is made on the basis of Article 51 rules "*Classification of devices*" with Annex VIII "*Rules for classifying*", are contained in Article 2 "*Definitions*". As regards the fulfilment of the essential requirements reference is made to Article 5

"*Placing on the market and putting into service*", Chapter 1 of Annex I "*General safety and performance requirements*". For subsequent conformity assessments and clinical evaluations, the articles contained in Chapter V "*Classification and conformity assessment*", with the exception of Articles 51 and 59, shall be considered together with Annexes IV "*EU declaration of conformity*", IX "*Conformity assessment based on quality management system and assessment of the technical documentation*", X "*Conformity assessment based on type examination*" and XI "*Conformity assessment based on product conformity verification*", Articles of chapter VI ("*Clinical Evaluation and Clinical Investigations*", with reference to annexes XIV "*Clinical evaluation and post-market clinical follow-up*" and XV "*Clinical Investigations*".

2.3 Medical Device Regulation 2017/745 versus 93/42/EEC Directive

From the previous description given on the articles and annexes both for 93/42/EEC Directive and MDR concerning the procedure to be followed for the marketing of a medical device, reference may be made to Annex 1 of this thesis (cf. Annex 1 - "*Marketing path of a medical device*" p.74) which gives an example of all the steps to carried out. This scheme is valid for both the Directive and the Regulation because the steps that the manufacturer will have to take to allow the marketing of a device not yet on the market are the same.

With regard to structural differences, an accurate technical analysis by means of two comparison tables, both for articles (cf. Annex 2 - "*Correlation table of the Articles between 93/42/EEC Directive and the (EU) Medical Device Regulation 2017/745*" p.75) and for annexes (cf. Annex 3 - "*Correlation table of the Annexes between 93/42/EEC Directive and the (EU) Medical Device Regulation 2017/745*" p.77). The table in Annex 2 of this thesis parallels the articles of the first Directive with the articles of the new MDR, noting that there are articles of Directive that do not find an equivalent in Regulation, and also many articles of the new regulation that are not present in the comparison made. This is a proof of the fact that new issues not included in the previous directive have been addressed in the drafting of the Regulation, or that the same issues have been addressed in more detail. The table in Annex 3 of this thesis represents the comparison between their annexes and also here there are annexes that do not find matches of comparison from both sides. In particular, the number of annexes to the new regulation is greater and more detailed issues than the directive.

Chapter 3

New European Medical Device Regulation (MDR) 2017/745

As mentioned in the previous chapter, the EU needs to have a more robust legislative framework that included high standards of quality and safety for medical devices to keep up with advances in medical device technology. These facts lead the European Community to create the new European Medical Device Regulation.

3.1 General information

The (EU) Regulation 2017/745 was officially published in the GUCE on 5 May 2017 and entered into force on 25 May 2017. Theoretically, manufacturers of medical devices should have a transition period of 3 years before the mandatory application of the new regulation. However, because of the fight against Covid-19 pandemic it was given the opportunity to medical device manufacturers to fully focus on this challenging situation. In order to avoid shortages or delays of some medical devices during this period has been postponed the entry into force of MDR from 26 May 2020 to 26 May 2021. More precisely, certificates issued in accordance with Directive 93/42/EEC before 26 May 2017 shall remain valid until the expiry of the period reported on the certificate, while those issued from 26 May 2017 remain valid until the end of the period reported on the certificate, but shall become valid no later than 26 May 2025, so four years after the date of application of the new Regulation [16] [15]. All products that have already been manufactured can be sold under the Directive until 2025, while for all new products manufactured later, from May 2021 it is mandatory to apply new Regulation (Figure 5).

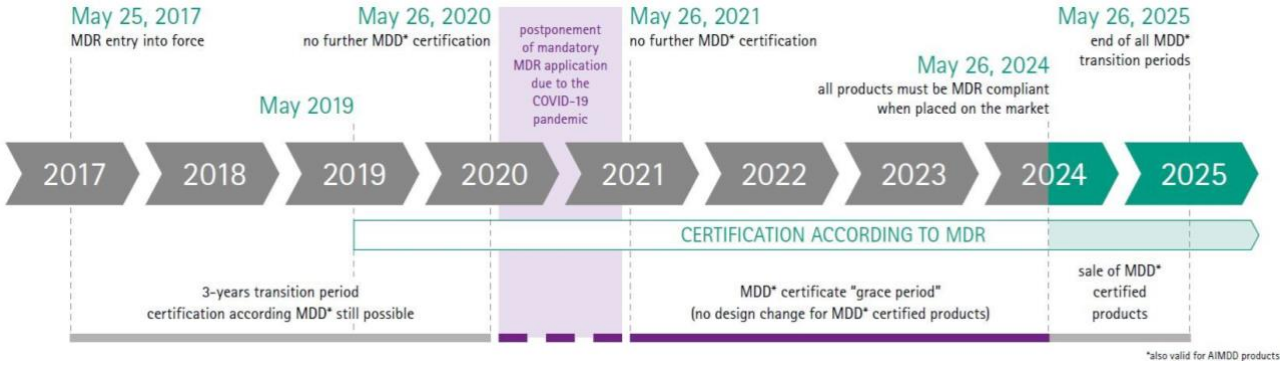


Figure 5: Timeline and transition to the MDR 2017/745 [17].

From a structural point of view, it is composed of 123 articles, grouped into 10 chapters, and XVII annexes. The main innovations introduced are [13]:

- **Scope and Definitions**: the scope is extended to include devices which do not have a specific medical purpose. As a result, the definition section of the medical device sector has been extended.
- **Responsibilities of Economic Operators**: definition of the role and responsibilities of Economic Operators (manufacturer, authorized representative, importer and distributor) involved in the import and distribution of medical devices. For each of these positions are provided specific requirements.
- **Person Responsible**: identification of the "person responsible", who has the necessary expertise in terms of medical devices and compliance with the MDR. Therefore, the person responsible must: check the compliance of the device in accordance with the company quality system before the device is released, verify that the technical documentation and the declaration of conformity are present and updated, ensure that post-market surveillance requirements and reporting requirements are met.
- **Common Specifications**: introduction of specifications that implement the essential and safety requirements, called "common specifications".
- **Notified Bodies**: strengthening the role of notified bodies in the pre-commercialization evaluation process of medical devices and stricter rules for the designation and supervision of notified bodies by competent authorities.
- **Medical Devices Coordination Group**: establishment of Medical Devices Coordination Group (MDCG) with the aim of increasing cooperation between Member States.
- **Classification Rules**: introduction of stricter classification rules to be followed by producers in the conformity assessment process.

- **Clinical Evaluation and Clinical Investigations**: clinical evaluation proportionate with the risk associated with a given device. Manufacturers may be required to obtain additional data from clinical studies and should look to review all their clinical evaluation reports if not reviewed within the last one to two years and guarantee they include post market surveillance data. Then, the improvement of clinical investigations and more stringent clinical assessments with the aim of increasing the availability of clinical data.
- **Post-market, Vigilance and Market Surveillance**: increased responsibility to manufacturers for post-market surveillance controls in terms of safety, quality, performance and reporting of adverse and accidents of devices placed on the market.
- **Traceability and Transparency**: improved traceability of devices by using the Unique Device Identification (UDI) system and transparency due to creation of European Data Bank on Medical Devices (EUDAMED).
- **Technical Documentation**: more detailed technical documentation as a result of the requirements introduced.

The following paragraphs will go into more detail on previous innovations.

3.2 Scope and Definitions

In MDR the Chapter 1 "*Scope and Definition*" is the section dealing with these issues. In detailed, Article 1 *"Subject matter and scope"* introduces the scope as a combination of fields of application of 93/42/EEC and 90/385/EEC Directives and establishes the rules concerning the placing on the market, making available on the market of medical devices for human use and accessories for such devices in the EU. The including products, also non-viable human tissues or cells and reconditioned disposable devices, are listed in Annex XIV "*List of groups of products without an intended medical purpose referred to in Article 1(2)*". Some examples are elements to be introduced into the eye, equipment used to destroy or reduce adipose tissue, equipment with high intensity electromagnetic radiation emission for dermal treatments, and so on.
In addition, point 6 of Article 1 reports a list of products that does not apply to the regulation, such as in vitro diagnostic medical devices. It includes several devices already in use in current regulations and also new devices.

For what concern the definitions on medical devices, reference is made to Article 2 "*Definitions*" which includes includes 71 definitions useful in the medical device sector. These definitions are the

result of the combination of the definitions in the previous medical devices and that concern active implantable medical devices directives with addition of further new ones.

It rewords the definition of a medical device expanding the scope as follow:

"*The following products shall also be deemed to be medical devices:*
-devices for the control or support of conception.
- products specifically intended for the cleaning, disinfection or sterilization of devices" [18].

Among the most recurrent and important definitions to keep in mind are:

- *Manufacturer* defined as a natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under its name or trademark [18].
- *Authorised representative* is defined as any natural or legal person established within the Union who has received and accepted a written mandate from a manufacturer, located outside the Union, to act on the manufacturer's behalf in relation to specified tasks with regard to the latter's obligations under this Regulation [18].
- *Importer* defined as any natural or legal person established within the Union that places a device from a third country on the Union market [18].
- *Distributor* defined as any natural or legal person in the supply chain, other than the manufacturer or the importer, who makes a device available on the market, up until the point of putting into service [18].

3.3 Responsibilities of Economic Operators

Chapter 2 "*Making available on the market and putting into service of devices, obligations of economic operators, reprocessing, CE marking, free movement*" aims to clarify the obligations of economic operators involved in the production and placing on the market of medical devices. The economic operators referred to in the new Regulation are the manufacturer, the authorized representative, the importer and the distributor (Figure 6). In detail, the chain starts with the supplier figure, selected by the manufacturer that provides for the realization of the medical device, and finishes with the customer, both represented with green circles in Figure 6. The process continues with the manufacturer and distributor figures defined in EU, represented with blue circles in Figure

6 and with dashed light blue circles in Figure 6 the importer and authorized representative, named in the case of no-EU manufacturer [19].

As a first step there is the registration of these figures. In particular, Article 30 "*Electronic system for registration of economic operators*" states that the Commission, after consulting the MDCG, operates an electronic system to create the single registration number in order to identify the manufacturers. In parallel, Article 31"*Registration of manufacturers, authorized representatives and importers*" states that prior to the placing on the market of the device, economic operators must necessarily submit to the electronic system.

All this information referred to Section 1 of Part A of Annex VI "*Information to be Submitted Upon the Registration of Devices and Economic Operators in Accordance with Article 29(4) and 31, Core Data Elements to be Provided to the UDI Database Together with the UDI-DI in Accordance with Article 28 and 29, and the UDI System*"

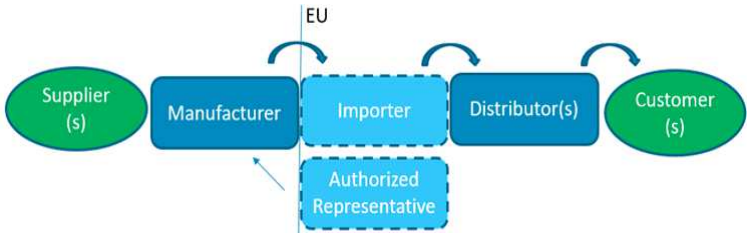


Figure 6: Economic Operators in the supply chain of the new Regulation [19].

Manufacturer

The steps that must be complied by the manufactures to place their devices on the market are reported on Article 10 *"General obligations of manufacturers"* "and vary according to the risk class of the devices they produce.

The manufactures are responsible for the quality management system. In fact, they ensure that the device is accompanied by the information concerning general requirements, they manage the risk management. They implement and keep up to date the post-market surveillance system in accordance with Article 83 *"Post-market Surveillance",* without the possibility of delegating this obligation. This duty includes the collection of technical and clinical data, reports and complaints, and the documentation must follow the indications contained in Annex III "*Technical documentation on post-market surveillance*". In the case of custom-made devices, the manufacturer shall draw up documentation containing the information listed in Annex XIII "*Procedure for custom-made devices*". Furthermore, they shall be responsible for conformity assessment and related technical

documentation. In particular, the manufacturers must ensure that the device meets the essential requirements set out in Annex I "*General Safety and Performance Requirements*" in order to issue the declaration of conformity for the marketing of the device and the conformity assessment must follow indications reported on Article 52 "*Conformity assessment procedures*" [18].

Under certain circumstances, the manufacturers obligations are applied to importers, distributors or other persons. In such cases, reference shall be made to Article 16 *"Cases in which obligations of manufacturers apply to importers, distributors or other persons"*. The circumstances are:

- When importers or distributors or other persons place on the market a device bearing their name or first mark.
- When importers or distributors or other persons change the intended use of a product already on the market.
- When importers or distributors or other persons modify the device already on the market resulting in a compromise of compliance with the applicable requirements.

Authorized Representative

The authorized representative position and the tasks are described in Article 11 "*Authorized representative*". The tasks must be described in a written statement drawn up by the manufacturer setting out the tasks he/she is to perform and the minimum obligations to which he/she is subject. In addition, the authorized representative must have at disposal a group of persons with particular qualifications. Moreover, Article 12 "*Change of authorized representative*" reports the procedure to be followed in the case of a change of authorized representative which must necessarily take place in the presence of the manufacturer, the outgoing and the incoming authorized representatives [18].

Distributor and Importer

All the obligations incumbent on distributors and importers are listed on Article 13 *"General obligations for importers"* and Article 14*"General obligations of distributors"*. Both the importer and the distributor have a duty to carry out an appropriate conformity assessment of the products before they are made available on the market.

Distributors steps:

- The device has been CE marked and the EU declaration of conformity of the device has been drawn up [18].
- A manufacturer is identified and that an authorised representative in accordance with Article 11 has been designated by the manufacturer [18].
- The device is labelled in accordance with this Regulation and accompanied by the required instructions for use [18].
- Where applicable, a Unique Identification Device (UDI) has been assigned by the manufacturer in accordance with Article 27 [18].

Importers steps:

- The device has been CE marked and the EU declaration of conformity of the device has been drawn up [18].
- The device is accompanied by the information to be supplied by the manufacturer in accordance with Article 10 [18].
- For imported devices, the importer has complied with the requirements set out in Article 13 [23].
- UDI code [18].

3.4 Person Responsible

According to this new regulation, another figure comes into play, the person responsible. It is described, together with its obligations and the skills required, in Article 15 "*Person responsible for regulatory compliance*". Specific qualifications are required to occupy this role: degree from a university or a higher institute of technology, qualification in appropriate disciplines or professional experience in quality control of medical devices [18].

The tasks to be performed by the designated qualified persons shall be:

- Establish that the quality management system controls of the devices are respected before they are issued.
- Verify that the technical documentation and the declaration of conformity are correct.
- Carry out post-market surveillance and surveillance.
- Assume that the declaration referred to Section 4.1 of Annex XV "*Clinical investigations*" has been issued.

3.5 Common Specifications

The common specifications are defined by Article 2 as "*a set of technical and/or clinical requirements, other than a standard, that provides a means of complying with the legal obligations applicable to a device, process or system*" [18]. The Commission may adopt these common specifications when harmonized standards are not present or are insufficient, with regard to general safety and performance requirements, technical documentation and clinical evaluation and follow-up post-marketing. The latter information is reported on Article 9 "*Common specifications*".

3.6 Notified Body

In order to ensure a high level of protection for health and safety and also to increase patient confidence in the clinical assessment carried out by the manufacturer, Notified Body (NB) figure is important [20].

According to Chapter 1, a NB is defined as a conformity assessment body [18]. They are an indispensable part of the regulatory system since they grant a CE mark to each device before it can be placed in the EU market. The NBs already notified in 93/42/EEC and 90/385/EEC Directives shall retain their identification number assigned and the authority responsible to the NB will supervise them. In order not to underestimate the proper functioning of the latter, the new regulation provides for enhanced supervision of notified bodies. In particular:

- New designation and monitoring procedure through joint evaluations.
- Strengthening of the minimum requirements such as independence, impartiality and competence.
- Greater investigative obligations in establishments.
- Rotation of the staff responsible for inspection visits.

Indeed, the new standard allows notified bodies to carry out surprise inspections and physical or laboratory tests on medical devices in establishments. The new regulation also proposes the possibility of increasing the knowledge and experience as well as the objectivity and neutrality needed to carry out the appropriate assessments required, by the rotation of staff working in the notified body and carrying out the required examinations. In addition, the Regulation introduced an extra figure, the "special" NB. This special NB is specialized in high-risk medical devices (Class III or medical

device with medicinal products) and is composed of experts in clinical investigations or pharmacology and product specialists.

Article 26 *'Requirements related to the notified bodies'* and Annex VII *'Requirements to be met by notified body'* explained that NBs shall have permanent availability of sufficient administrative, technical and scientific personnel in order to achieve their requirements.

In Italy there are several NBs (Table 1). As shown in Figure 7, the manufactures will have to turn to the designed NB to obtain the CE mark with a four digit-number. The four-digit is only used for medical devices requiring NB involvement. Therefore, NBs assess:

- All medium and high risks devices (class IIa, IIb and III) for conformity.
- Class I devices with a measuring or sterile function.
- All active implantable medical devices.
- *In-vitro* diagnostic medical devices according to the relevant legislation.

Figure 7: CE mark with NB number.

Subsequently, NBs can annually audit manufacturers focusing on the post-market surveillance plan and on the quality management system also without announce. Article 50 "*List of Standard Fees*" states that all these activities to test the conformity are performed under remuneration established by NB. Lastly, NB shall issue a certificate to the manufacturer that identifies the device, including the name and address of the NB and of the manufacturer, a unique number that identifying the certificate, the date of issue and of expiry and examinations and test performed and conclusions of the notified body's conformity assessment. All this information is reported on Annex XII *"Certificates issued by the notified body"*.

Regarding the NB designation reference is made to Article 38 *'Application by conformity assessment bodies for designation'* and Article 35 *'Authorities responsible for notified bodies'* application for designation to the authority responsible to the NB. The latter set up and carry out the necessary procedures for the assessment, design and notify of conformity assessment bodies and to monitor NBs. Each step is described from Article 39 *"Assessment of the application"* to Article 48 *"Peer*

review and exchange of experience between authorities responsible for notified bodies" which explain that: It starts with the notification application from NBs to the national authority responsible to the NB. The latter draw up a preliminary evaluation report to the Commission. The Commission transmits the application to the medical device coordination group (MDCG) and joint assessment team made up of three experts, within 14 days. The joint assessment team evaluates the conformity assessment activities and the types of devices subject of the application. Within 90 days, the joint assessment team together with the national authority shall plan and conduct an evaluation of the NB. The assessment report is led by the authority responsible and within 21 days, the joint assessment team shall document any remaining diverging opinions with respect to the assessment send them to the authority responsible. Within 21 days, MDCG provides recommendation with regard to the draft designation of the NB. The final decision rests with the authority responsible to the NB, who elaborates a final report with the results of the assessment, the confirmation and the implementation of the corrective actions, the diverging opinion and the recommended scope of designation. This report is sent to the Commission, MDCG and to the joint assessment team. At the end, the Commission assigns an identification number to the choose NB and makes available to the public a list of NBs in electronic notification tool within the database of notified bodies, the New Approach Notified and Designated Organisations (NANDO) [18].

3.7 Medical Devices Coordination Group

Medical Devices Coordination Group (MDCG) is introduced by MDR 2017/645, which provides advice to the Commission and assists the Commission and the Member States in ensuring a harmonized implementation of medical devices Regulation. The necessary information can be found in Article 103 "*Medical Device Coordination Group*" that states that the members of the coordination group must be appointed by the Member States in accordance with their competence and experience in the field of medical devices. The task concerned with playing a central role in assisting and advising the authorities in the correct interpretation and implementation of the provisions of this legislation, as reported on Article 105 "*Tasks of the MDCG*". Some main tasks are:

- Advising the Commission on the supervision of notified bodies.
- Contribution to the correct implementation of the indications in the legislation such as compliance with safety and performance requirements, conduct of clinical investigations by manufacturers and assessments by notified bodies.
- Assistance to Member States in their post-market surveillance and surveillance tasks.

- Creation of sub-groups to provide opportunities for the exchange of information between the authorities concerned through Union-wide discussion forums on medical device issues.

3.8 Classification Rules

The proposal of the new Regulation is based on the approach already defined in the previous Directive, which is to divide medical devices into four classes (Annex VIII "*Classification Rules*"). All of the rules are based on the potential risks associated with the device, its technical design, and how the device is manufactured Moreover, the MDR contains 22 rules for classification, four more with respect the previous 93/42/EEC Directive, as shown in Figure 8.

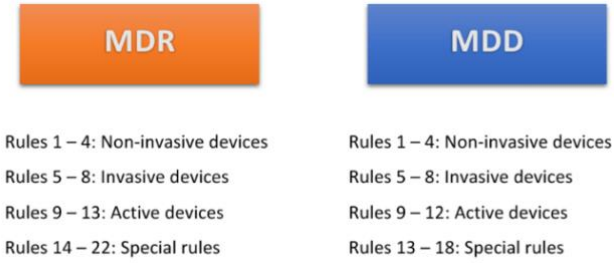


Figure 8: Rules comparison between MDR and MDD [21].

The new rules introduced are:

- Rule 19: all devices which are made up or consisting of nanomaterials.
- Rule 20: all invasive devices which are related to body orifices and intended to administer medicinal products by inhalation.
- Rule 21: all devices consisting of substances or combinations of substances and intended to be introduced into the human body by orifice or applied to the skin and then absorbed by the body or locally dispersed in the body.
- Rule 22: all active therapeutic devices which have a diagnostic function.

In addition, in MDR there is a further subdivision of the Class I medical devices in sterile (Is), reusable (Ir) and measurable (Im). Also, some products will be classified in Class III from 2020 onwards, especially the products used in the heart or in the central circulatory system. Then, one of the biggest changes in the MDR is its focus on medical software. Previously, some of them, did not fall under the definition of medical devices but now, with the new regulation, will become so. Also, some medical software in class I will pass in class IIa and IIb. It must be taken into account Rule 11

of the MDR which differ from MDD. Software classification is reported on Figure 9 through an infographic [22].

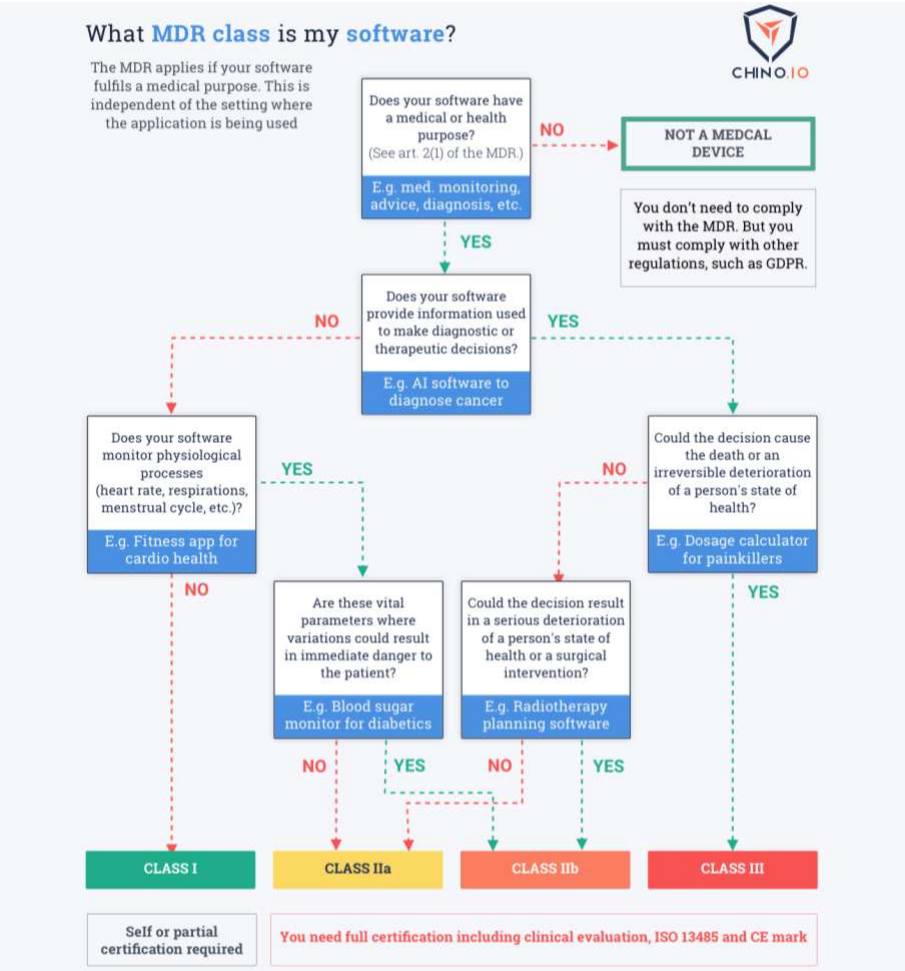


Figure 9: Classification to determine what MDR class a software is [22].

3.9 Clinical Evaluation and Clinical Investigation

The MDR provides for a strengthening of the provisions relating to clinical evaluation and clinical investigation, Chapter 6 "*Clinical Evaluation and Clinical Investigations*" as reference. Simultaneously, Annex XIV "*Clinical evaluation*" deals to define clinical evaluation term for pre-commercialization (Part A) and states provisions affecting clinical evaluations in the post-market period (Part B) and Annex XV "*Clinical investigations*" deal with general requirements including ethical principles and methods by which clinical investigations shall be carried out and also the list of information to be included in the clinical investigation documentation.

Clinical Evaluation

According to MDR, a clinical evaluation is defined as "*a systematic and planned process to collect, assess and analyse the clinical data in order to verify the safety and performance of a medical device*" [18]. This process is described in Article 61 '*Clinical evaluation'* and include [18]:

- A critical analysis of the scientific literature related to the safety, performance, design characteristics and intended purpose of the device.
- All relevant scientific data available (technical data, preclinical data, etc.).
- A critical analysis of the results of the clinical investigations.
- An evaluation of the post-marketing data.

Figure 10 shows the main stages of clinical evaluation: pre-clinical data, clinical investigations, post-marketing data and literature search. These stages are not mandatory for all the devices, depends on the class to which the device corresponds. In a detailed clinical evaluation, the manufacturer should demonstrate through a clinical investigation that its device achieves the performance intended, safety and the expected clinical benefits. Instead, in presence of devices with already the CE mark affixed according to the MDD (valid until May 2024), for devices with a non-substantial modification, for devices produced by the same manufacture and with already the CE mark and for devices produced by another manufacturer with already CE mark and demonstrated to be equivalent to the previously marketed device also accepted by the NBs, a less detailed clinical evaluation is required [1] [2].

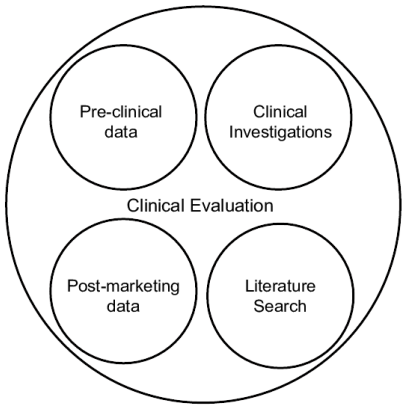


Figure 10: Main components of clinical evaluation of a medical device [23].

Clinical Investigation

From Figure 10, one of the main components of clinical evaluation is the clinical investigation. According to MDR, a clinical investigation is "*any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device*" [18].
The clinical investigations process is described by Article from 62 to 69 and Annex XV *"Clinical investigations"* conducted, designed, authorised and recorded to establish and verify the intended use, the clinical benefits, performances and le safety of medical devices always protecting rights, safety, dignity and well-being of the subjects [18].

The investigations are performed by figure called *sponsor*, set by the European Union, who requests to carry out the clinical investigations by submitting an application for the clinical investigations, valid at least 10 years (Article 70) and coupled with a precise documentation (Chapter 2-Annex XV) [18]. Therefore, the new Regulation introduces the figure of "sponsor". According to Article 2 "*Definitions*", a sponsor is "*any individual, company, institution or organisation which takes responsibility for the initiation, for the management and setting up of the financing of the clinical investigation"* [18]. Sponsors are mostly research organizations available to the manufacturers and conduct clinical investigations on their behalf. Their investigations are aimed at obtaining or confirming the device's access authorization to the European Union market.

As defined in Article 70 "*Application for clinical investigation*", the sponsor shall draw up and submit the application to the Member States, accompanied by documents listed in Annex XV, Chapter II "*Documentation regarding the application for clinical investigation*". In this case, the aim of Member States is to ensure objectivity by the persons responsible for assessing and validating applications.

Once the requested investigations have been carried out, As defined in Article 73 "*Electronic system for clinical investigations*", Member States and the Commission should operate an electronic system with the aim of generating a unique identification number for the clinical investigations, to report the serious adverse event, any device deficiencies and to exchange the information related to the clinical investigations between them. The unique identification number may be used for various purposes including the submission of an inquiry request, reporting of adverse events and sorting of information between the various sponsors.

3.10 Post-market, Vigilance and Market Surveillance

In order to identify any risks and accidents and to regulate a corrective safety plan, the Regulation introduced reinforcements in vigilance and surveillance measures of devices in the post-market phase. This information is reported on Chapter VII "*Post-market Surveillance, Vigilance and Market Surveillance*" and it is divided into 3 sections [18].

Section 1 *"Post-market surveillance"* described the phase subsequent to market placing of the devices in which the manufacturers are obliged to collect, plan, apply and update a specific Post-Market Surveillance (PMS) plan. Therefore, manufacturers shall be obliged to collect information on the experience of the devices in the post-market phase in order to fix problems which may arise in the device and which cannot be identified before they are placed on the market trade. The aim is to detect safety risks and then to take both preventive and corrective action, which in turn will serve to update the technical documentation of the device, the risk assessment, the clinical evaluation and will also increase the transparency of the properties of the product itself.
Obviously, the PMS plan depends on class of risk of the device. For the class I device, the manufacturers draw up a report showing the results of the surveillance analysis and the preventive and corrective actions taken, called post-market surveillance report. For class IIa, IIb and III devices, the manufacturers prepare a Periodic Safety Update Report (PSUR) that sets out the conclusions of benefit-risks determination. Usually, the manufacturers of class IIb and III update the PSUR at least annually and they submit the report via electronic system to the NBs, instead, for class IIa at least every two years.
In the PMS is treated the Post-marketing Clinical Follow-up, reported Part B of Annex XIV "*Post-marketing Clinical Follow-up*" of the Regulation. Here, the PMCF is defined as "*a continuous process that updates the clinical evaluation after the device is launched and it shall be addressed in the manufacturer's PMS plan*" [18]. The PMCF plan is carried out on devices already bearing the CE marking in order to confirm the safety and performance of the device, to identify risks, benefits and the side-effects the manufacturer must collect clinical data corresponding to the use of the device in question, which must be used within the scope of the intended purpose, no further analysis may be included. The results obtained are added to the clinical evaluation of the device.

Section 2 "*Vigilance"* deals with vigilance of medical devices made available on the EU market. In this phase, manufacturers can trace possible complications in the operation of the device that may not occur immediately but only after it is placed on the market. Manufacturers will be able to report any

serious incidents and any field safety corrective action, also undertaken in a third country, through an electronic system to the competent authorities.

Lastly, Section 3 *"Market Surveillance"*. The obligations of the competent authorities are reinforced. They verify the conformity characteristics and performances of the devices and draw up annual surveillance activity plan that will be evaluate by the Member States and share with the European Commission. If the risk will result unacceptable for health and safety of the patient, the competent authorities notify immediately to the manufacturer the problem in order to proceed with corrective actions. Even in this case, the Commission with the Member States prepares and manages an electronic system that contains the summaries of the results of surveillance, information about devices with high risk and about the preventive health protection activities [18].

3.11 Traceability and Transparency

One aims of the Regulation is to make the traceability of medical devices more transparent along its supply chain, starting from the manufacturer to the end user.
Indeed, the Chapter III "*Identification and Traceability of Devices, Registration of Devices and of Economic Operator, Summary of Safety and Clinical Performance and European Database on Medical Devices*" brings some news about the identification and traceability of medical devices.
A real chain of control and traceability is created between economic operators (Article 25 *"Identification within the supply chain"*) and includes:

- Medical device nomenclature to assign an international and free name to the device, available to the manufactures and other legal or natural persons (Article 26) [18].
- Introduction of a European Database on Medical Devices called Eudamed. It includes seven modules, controlled by an electronic system, by which it is possible to freely access in order to visualize the life cycle of the device (Article 33*"European database on medical devices ('Eudamed')*" [18].
- UDI system to ensure the identification and traceability of the medical devices. Each type of device is constituted by an UDI code, assigned by the manufacturer, divided in UDI-PI and UDI-DI (Article 27 *"Unique Device Identification (UDI) System"*). All these codes recognize the device in a unique and global manner, are recorded UDI database (Article 28) in Eudamed and are available to know information about the device, whenever the companies want [18].

- Electronic system for registration of economic operators to identify the person (Article 30) [18].
- Use of an implant card to accompany the implantable devices with different info about the device.

3.11.1 Unique Device Identification (UDI)

According to Article 2, UDI is "*a series of numeric or alphanumeric characters that is created through internationally accepted device identification and coding standards and that allows unambiguous identification of specific devices on the market*"[18]. Therefore, the main objective of UDI system is to allow greater traceability of devices from the manufacturer to the end user, through the entire supply chain, described above. The identification code may also be used to improve incident reporting, safety corrective actions, surveillance by authorities, and to participate in the reduction of medical errors and in the detection of falsified devices.

Article 27 is responsible for defining in detail the key features of the UDI code. In particular, in that article, it is said that the UDI code includes two distinct parts:

- "UDI-DI" is a device identifier. It is represented by a unique numeric or alphanumeric code for model of device and it is also used as "access key" in UDI database. It helps to distinguish if medical device is for example an artificial limb or a plaster. Whenever a change on the original performance safety and interpretation of data is made, the UDI-DI code must change [24].
- "UDI-PI" is a production identifier. It is represented by a unique numeric or alphanumeric code and identifies the unit of device production and if applicable the packaged devices. The latter include the serial number, lot number and expiration date (Figure 11). It is placed on the label of the device or on its packing in text format or bar code (Figure 12) [24].

Figure 11: Unique Device Identifier [25].

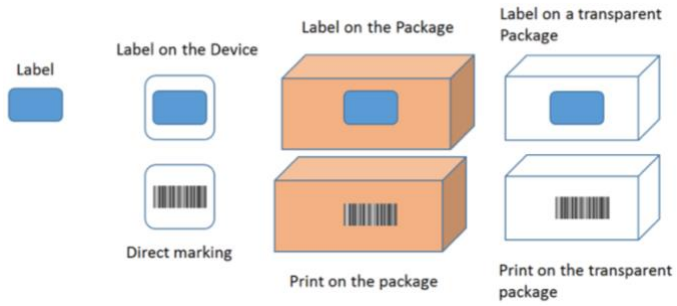


Figure 12: Option for placing the UDI [24].

The UDI codes must be collected into a database, Article 28 "*UDI database*" and registered according to Article 29 "*Registration of devices*". The first one defines the UDI database which purpose is to collect, process, make available specific information. The second one reference to the issue of device registration is addressed before being placed on the market. Accordingly, the manufacturer shall assign a UDI-DI to the device and then provide it to the UDI database together with other data.
In detailed, Annex VI *"Information to be submitted upon the registration of devices and economic operators in accordance with articles 29 and 31, core data elements to be provided to the UDI database together with the UDI-DI in accordance with articles 28 and 29 and the UDI system",* articulated in three parts:

- Part A: the manufacture or the authorised representative or importers provide the information relating to the economic operators (name, address, type etc) and the information relating to the device (Basic UDI-DI, risk class, presence of tissues or cells etc.) [18].
- Part B: the manufacturer provides to the UDI database the UDI-DI and information relating the manufacturer and the device [18].
- Part C: It defines the UDI system with a series of definition, including UDI-DI, UDI-PI and UDI carrier and gives the general principles about UDI database.

The period of time required for affixing the UDI code to the product label shall be between one and five years from the date of application of the Regulation and based on the risk of the device. Manufacturers of high-risk medical devices must also make available the clinical data of investigations carried out as a safety guarantee. The new regulation will require that all the devices have the UDI code in place to allow maximum traceability.

The UDI system is controlled and assigned by an 'issuing entity' at least 10 years [18]. These entities are embodied by a global organizations and standardizing bodies that define rules for the identification. In Italy the issuing entity is embodied by the GS1, which is the only Italian organization authorized by the European Commission to support companies with UDI codes.

3.11.2 European Database on Medical Devices (EUDAMED)

As mentioned above, another new in the Regulation is the creation of a European Database for Medical Devices, called EUDAMED, with the aim to enhance the transparency, including the information for the public and for healthcare professionals with regard to the devices placed on the market, to the economic operators, to the notified bodies and about the clinical investigations [23], [26]. In EUDAMED will have to be present the UDI of all the devices on the market. Indeed, in this database must be registered all the devices that must be placed on the market in the European Union. Other information to be included in the database are the information relating to conformity assessment, notified bodies, certificates relating to both clinical investigations and post-market surveillance. The reference article is Article 33 "*European database on medical devices*" which defines the purposes of EUDAMED, and the electronic systems include on it relating to the registration of devices, of the economic operators, of the notified bodies, of the clinical investigations, on vigilance and post-market surveillance, UDI-database [18]. According to it, EUDAMED database should contains (Figure 13):

- Electronic system concerning the recording of devices.
- UDI database.
- Electronic system concerning the registration of economic operators.
- Electronic system concerning clinical investigations.
- Electronic system concerning market surveillance.
- Electronic system concerning vigilance.

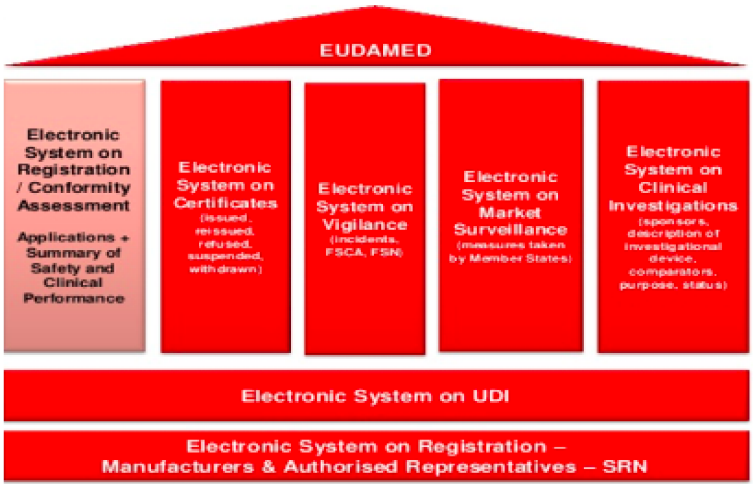


Figure 13: Eudamed database system.

The electronic system is available from December 1st, 2020, useful for EU manufacturers, competent authorities and importers to register to the Eudamed themselves, to provide necessary information and to obtain Single Registration Number (SRN) for each actor role. The SRN is made of three different parts (Figure 14). The first part is a two-letter country code for the actor (e.g., CH for Switzerland), the second part is the two-letter abbreviation of the actor's role (e.g., IM stay for Importer) and the third part is a 9-digit number code [27], [28].

Figure 14: Single registration number [28].

3.12 Technical Documentation

Technical documentation is an essential part of the approval process for medical devices. Without this documentation, the manufacturer cannot perform the conformity assessment procedure for his medical device. The MDR 2017/745 adds additional elements and requirements, which results in considerable additional effort to keep the technical documentation in line and up to date. In addition, manufacturers must undertake to renew the document on an ongoing basis to provide up-to-date information on devices [29].

The information to be included in a technical documentation is listed in Annex II *"Technical documentation"* and it includes:

- Device description and specification, including variants and accessories.
- Information to be supplied by the manufactures.
- Design and manufacturing information.
- General safety and performance requirements.
- Benefit-risk analysis and risk management.
- Product verification and validation, in particular pre-clinical and clinical data.

The technical documentation will also cover post market surveillance information. The manufacturer will have to draw up a technical report on the information found during the post-market control process in a clear and unambiguous manner and shall including elements described in Annex III "*Technical Documentation on Post-market Surveillance".*

Chapter 4

Technical Documentation for Medical Device According to MDR 2017/745

The term technical documentation is a generic term for product documentation, which gives the evidence, that a medical device conforms to the Regulation, meeting the general safety and performance requirements. Technical documentation is a core part of the process of approval of medical devices. Without this documentation, a product cannot be approved because the manufacturer cannot perform the conformity assessment procedure with his medical device. Therefore, it is of great importance to maintain a technical documentation compliant with the standard [30].

No matter the class of the medical device, a technical documentation must always be available. In particular, for the technical documentation must comply with the requirements of the authorities in order to obtain CE conformity for their medical device. Products of simple Class I devices conformity assessments shall only be carried out by manufacturers without the intervention of any notified body, Class Is, Im, Ir need comply in parts with the requirements of the notified body, products of the class IIa, IIb and III must comply completely.

In fact, the MDR does not give an explicit information in terms of structure and uniformity of the technical documentation but just provides guidelines as to which content must be present in a technical documentation for approval in the EU. MDR clarifies that must be "*clear, organized, readily searchable and unambiguous manner*" [18]. Meaning that, every technical documentation has the same form of content, but there may well be differences between individual authors.

In Annex II "*Technical Documentation*" and Annex III "*Technical Documentation on Post-market Surveillance*", the MDR depicts precisely what every documentation must contain (Figure 15). In detail, Annex II contains a list of the information to be included by the manufacturer in the technical documentation to be kept at the disposal of competent authorities together with the declaration and certificate of conformity for a period of less 10 years and 15 years for active implantable devices. With respect to 93/42/EEC Directive, the new Regulation adds further elements and requirements which result in a notable extra effort for the technical documentation.

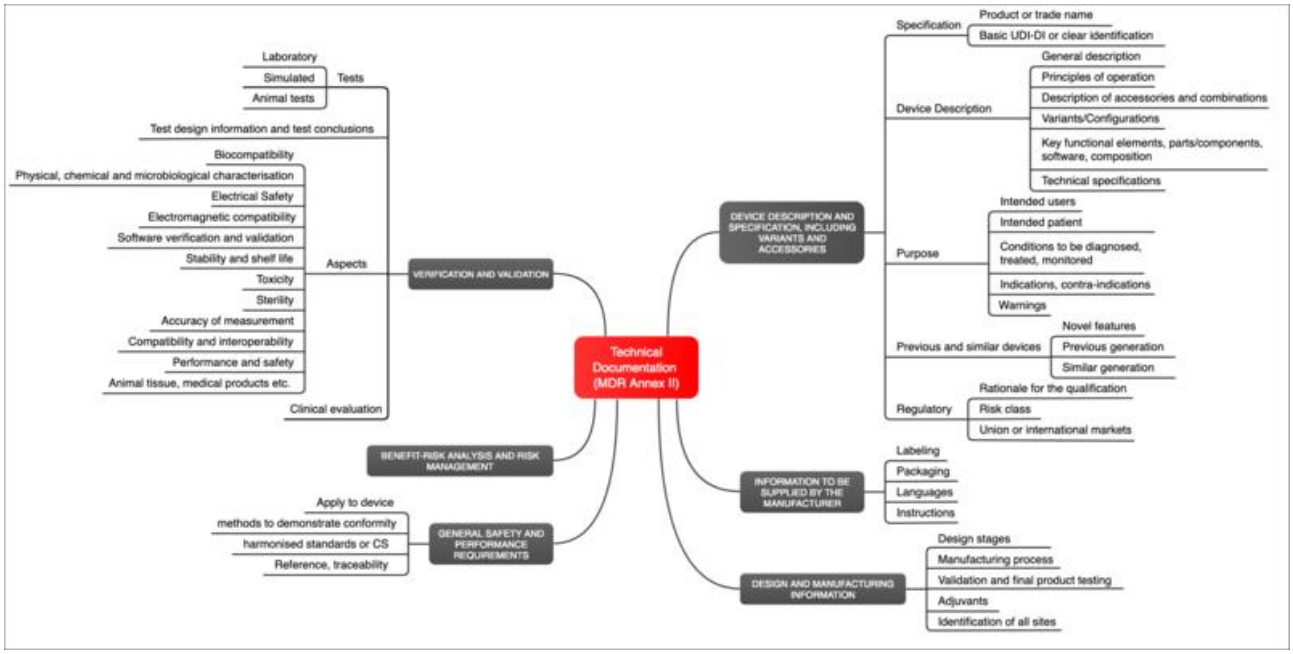


Figure 15: MDR specifies the requirements for the technical documentation in Annex II [31].

Elements set out in the Annex II are [18]:

- Description and specifications of the device: the name of the product with its description including the technical specifications, such as size and performance, the target patient group, the device classification, the description of the raw materials used, references to similar devices previously produced and the UDI-DI code.
- Information to be provided by the manufacturer: the manufacturer shall provide the label of the device on the package, together with the instructions for use.
- Design and manufacturing information: the manufacturer shall provide all information relevant to the design and manufacturing stage of the device in question.
- General safety and performance requirements: a proof of compliance with the general safety and performance requirements are required. As a consequence, it is necessary to provide information on the applicability of the requirements and their explanation, the criteria used for the demonstration, the technical standards and the technical specifications used.
- Risk, benefit and risk management analysis: the technical documentation shall contain the risk analysis and the results of risk management.
- Verification and validation of the device: they must be included in the clinical and pre-clinical data of tests that are carried out on the device, information about the design and conduct of tests, software verification, the report of the clinical evaluation and also the PMCF plan carried out together with the validity report of the same; are also included in the

documentation of information concerning special devices such as those containing a medicinal product or those that are manufactured using human or animal tissues or cells or particular substances which must be introduced into the human body, sterile or measuring devices.

Instead, Annex III sets out the requirements for the post-market surveillance system as defined in Article 83 "*Post-market Surveillance System of the Manufacturer*". The documentation shall include the information that the manufacturer has available concerning major accidents, together with the related data found, side effects, any comments and complaints following the use of the device. Instead, the surveillance plan should contain a description of the methods used to collect all the information previously described the threshold indicators on the data found relating to the risks-benefits relationship of the device, a description of the methods used to carry out the surveys, the methodologies used to warn the competent authorities about the investigations carried out and the PMCF plan carried out. The documentation shall be regularly updated by the manufacturer and a post-market surveillance report shall also be drawn up in accordance with Article 85 "*Post-market surveillance report".*

In the following paragraphs we will deepen what are the key points for the writing of technical documentation: classification of a medical device, essential requirements and conformity assessment.

4.1 Classification Procedures

The new MDR 2017/745 understands the relevance of medical devices classification as classifications of potential risk of harm to the patient. As Class I denote the lowest risk, Class III populates the other end of the risk range. Similarly to 93/42/EEC Directive, the manufacturer must first declare whether the device falls within the definition of "*medical device*" reported on Article 2. Only after certifying that the product is a medical device, the manufacturer can proceed with the classification of the same. In order to be able to classify the device, the manufacturer shall refer to Article 51 "*Classification of devices*" together with Annex VIII "*Classification rules*".
According to Article 51, the devices should be divided into the same four classes as those already defined in 93/42/EEC Directive. The classification shall take into account the risk of the device and the manner in which it is used, considering the potential risks arising from its design and manufacture. In the classification process, the involvement of competent authorities may also be necessary in the event of a dispute over the classification conclusions between the manufacturers and the notified body. Then, the competent authorities will inform the MDCG of the decision that has been taken on

this matter. Whereas Annex VIII is divided into three chapters, which contain:

- Chapter I "*Definitions specific to classification rules*": definitions relating to the duration of interaction of the device in question with the human body, definitions relating to invasive devices and active devices. The differences with respect to 93/42/EEC Directive is the addition oof "active device", "implantable device" and "active medical device" definitions [18].
- Chapter II "*Implementing rules*": implementing rules in case there is software or a combination with another devices [18].
- Chapter III "*Classification rules*": classification rules on which the correct risk class of the device is based. In this chapter additional rules have been introduced with the aim of entrusting appropriate classification to those devices which pose a higher risk because they are composed of substances or combinations of substances, which are absorbed by the human body or are locally dispersed [18].

Thus, the subdivision of medical devices into risk classes is considered to be of fundamental importance in order to proceed with the other assessments.

4.2 Essential Requirements

In order to affix the CE marking to a medical device, it is necessary that the device meets the essential requirements listed in Annex I "*General safety and performance requirements*". The latter is divided into three Chapters, which analyze the characteristics that a device must possess to ensure its normal use and safety conditions.

- Chapter I "*General requirements*" describes the general safety aspects of the device, including measures to be taken by the manufacturer in order to reduce risks related to misuse, lack of adequate safety status of the device, side effects, conditions of transport and storage. In addition, the new Regulation introduces the provisions that the manufacturer should comply with in order to run an updated risk management system throughout the life of the device [18].

- Chapter II "*Requirements regarding design and manufacture*" listed the requirements [18]:
    - Chemical, physical and biological properties.
    - Infection and microbial contaminations with insights for devices containing a substance considered a medicinal product, devices consisting of a combination of substances that are absorbed by the human body and devices containing materials of biological origin.
    - Construction of devices and its interaction with the environment.
    - Device with a diagnostic or measuring function.
    - Protection against radiation.
    - Devices that incorporate electronic programmable systems, including software, active devices and devices those connected to them, for protection against mechanical and thermal risks and those caused by devices that emit energy or administer real substances to patients and users.
    - Active implantable devices in order to minimize risks connected with the use of energy source, with medical treatment (e.g., defibrillators or high frequency surgical equipment).
    - Protection against the risks of devices intended for use by lay person.

- Chapter III "*Requirements regarding the information supplied with the device*" contain safety and identification information of the device and of the manufacturer to be supplied together with the device. The information must be given by the manufacturers with accuracy on the labels or on the instructions for use. Technical standards and technical specifications are used to meet a large number of essential requirements. The technical documentation must therefore contain, in addition to the information necessary to demonstrate the compliance of the device with the essential requirements, also the technical rules that have been used to meet them [18].

According to Point 3 of Article 5 "*Placing on the market and putting into service*" a clinical evaluation is necessary in order to be able to verify the conformity of the general safety and performance requirements for medical devices. Indeed, clinical evaluation is one of the most important moments in the life of a medical device. It is a periodic appointment in which the manufacturer analyses the clinical data identified to decide whether the device meets the legal requirements and, in particular, whether the device is safe. The adverse events which it may cause shall be commensurate with the benefit which it brings if it is really effective in carrying out its

intended use, even in the light of the most up-to-date medical knowledge [18]. In the next section, depth analysis on clinical evaluation.

4.2.1 Clinical Evaluation

According to MDR 2017/745 and its Article 2, clinical evaluation is defined as "*a systematic and planned process to continuously generate, collect, analyze and assess the clinical data pertaining to a device in order to verify the safety and performance, including clinical benefits, of the device when used as intended by the manufacturer*" [18].

The provisions concerning the clinical evaluation refer to Article 61 "*Clinical evaluation*". This article states that manufacturers must carry out a clinical evaluation which aims to certify compliance with the essential requirements listed in Annex I, but also to assess any serious side effects or events that may occur during the use of the same device together with a risk-benefit analysis. Thus, the deepening of the evaluation is chosen according to the state of risk and the destination of the use of the device.
As a consequence, depending on the intended use of the device and its characteristics, manufacturers shall choose the level of clinical evidence best suited to demonstrating the general safety and performance requirements.

The clinical assessment plan to be carried out by the manufacturer shall contain the information listed in Annex XIV, Part A "Clinical evaluation" and the obtaining results, both positive and negative and both clinical and non-clinical, shall be documented in a report which provide evidence of compliance with the essential requirements. Then, this report will be included in the technical documentation of the device and assessed by the authorities responsible for the notified bodies. An update process throughout the life of the device is required for the clinical evaluation and updates are possible through the introduction of the post-market surveillance plan. So, in support of clinical evaluation, the post-market surveillance plan aims to collect clinical data in order to confirm the safety and fulfilment of the essential requirements, and to identify any side effects and risks arising after the marketing of the device [18]. The procedures that may be followed in implementing this plan shall cover the possibility of referring to clinical data relating to equivalent or similar devices and to the common technical specifications or harmonized standards used.

Three methods are available to carry out the clinical evaluation procedure:

- Analysis of available scientific literature provided that the device to which the data are based is equivalent in terms of technical, biological and clinical characteristics to the device being assessed.
- Critical analysis of results of other clinical investigations provided that it is in accordance with the articles ranging from 62 "General requirements for clinical investigations conducted to demonstrate compliance of devices" to Article 81 "Implementing acts" and Annex XV - "Clinical investigations"
- Examination of possible alternative treatment options.

In order to demonstrate the compliance of medical devices with the general safety and performance requirements and as part of the clinical evaluation, clinical investigations must be carried out. According to MDR 2017/745 and its Article 2, clinical evaluation is defined as "*any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device*" [18]. The clinical investigations that are carried out in the field of clinical evaluations, aim to verify the use of medical devices and to identify both the benefits resulting from their use, and any side effects not expected. The rules are laid down in Annex XV "*Clinical investigation*" and clinical investigation plan is described in Point 3 Chapter II of the same Annex, which list the objectives, the methodology, the implementation, the recording of the results and everything relating to the planning of the clinical investigations to be carried out.

As previously mentioned, in the new Regulation is introduced the sponsor figure. The sponsor must submit an application stating that it wishes to initiate clinical investigations. The information to be included in this application is listed in Chapter II of Annex XV "*Documentation regarding the application for clinical investigations".* The application must be submitted via an electronic system (Article 73 "*Electronic system on clinical investigations*"), which generates a unique identification number, which, in turn, will notify all information relating to the clinical investigations that have been carried out, and to record it in a database. The assessment of the application and subsequent authorization shall be entrusted to the Member States or to the competent authorities designated by them. After ten days from the receipt of the application, the sponsor will be informed of the outcome of the evaluation and may undertake clinical investigations after the application has been approved [18]. The application could be considered:

- Suitable
- Lacking some information. In these cases, the sponsor has ten days to be able to heal them.

- Refused. It occurs when the sponsor is sure to have complied with the required provisions, but the Member States consider the application documentation not suitable.

The application to be submitted by the sponsor should also include the clinical investigation plan and the dossier of investigator ("*an individual responsible for the conduct of a clinical investigation at a clinical investigation site*" Article 2 [18]). The latter is a manual containing the information available at the time of submission of the application and relating to the device being surveyed which is then useful to the investigator during the conduction of the investigation. The investigator collaborates with the sponsor in the collection, recording and processing of the data that are collected from the surveys carried out, and in the subsequent preparation of a written documentation. At the end of the investigation, the sponsor shall submit a summary of the clinical data obtained together with a written report on the investigations to be made available to the competent authorities for a period of at least 10 years after the placing on the market of the device [18]. The specific information that must be contain in the documentation, the purpose of the investigations, the description of the arrangements under investigation, the results obtained and the summary of adverse events that occurred are listed in Chapter III of Annex XV "*Other obligations of the sponsor*".

To continue, the sponsor is able to interrupt the investigation in a temporary way informing with a justification the Member State with a preventive timetable of 15 days and through the electronic system, as reported in the Article 77 "*Information from the sponsor at the end of a clinical investigation or in the event of a temporary halt or early termination*". Usually, interruptions are made when the safety and immunity of the subjects submitted to such investigations are lacking. The sponsor shall also report to the competent authorities, via electronic system, any adverse events or defects that occur during the conduction of clinical investigations.

All patients should sign an informed consent. In particular, patient protection mainly concerns people with the need for more specific protection measures and a legal representative, appointed by the Member States, who can sign informed consent on their behalf: incapacitated persons (Article 64 "*Clinical investigations on incapacitated persons*"), minors (Article 65 "*Clinical investigations on minors*") and pregnant or breastfeeding women (Article 66 "*Clinical investigations on pregnant or breastfeeding women*") [18].

Moreover, the activity of clinical evaluation is intimately intertwined with that of carrying out the risk analysis. The clinical evaluation shall include the task of providing accurate and rigorous information on the risk profile of the device when applied in the clinical setting, so that the risk

analysis team can correctly assess what damage it may cause, the severity, likelihood and appropriate risk reduction measures.

4.2.2 Risk Management

Medical device Risk Management is a central component of MDR compliance. Risk Management is a direct component of clinical evaluation and a benefit-risk analysis is one of the required technical documents specified in Annex II. Indeed, Risk management must be carried out in parallel with the clinical evaluation of the device, the two processes should be interdependent, and the topics addressed must reflect those in depth in the clinical evaluation. Risk Management is the structured process of identifying, analyzing, mitigating, eliminating and drawing conclusions from medical risks associated with use of a medical device and must be carried out throughout the life of the device in question, from design to post-production. This process does not eliminate every conceivable risk that could emanate from use of a device, but concern with the elimination of unacceptable risks and the reduction of any risks that cannot reasonably be eliminated. As a consequence, risk management allows the formulation of a benefit-risk assessment that will determine whether the potential benefits of using a device outweigh any residual risks [32].

The risk management system is described in the new Regulation in Point 3 of Annex I as "*a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating*" [18]. It is manufacturers who have to set up and maintain a risk management system to identify known and foreseeable hazards, to estimate the risks that may occur during the use of the device itself by assessing the data found during the post-market assessment. The conclusions that are identified during PMCF are taken into account for both clinical evaluation and risk management. Also, Annex I require that devices are designed to be able to withstand stresses, strains, temperature fluctuations, conditions of storage and transport, and environmental conditions to which they can be expected to be subject. Risk analysis therefore becomes a component of product design.

All these steps of risk analysis to be carried out in order to be able to place a device on the market or to carry out a post-market, refer to the diagram in Annex 4 (cf. Annex 4 – "Overview of risk management activities as applied to medical devices" p.78).

The analysis shall be conducted in accordance with the requirements contained in ISO 14971:2019 "*Application of Risk Management to medical devices*". It is the most up-to-date version of the ISO 14971:2012 standard in order to reflect changes to risk management imposed by the MDR. This standard outlines a process for risk management and extends its coverage to software as a medical

device and in-vitro diagnostic medical devices. It can be applied to all phases of a product's life cycle [32].

Exist different techniques that can be used to support a risk analysis procedure. Some of them start with the possible harm and analyze the variety of events that can cause that harm, while others start with an initiating event and analyze the subsequent sequence or combinations of events that could lead to harm. The basic principle is that the sequence of events is analyzed [33].

In particular, ISO/TR 24971:2020 provides a guidance on the development, implementation and maintenance of a risk management system for medical devices according to UNI CEI EN ISO 14971:2020. The ISO 31010:2019 discusses the risk assessment techniques:

- Preliminary Hazard Analysis (PHA) is a technique that can be used early in the development process to identify the hazards, hazardous situations, and events that can cause harm when few of the details of the medical device design are known [34].
- Fault Tree Analysis (FTA) and Event Tree Analysis (ETA) are especially useful in safety engineering, early in the development process, for the identification and prioritization of hazards and hazardous situations and possible risk control measures as well as for analyzing the consequences of adverse events [34].
- Failure Mode and Effects Analysis (FMEA) is a technique by which effects or consequences of individual components are systematically identified and is more appropriate as the design matures and the failure modes are better understood [34].
- Hazard and Operability Study (HAZOP) is typically used in the early stages of the development process to study deviations from the intended performance [34].
- Hazard Analysis and Critical Control Point (HACCP) is typically used in the later stages of the development process to verify and then optimize design concepts or changes [34].

4.3 Conformity Procedures

Conformity assessment is the main objective of the technical dossier. It is defined in this Regulation as the "*procedure to demonstrate whether the requirements of this Regulation relating to a device have been met*" in Article 2 [18]. Responsibility for compliance with the provisions of the Regulation is the responsibility of the manufacturer who has the duty to draw up an EU declaration of conformity declaring compliance with the requirements of the Regulation in relation to the device being analyzed. The declaration of conformity shall then be submitted together with the technical documentation and

shall contain specific information which is listed in Annex IV "*EU declaration of conformity*" to this Regulation. The data that should be reported by the manufacturer, when compared with those of the current Directive, are the same with the exception of the UDI-DI index and any common specifications used. The declaration of compliance shall be continuously updated. Therefore, the conformity assessment determines whether the device is suitable for placing on the market and for obtaining the CE mark. According to Article 20 "*CE conformity marking and complete it in the language required by the Member State concerned*", the CE mark shall be affixed to the device or its casing in a visible and legible manner before it is placed in the market.

In order to strengthen health and safety protection measure, the new Regulation proposes stricter conformity assessment procedures. One of them concern the notified body figure. They come into action both before marketing is granted and the subsequent phases, through audits of the quality management system. In addition, notified body should be responsible for informing a committee of experts of the need to carry out more detailed monitoring procedures for high-risk devices and for carrying out such monitoring, a preliminary assessment of these arrangements which will then be made available to the committee. The latter will make comments on the matter through a further check, before the terms of issue of the certificate by the notified bodies themselves. Conformity assessment for Class I devices, without measuring functions and is not sterile, does not require the intervention of a notified body, but is carried out exclusively by the manufacturer, who will be solely responsible for the outcome of the latter. For sterile or measurable Class I devices, IIa, IIb and III instead, the intervention of notified bodies is mandatory. When the devices need the intervention by a notified body, the manufacturer may apply to only one body of his choice, without submitting the same conformity assessment procedure with another body. Indeed, thanks to the use of the electronic system by the notified body, it allows to inform the other bodies of the withdrawal of the assessment application by the manufacturer before the decision on the conformity assessment of the body (Article 53 " *Involvement of notified bodies in conformity assessment procedures* "). The elements that should be contained within the electronic system are listed in Article 57 "Electronic system on notified bodies and on certificates of conformity " listed the elements should be contained into electronic system and the various notifications relating to conformity assessments and the withdrawals or refusals of applications for assessment. Therefore, for each class of devices, Article 52 "Conformity assessment procedures" report the applicable annexes and possible combinations thereof (Table 2) [18].

Table 2: Corresponding annexes for each type of medical devices classes.

Classes	**Annexes**
Class I	Article 19 (conformity assessment) Annex II and III (technical documentation)
Class Im and Is	Chapter I and III of Annex IX Part A of Annex XI
Class IIa	Annex II and III (technical documentation) + Chapter I and III of Annex IX + Point 4 of Annex IX (technical documentation) + Point 10 (or 18) of Annex IX
Class IIb	Chapter I and III of Annex IX + Point 4 of Annex IX (technical documentation) + Point 4 of Annex IX (technical documentation) + Annex XI
Class III	Annex IX Annex X Annex XI
Custom-made devices	Chapter I of Annex IX [class III implantable device] Part A of Annex XI [class III implantable device] Annex XIII
Devices incorporating a medicinal substance	Point 5.2 of Annex IX or Point 6 of Annex X [depending on the situation]
Devices manufactured utilizing, or incorporating, tissues or cells of human or animal origin, or their derivatives,	Point 5.3 of Annex IX or Point 6 of Annex X [depending on the situation]
Devices that are composed of substances or of combinations of substances that are absorbed by or locally dispersed in the human body	Point 5.4 of Annex IX or Point 6 of Annex X [depending on the situation]

Particular attention to Class III implantable devices and Class IIb active devices intended to administer or remove medicinal product from the human body. In these cases, the procedure to follow is described through Article 54 "*Clinical Evaluation Consultation Procedure for Certain Class III and Class IIb Devices*" and 5.1 of Annex IX or Point 6 of Annex X. Once the conformity assessment

has been carried out according to Article 54, the notified body shall be responsible for notifying the various certificates issued to the devices subject to such assessments to the competent authorities via the electronic system. The information to be included in that notification is reported on Article 55 "*Mechanism for Scrutiny of Conformity Assessment of Certain Class III and Class IIb Devices*".

In the Regulation, the procedures to be followed for carrying out the conformity assessment are described in Annexes IX, X and XI.

Annex IX "Conformity assessment based on a quality management system and assessment of the technical documentation"

Annex IX is divided into three Chapters:

- Chapter I "*Quality Management System*" deals with the provisions that are followed in the assessment of the quality management system. It certifies that the notified body must carry out the assessment of the quality management system which is carried out by the manufacturer throughout the life of the device in order to ensure that the devices meet the requirements of the Regulation. Once drawn up the quality management system, the manufacturer shall submit an application for assessment for the same to a notified body together with precise documentation for the assessment of the management plan. Subsequently, notified bodies will then have to carry out an audit of the quality management system. Audits must be carried out by qualified personnel, either in the manufacturer's premises or in those of suppliers, either with due notice or without. Unannounced audits shall be carried out at least once every five years and scheduled audits at least once a year. If the quality management system complies with the provisions of the Regulation, an EU quality management system certificate shall be issued by the notified body. In the case of class IIa, IIb and III devices, the assessment of a technical documentation is also envisaged [18].
- Chapter II "*Assessment of the Technical Documentation*" provide guidance for carrying out the assessment of the technical documentation and describe the additional specific procedures for the special devices and for certain devices of Class IIb and III. Manufacturers shall submit to notified bodies a request for assessment of the technical documentation containing information concerning the design, manufacture, performance and a technical documentation of the device. The notified body shall be responsible for verifying the suitability of the clinical evidence and clinical assessment provided by the manufacturer and for providing a report on the outcome of the assessment which has been carried out in the documentation. In case of a positive result, an EU assessment certificate shall be issued by the notified body [18].

- Chapter III "*Administrative Procedures*" lists the information which must contain the documentation to be kept by the manufacturer or his authorized representative at the disposal of the competent authorities. Such equipment must be kept at the disposal of the competent authorities for at least 10 years in the case of devices which can be implanted for at least 15 years from the date on which the equipment is placed on the market [18].

Annex X "Conformity assessment based on type examination"

Annex describe the conformity assessment procedures that are based on the type examination. In addition to the technical documentation, the manufacturer makes available to the notified body a representative sample of the device under analysis, which is called "type". As in the previous case, all assessments of the technical documentation and clinical evidence provided by the manufacturer are carried out to verify the suitability of the "type". In the case of positive assessment, the notified body will issue an EU "type" examination certificate containing specific information listed in point 4 of this Annex. Then, the manufacturer should draw up the post-assessment documentation and shall be made available of competent authorities for at least 10 years, or 15 years for implantable devices [18].

Annex XI "Conformity assessment based on product conformity verification"

Annex XI describe the conformity assessment procedure which is based on the verification of conformity of a product. The aim is to ensure that the devices being analyzed comply with the "type" for which documentation has already been issued stating that it complies with the EU-type examination. When an EU-examination certificate has actually been issued in accordance with Annex X, the manufacturer may choose to apply either the procedure described in Part A or the procedure defined in Part B. For both of them the timing of maintenance of the required documentation is the same as the annexes described above, while change the information to be included in the documentation.

- Part A "*Production Quality Assurance*" describes the production quality assurance procedure. The manufacturer shall submit to the notified body an application for assessment of its quality management system, together with a technical documentation and a copy of the EU "type" examination certificates. Subsequently, the notified body shall carry out the audits and surveillance procedures. If the notified body declares that the manufacturer has met all the requirements, an EU certificate of conformity shall be issued, according to Article 19 of Annex IV. The declaration shall state that the device under examination complies with the

"type" described in the EU-type examination certificate and also meets the requirements of this Regulation [18].

- Part B "*Product Verification*" outlines the verification of the product. In this case, the Notified Body performs checks and tests on each individual product in order to verify the conformity of the device with the provisions of the Regulation [18].

In addition, Annex XII "*Certificates issued by a notified body*" defines the general requirements and minimum content of certificates issued. Among the requirements to be met, it is necessary to underline the language and timing of validity of the certificate: the language must be the official language of the Union chosen by the Member State of which the notified body is a member, or it must be a language chosen by the Notified Body to carry out the conformity assessment; the period of validity of the certificate may not exceed five years and shall be indicated in the information contained in the certificate.

Annex XIII "*Procedure for custom-made devices*" treats the procedure in presence of custom-made devices. In these cases, the manufacturer shall draw up a declaration containing specific information (listed in Point 1 of that Annex) and documentation containing the relevant information to enable the conformity of the device with the requirements of this Regulation to be assessed. This information shall be kept at the disposal of the competent authorities for at least 10 years after the first device has been placed on the market [18].

Chapter 5

Technical Documentation for Class I Medical Device

In order to apply the MDR 2017/745 aimed at obtaining the CE marking necessary for the placing on the market a product to a real problem, with Consultek Group srl it is proceed with the drafting of technical documentation of class I medical devices for some of their customers. Specifically, work was done on technical documentation for a nasal pad, a three-points hyper extender, an anti-bedsore mattress and a motorized bed base. All these devices comply with the definition of "medical device" reported on Article 2 and fall within rule 1 of Chapter III of Annex VIII to the Medical Device Regulation 2017/745.

5.1 FIDPAD Nasal Pad

FIDPAD nasal pad was designed and built by FID s.r.l. It is a reusable mono-patient pad for nose protection during mask use. It is made of medical silicone (a silicone complying with the USP Class VI provisions from ISO 10993) available in three sizes: Small, Medium, Large (Figure 16) (Table 3) chosen according to the type of face and the type of masks. The types of masks with which this nasal bearing can be used are nasal masks, oronasal masks, continuous positive airway pressure (CPAP) and personal protective equipment (PPE). FIDPAD has been created with such a shape that it can best shape on the back of the nose and then apply the mask. It shall be positioned above the nose as shown in Figure 17.

Therefore, the patient or end user of the device is a person who uses nasal masks, gold-nasal masks, CPAP and PPE and its intended use is to limit the formation of bruises and to facilitate the sealing operations between mask and skin increasing the comfort during the use of the mask. The user, before each use, must wash the device with warm water and mild soap and rinse thoroughly, finally leave to air dry. There are no limitations to the use of the device and no minimum functional abilities are defined necessary for the use of the device itself. However, it is recommended that only one patient use the nasal pad and in case the device is used by another person, the parts in direct contact with the skin could pose hygienic or functional risks. In particularly sensitive individuals, contact between the skin and the device may cause redness and/or irritation.

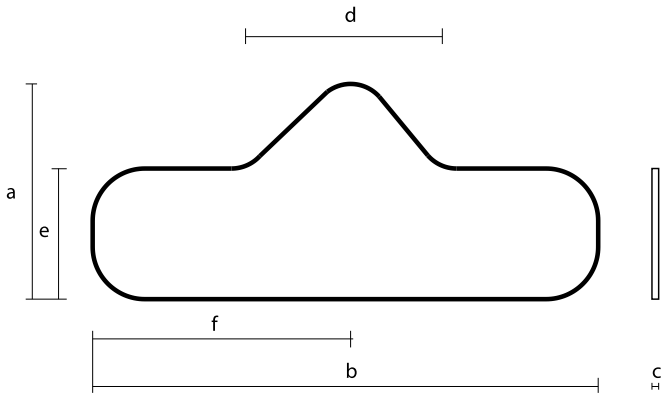


Figure 16: FIDPAD structure.

Table 3: Dimensions and weight of size available.

Size	Dimensions a-b-c-d-e-f (mm)	Weight (g)
Small	34 – 80 – 4.5 -35 - 21 - 37	6.5
Medium	41 – 95 – 4.5 – 39 – 24 – 49	8.8
Large	52 -120 - 4.5 – 47 – 32 - 61	13.5

Figure 17: How FIDPAD nasal pad should be positioned.

The environmental conditions to be observed during transport, the storage and the place of use of the device are:

- Temperature: from -20°C to +60 °C.
- Humidity: from 0% to 95%

The identified warnings to be taken into account are:

- Do not wash the device in the dishwasher or with aggressive shampoos or detergents
- Do not expose the device to direct sunlight or to heat sources greater than 60 °C

- The device is not fireproof so keep it away from open flames
- Replace device after 40 days of use
- Do not use the device if damaged or broken
- Do not ingest or put into the mouth
- Wash with soap and water when in contact with eyes
- In case of redness and/or irritation to the skin, contact your doctor (particularly sensitive skin)

For what concern the disposal, the device should be disposed of in undifferentiated collection. Its packaging must be disposed of in the collection undifferentiated and for no reason disperse the device in the environment.

5.2 Three-Points Hyper Extender

The three-points hyper extender was designed and built by Tecnoway s.r.l. It is mainly composed of a supporting structure in anodized aluminum alloy and supports (padded) in non-toxic material, making the device light, comfortable and safe (Figure 18). Figure 19 indicates and lists all the components of the three-points hyper extender. It is suitable for traumatic and/or pathological fractures of the dorso-lumbar tract, dorsal vertebral failure, specific or non-specific vertebral pain, dorso-lumbar osteoarthritis, spondylarthrosis associated or not with arthritic scoliosis. In addition, it also has a "water line" made of water-repellent materials, suitable for therapies in the pool. Therefore, the patient of the device is the one who presents these problems at the level of the trunk, but also elderly patients who have globose abdomen. The purpose of use of this device is specifically to ensure excellent stabilization, thanks to the three points of thrust: two anterior (sternum and pubis) and one posterior (lumbar spine), allowing to maintain a physiological and natural position, without compromising normal breathing and blood circulation. The device is produced in size variants, as shown in the Table 4.

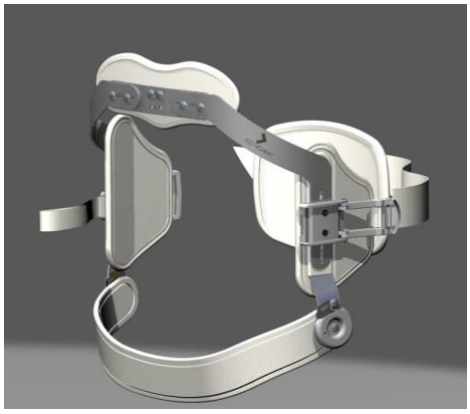
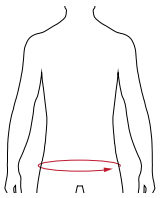
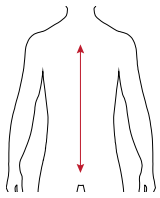


Figure 18: Three-points hyper extender.

1. Sternal pelota	10. Sub axillary adjustment
2. Connection plate	12. Link bar
3. Side	13. Sternal pelota
4. Upper lateral side	14. Latch with belt
5. Lumbar plate	15. Lower lateral side pubic plate
6. Coupling buckle and pin	16. Lower lateral side
7. Pelvic band	17. Arm part
8. Pelvic band mechanism	18. Plate with buttonholes
9. Lateral side	

Figure 19: Three-points hyper extender components.

Table 4: Hyper extender available sizes.

Size	Pelvis girth (cm) 	Sternum-Pubis Length min/max (cm) 
XS	50/60	36/40
S	60/75	39/46
MS	75/90	39/43
M	75/90	42/49
ML	75/90	45/52
LS	90/105	42/49
L	90/105	45/52
XLS	105/115	45/52
XL	105/115	49/56
XXL	115/125	53/60

The medical device in question must be prescribed and applied by an orthopedic doctor, who will instruct the patient on the correct and safe use of the device itself. It is recommended that only one patient use the device, in case the device is used by another person, the parts in direct contact with the skin could pose hygienic or functional risks. However, even in particularly sensitive subjects, the contact between the skin and the device could cause redness and/or irritation.

Then, the identified warnings to be taken into account are:

- The pressure exerted by the device should not act on lesions, or cause symptoms arising from localized compression, nor compress nerve fibers and blood vessels.
- Direct contact between skin and device should be avoided by wearing a garment.
- The device is not fireproof, so do not use it near open flames.
- Do not use the device in the presence of strong electromagnetic fields.
- The strap shall be loosened by means of a release lever slowly to ensure that no sudden torso failure occurs.

In case of non-use of the device, even for short periods, must store it in the original packaging to maintain a good level of cleanliness, keep it in a cool environment, free of moisture and avoid direct sunlight. For what concern the disposal, the three points hyper extender should not disperse into the environment. The device must be disposed of through authorized collection centers.

5.3 Anti-bedsore Mattress

The anti-bedsore mattress was made by Castiflex, belonging to Eurogroup Italia srl company. It is ergonomic as it perfectly molds to every part of the body, creating a perfect and balanced support, ensuring the optimization of support pressures by limiting the risks of prolonged capillary occlusion. It is thermosensitive because the body temperature acts on the molecular structure of this material making it soft and winding, it also has slow memory as it is able to slowly recover the original form. Finally, it has outstanding hypoallergenic, antibacterial and antistatic qualities. The mattress is made and sold in both single and double bed version (Figure 20).

Figure 20: Anti-bedsore mattress.

Therefore, the purpose of use of anti-bedsore mattress is specifically to improve the user resting phase allowing an adequate posture of the body, ensuring the optimization of back-up pressures. Indeed, the patient or end user of the device is the one who during the day adopts incorrect postures for long periods and performs sedentary work. In particular, it is used by patients with the following diseases: lumbar sciatica, disk hernias and arthritis.

It is possible to request particular sizes according to the needs, but usually the standard sizes are:

- Lengths (cm): 190/195/200
- Widths (cm): 80/85/90/120/160/165/170/180

Specially designed in conjunction with motorized bed frame, which we will discuss in the next paragraph. The special design of the sheet in conjunction with the articulated parts of the bed base bends adapting your mattress in a homogeneous way for a perfect comfort.

The constituent parts of mattress are:

- External cover: it is the fabric covers the mattress and is removable according to the model chosen on 2 or 4 sides, allowing periodic washing. All the covers are composed of padding and palm fabric. if the device has been contaminated, the coating should be replaced, and the manufacturer contacted.
- Padding: depending on the type of cover chosen, the mattress has adequate padding both as regards the type of material it will be made of (polyester) and as regards the technical characteristics of weight and density. This is sewn to the covering and is reported in the specifications of each coating.
- Inferior support: polyester sheath that is sewn with the padding and the fabric.
- Under-lining with zipper: This fabric consists of stretch cotton (50%) and polyester (50%), covers and protects the internal structure of the mattress.

The identified warnings to be taken into account are:

• Avoid direct contact between the skin and the device, covering the mattress with any sheet.
• The device is not fireproof, so do not use it near open flames.
• Before its use must be intact both at the structural level and at the level of the coating (which is not contaminated, dirty and/or degraded).
• No foreseeable misuse has been found for the use of the mattress.
• Always perform the required maintenance.

For what concern the disposal, the mattress should not disperse into the environment, but must be disposed of through authorized collection centers.

5.4 Motorized Bed Base

The motorized bed base was built by Castiflex, belonging to Eurogroup Italia srl company. It is a motorized wooden bed base, designed and built to be used by people with disorders or diseases to the spine or neck, disabled and elderly people. The bed frame facilitates the operation of sitting, standing and relaxing the patient's body. It has the purpose of managing the declivous position of the lower limb, the maintenance of the bending of the trunk and of the head distributing the tensions in a balanced and harmonious way to the whole rachis without points of overload or of over distension (Figure 21). In addition, the device can be used in sanitary facilities and in private homes.

Figure 21: Motorized bed.

The device is produced in variants of dimensions (length, width, number of slats) as shown in Table 5.

Table 5: Available dimension of motorized bed. In yellow are reported the width, in green the number of slats and in pink the lengths available.

	80	85	90	120	160	165	170
190	30	32	35	40	60	63	70
195	31	33	36	41	61	65	72
200	32	34	37	42	62	67	74

The environmental conditions to be observed during transport but also for the storage and the place of use of the device are:

- Temperature: from +5 °C to +40 °C.

- Humidity: 80 % in the absence of condensation.
- Atmospheric pressure: 86kPa ~ 106kPa.

In addition, space requirements should also be considered to ensure that the medical device is used without hindrance or hindrance by other products/devices. Therefore, the room in which the medical device will be placed must have:

- Length of at least 4000 mm.
- Width of at least 2600 mm.
- Height of at least 2000 mm.

One of the main limits of the motorized bed concern the weight supported. The medical device can support a maximum weight of 120 kg per square provided that they are evenly distributed. Once the indicated weight is exceeded, the product is deprived of its therapeutic properties. Indeed, a prolonged use of the motorized net with an excessive weight, leads to permanent alterations that make less and/or ineffective its properties.

The accessories associated with the motorized network are the remote control, the control panel and the emergency batteries, necessary for its handling and regulation. Emergency batteries have the only function to return the engine to the resting position in the event of a power failure. While the functions of control panel and remote control are mainly lifting head side, head side return, lifting foot side, back foot side, lifting head and feet simultaneously and head and feet return at the same time.

Then, warnings for proper use are:

- The place where the operation, maintenance and cleaning of the device is carried out must have lighting of at least 200 lux.
- Never expose the device to open flame and/or heat sources.
- It is absolutely forbidden to make any modification on the equipment. Any damage to persons, animals or property resulting from the use of the medical device improperly modified by an unauthorized operator shall relieve the manufacturer of any liability.

Lastly, the construction materials of the device do not require special disposal procedures but must refer to local rules for the scrapping of electrical and electronic equipment.

5.5 Label and User and Maintenance Manual

In general, the presence of an appropriate user and maintenance manual and labeling is a very important requirement to obtain a product that complies with the requirements of MDR 2017/745. In fact, the information provided to the customer is considered fundamental in the risk management process, as, in addition to identifying the product, they allow to avoid risks arising from the incorrect use of the device and warn the user about any residual risks. It is important to note that the labels and user and maintenance manual were written in Italian, the official language used in the countries where the device will be marketed. The label contains information about the manufacturer, useful information about the device such as the symbols needed to identify the product. These symbols are very important to prevent the user from using the device incorrectly. The label must be applied to each product. This can be applied on the product itself or on the packaging or packaging, as long as it is guaranteed that the user can see before buying.

The general symbols used in the creation of the labels are represented in the Table 6. in addition, as shown in the Tables, depending on the device in question, other more specific symbols have been added to the previous.

Table 6: Generical symbols reported on the label and on the instructions for use of the devices.

	Consult instructions for use
	Manufacturer
	Country of manufacturer
	Waste stream disposal status

	CE mark
	Serial number
	Caution

Table 7: Additional symbols reported on the label and on the instructions for use of FIDPAD nasal pad.

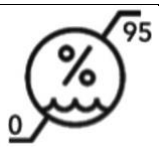
	Temperature limit
	Humidiy limit

Table 8: Additional symbols reported on the label and on the instructions for use of three-points hyper extender.

	Maximun washing temperature in normal condition
	Do not bleach

	Do not iron
	Do not dry clean
	Do not tumble dry

Table 9: Additional symbols reported on the label and on the instructions for use of motorized bed.

	Earth Ground
	RoHS mark (medical device complies with the requirements of Directive 2011/65/EC)
	Dangerous Voltage

5.6 Risk Analysis

The risk management plan is an important document to ensure a systematic approach throughout the process and it is required by UNI CEI EN 14971:2020.

Thus, ISO 14971:2019 requires that the manufacturer identify the characteristics of the medical device that could affect safety of the user, and, as a consequence, identify the hazards associated with it. The risk analysis was divided into two phases.

The first step consists in the analysis of the characteristics of the device that could affect safety according to Annex A of ISO/TR 24971:2020 concerning manufacture, the intended users, the intended use, reasonably foreseeable misuse and final disposal of the medical device. Such questions from the point of view of all the individuals involved (such as users, maintenance workers, patients, etc.) can give rise to a more complete picture of where the potential dangers are to be found.

The second stage consists in identifying known or foreseeable hazards, taking into account both normal use and failures or other unforeseen situations. Annex C of ISO 14971:2019 was used in correspondence with Chapter I of Annex 1 to MDR 2017/745, estimating the degree of risk for each identified hazard and including the mode of control or reduction of risk, according to the "semi-quantitative" method of analysis set out in Annex B ISO/TR 24971. Of course, for the motorized bed, having electrical components, was also consulted Article 3 of 2014/53/EU Directive, Annex I of 2014/30/EU Directive and Annex I of 2014/35/EU Directive. The risks that could not be eliminated were noted in the instructions of use where were given all those suggestions that reduce the danger of the device so as to operate safely. Thus, the method used for the risk assessment was the FMEA analysis for all the devices. From FMEA, the overall risk obtained is acceptable and its expected use brings greater benefits than possible risks, therefore it was not necessary to implement risk control measures.

FMEA Analysis

The FMEA is a technique by which the consequences of an individual fault mode are systematically identified and evaluated. It is an inductive technique using the question "*What happens if …?*". Components are analyzed one at a time, thus generally looking at a single-fault condition. The FMEA is not restricted to a failure of a component's design but can also include failures in the manufacturing and assembling of components and the use or misuse of the product by the end user. It can be extended to incorporate an investigation of the individual component fault modes, their probability of occurrence and detectability and also the degree of severity of the consequences.
Factors causing hazards that have been taken into account are:

- Energy (e.g., electromagnetic, thermal, mechanical, acoustic).
- Gravity (e.g., falls, suspended masses).
- Biological (e.g., bacteria, viruses, cross-infection).
- Chemicals (e.g., exposure of airways, strong acids, alkalis, strong bases, additives, contaminants, residues, cleaning agents, degradation products, medical gases, anesthetic products).
- Biocompatibility (e.g., toxicity of chemical components)
- Function (e.g., incorrect/inappropriate output, incorrect measurement, incorrect transfer, loss of function, error in use, attention error, memory error).

- Characteristics of the device: (e.g., incomplete instructions for use, inadequate description of operating characteristics, inadequate specification of intended use, inadequate explanation of limitations).
- Instructions for use: (e.g., inadequate specification of accessories, inadequate specification of controls before use, instructions too complicated).
- Warnings: (e.g., side effects, dangers related to reuse of disposable devices, service specifications and maintenance).
- Inadequate specifications (e.g., design parameters, operational parameters, operational requirements, service requirements, end-of-life usage).
- Production processes (e.g., changes in the production process, information on compatibility between materials).
- Transport and storage (e.g., inadequate packaging, contamination or deterioration, inappropriate environmental conditions).
- Environmental factors (e.g., heat, pressure, time, corrosion, degradation, susceptibility to electromagnetic disturbance, inadequate energy supply).
- Cleaning, disinfection and sterilization (e.g., missing or inadequate specification of validated procedures for cleaning, disinfection and sterilization).
- Disposal and destruction (e.g., missing or inadequate information, error in use)
- Formulation (e.g., biodegradation, biocompatibility, missing or inadequate specification, inadequate warnings about the dangers of incorrect formulations, error in use).
- Human factors, potential errors in use caused by project failures (e.g., complex or missing control system, ambiguous device status, ambiguous presentation of settings, incorrect presentation of results, insufficient visibility, incompatibility with accessories or other devices, incorrect metrological aspects, insufficient warnings).
- Failures, forgetfulness or errors (e.g., unexpected loss of electrical integrity, mechanical, fatigue failure).

In practice, for each factor were considered and calculate the damage, modes and causes of failure, risk control measures, probability (P), severity (S), detectability (RCM) and impact of control measures (R). The last four have been assigned a numerical value according to Table 10, Table 11, Table 12 and Table 13, still for each factor. From these there were revenues:

- Risk index, calculated as $S \times P$
- Risk index after checking, calculated as $S \times P \times RCM$

- Overall risk index, calculated as $S \times P \times RCM \times R$

Once the values for each factor have been assigned, the results obtained have been compared with the areas of definition of risk acceptability reported in Table 14.

Table 10: Probability assessment.

Probability (P)	Description	Value
Very high	Always tends to manifest itself	5
High	Tends to manifest often, frequently	4
Moderate	Tends to occur periodically	3
Low	Tends to manifest, but not frequently	2
Remote	Tends to occur rarely	1

Table 11: Severity assessment.

Severity (S)	Description	Value
Catastrophic / Fatal	Patient: death or permanent loss of primary functions (sensory, motor, intellectual) Operator: death or permanent loss of primary functions (sensory, motor, intellectual) Properties:- Envirorment:-	4
Critical	Patient: permanent decrease of primary functions (sensory, motor, intellectual), need for major surgery or clinical Operator: permanent decrease of primary functions (sensory, motor, intellectual), need for major surgery or clinical Properties: loss of innovative system or devices, serious damage to structure buildings Envirorment: massive pollution of water, air or soil	3
Seriuos / Major	Patient: increase in treatment time or increase in the level of care required Operator: medical care required Properties: loss of different devices or system, some damage to structures or buildings Envirorment: local environmental pollution	2

Minor	Patient: need for routine care Operator: need for intervention to correct or manage the situation Properties: loss of device in question Envirorment: pollution of structures or accessories	1

Table 12: Detectability assessment.

RCM Index	Description	Value
Negligible	Design: no control during design, no damage is detected during production Alarms and Protections: not activated, damage is not detectable during a routine check Warnings: no warnings on the label or instruction for use	1
Very low	Design: no control during design, damage can be highlighted during production by a 100% control Alarms and Protection: not activated, damage is detectable during a routine check Warnings: no warnings on the label or instruction for use	0.8
Low	Design: damage is easily evidenced during production by a 100% control Alarms and Protection: not activated, damage is definitely detected during a routine check Warnings: generic warnings on the label or instruction for use	0.6
Normal	Design: defined a quality control test to identify damage during production or the feature is made less risky during design, the damage is detectable with a sample control Alarms and Protection: activated after a certain time Warnings: warnings with symbol according to the label or instruction for use	0.4
HIgh	Design: feature is made safe at project level (design solution or process validation) Alarms and Protection: activated immediately Warnings: detailed and obvious warnings with symbols in accordance with the label or instruction for use	0.2

Table 13: Impact of control measures assessment.

R Index	Description	Index
No impact	Design: does not alter other features of the device Alarms and Protection: does not alter other alarms or protections, it is not a source of misunderstandings Warnings: does not alter other warnings, it is not a source of contradictory information	1
Medium impact	Design: alter other features of the device that are not functional features Alarms and Protection: activated at the same time as other alarms/protections Warnings: require changes in the labelling project	1.5
High impact	Design: alter functional features of the device Alarms and Protection: disable other alarms/protections Warnings: source of conflicting information	2

Table 14: Risk Acceptability Criterion.

Risk (R)	Risk Degree
$R < 3$	Low risk – acceptable
$4 < R < 10$	Medium risk - controllable
$R > 12$	High risk – to reduce

This analysis showed that for all devices it was not necessary to carry out a risk management review, as the risk was always found to be acceptable. Therefore, the analysis of the results of the risk management makes it possible to declare that the planned use of the facility entails risks that are abundantly outweighed by the expected benefit.

5.7 Technical File

The technical file of the devices has been drawn up in such a way that any information contained therein can be easily identified. It has been divided into 8 chapters:

- Chapter 1 "*Generality*" aims to standardize the terms used and describe the product in question, presenting the construction features and technical characteristics. In particular, it is prepared to demonstrate the application of the applicable Directives to the device, allowing the verification of design choices and not applied to ensure compliance with the essential safety requirements.
- Chapter 2 "*Development and Design*" illustrates the design solutions chosen for the device construction.
- Chapter 3 "*List of standards consulted*" lists all the harmonized standards that could be considered applicable to the device.
- Chapter 4 "*List of directives and laws consulted*" lists the regulations, legislative decrees and directives consulted for a more extensive and complete documentation on the state of the art regarding the safety of the device.
- Chapter 5 "*Risk management*" reports on risk management activities.
- Chapter 6 "*Risk analysis*" define the risk analysis presented by the device and the risk assessment with the consequent solutions adopted to prevent them, all this in the phases of design and construction of the device itself.
- Chapter 7 "*Documentation concerning the components of the device*" collects and catalogues all the information, documentation and certifications relating to all the commercial sub-parts of the device in order to clarify on what basis the choices of the material to be purchased were made to introduce and use it in the device itself.
- Chapter 8 "*Provision for maintaining conformity*" define the internal provisions and the test procedures that allow the verification of conformity of device and its approved design, in relation to the minimum safety requirements described in this technical file and to maintain such compliance for all subsequent models.

Conclusion

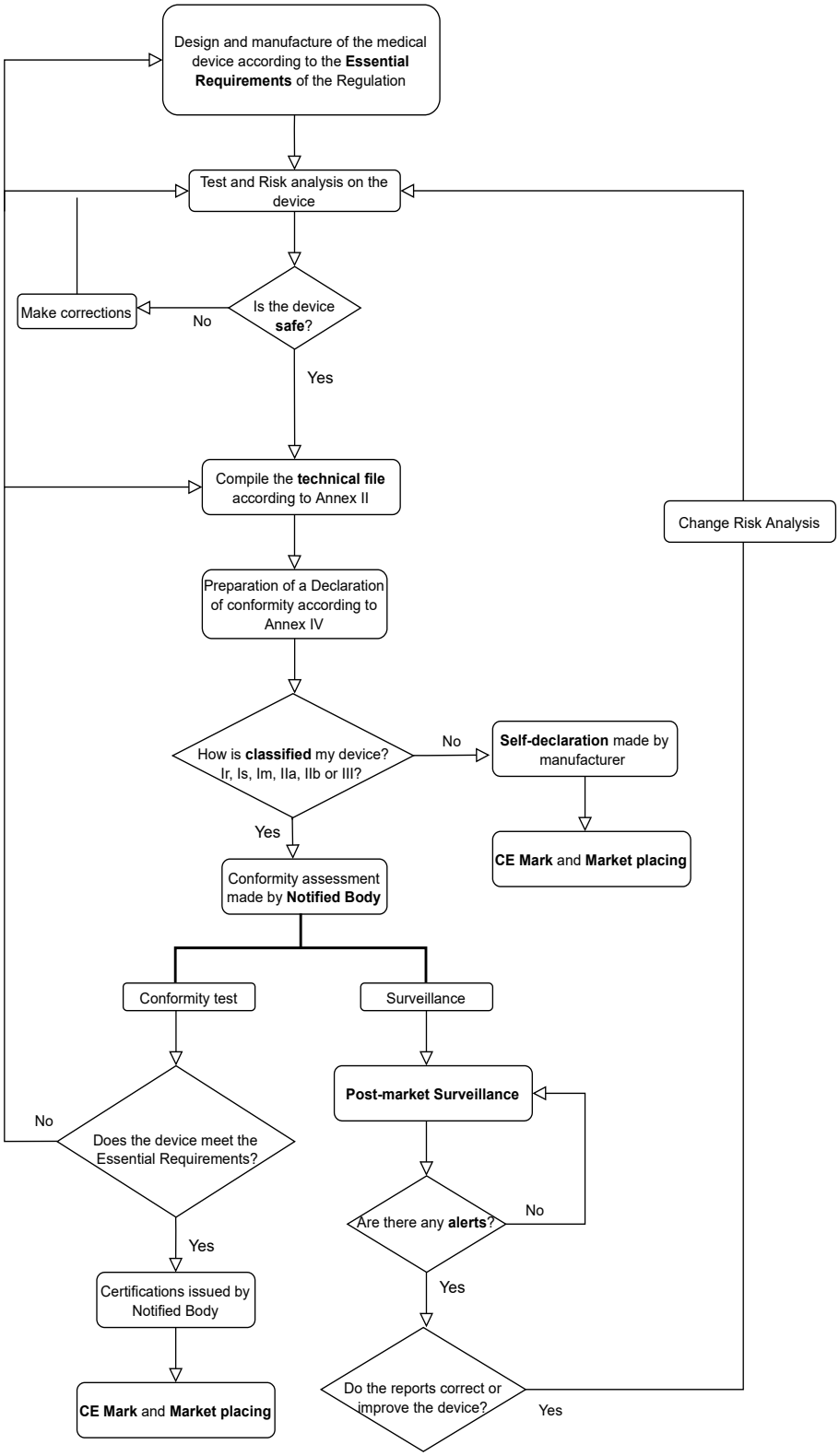
The aim of this thesis work was to highlight the role of drawing up a technical documentation for a medical device in order to obtain the CE marking for its subsequent placing on the market according to the new EU Medical Device Regulation (MDR) 2017/745. The MDR redefines the medical device field, leading to some problems, positivity and challenges for the future that the companies have to fight to market their products. The entire work is articulated in five chapters, starting from the definition of a medical device up to the implementation of the new MDR 2017/745 for real cases. Initially, the general features of the medical device have been analyzed, moving to the properties of the old 93/42/EEC Directives and the new Regulation to make a comparison between them and to understand what MDR upsets or maintains. An accurate and direct consultation of the Directive and Regulation allowed a clear and detailed reconstruction.

Therefore, all the contents for the drafting process of the technical file of a medical device were addressed, dealing with the information which should be included in the technical documentation and the various provisions to be followed by the manufacturer in order to obtain the CE marking. For this purpose, the technical documentation for products defined as "medical devices" by the regulation was developed. The drafting of the technical documentation was carried out through joint work with the company Consultek Group.

The preparation of dossier has seen initially the study of the technical and physical characteristics of the devices, together with the information that the manufacturer has provided us. Subsequently, on the basis of the information available, each device was classified as Class I devices, according to MDR 2017/745. As regard the route for conformity assessment, the technical file has been produced by inserting a description of the device in question, the basic concepts of the new Regulation, the application of the risk analysis with subsequent application of FMEA method and, finally, analyzed and responded points related to the essential requirements. Moreover, the label, the instructions for use and the form of the declaration of conformity have been developed, which are a key part of all the information to be provided by the manufacturer to users and competent authorities. Finally, it has been drawn up a list of the directives, legal provisions and technical standards to which reference has been made.

This thesis was to provide all the documentation necessary to the customer in order to obtain the CE marking and the consent of a subsequent marketing, but also to be a kind of help to the medical devices companies in understanding the main features and changes of the MDR that, they will follow from May 2021.

Annex 1
Marketing path of a medical device



Annex 2

Correlation table of the articles between 93/42/EEC Directive and the MDR 2017/745

Council Directive 93/42/EEC	Regulation 2017/745
Article 1 *"Definitions, Scope"*	***Article 1*** *"Subject matter and scope" Chapter I "Scope and definitions"*
Article 1, first paragraph (1)	Article 1 (1)
Article 1 (2)	***Article 2*** *"Definitions"*
Article 1 (3), first subparagraph	Article 1 (9) first paragraph
Article 1 (3) second paragraph	Article 1 (9) second paragraph
Article 1 (4)	Article 1 (8) first paragraph
Article 1 (7)	Article 1 (11)
Article 1 (5)	Article 1 (6)
Article 1 (6)	–
Article 1 (8)	Article 1 (13)
Article 2 *"Placing on the market and putting into service"*	***Article 5*** *"Placing on the market and putting into service", Chapter II "making available on the market and putting into service of devices, obligations of economic operators, reprocessing, CE marking, free movement* (1)
Article 3 *"Essential Requirements"*	Article 5 (2)
Article 3 (1)	Article 5 (1)
Article 3 (2)	Article 5 (2)
Article 4 *" Free movement, devices intended for special purposes"*	***Article 24*** *"Free movement"*
Article 4 (1)	Article 24
Article 4 (2)	Article 21 (1) and (2)
Article 4 (3)	Article 21 (3)
Article 4 (4)	Article 10 (11)
Article 4 (5), first subparagraph	Article 20 (6)
Article 4 (5) second paragraph	–
Article 5 *"Reference to standards"*	***Article 8*** *"Use of harmonized standards"*
Article 5 (1)	Article 8 (1)
Article 5 (2)	Article 8 (2)
Article 5 (3)	–
Article 7 *"Committee Medical Devices"*	***Article 114*** *"Committee procedure", Chapter X "Final provisions"*
Article 7 (1)	Article 114
Article 8 *"Safeguard clause"*	***Article 94*** *"Evaluation of devices suspected of presenting an unacceptable risk or other non-compliance"* ***Article 97*** *"Other non-compliance"*
Article 9 *"Classification"*	***Article 51*** *"Classification of devices", Chapter V "Classification and conformity assessment"*
Article 10 *"Information on incidents occurring following placing of devices on the market"*	***Article 87*** *"Vigilance" and* ***Article 89*** *"Analysis of serious incidents and field safety corrective actions"*
Article 10 (1)	Article 87 (1) and 89 (2)
Article 10 (2)	Article 87 (10), Article 87 (11) first subparagraph
Article 10 (3)	Article 89 (7)
Article 10 (4)	***Article 91*** *"Implementing acts"*
Article 11 *"Conformity assessment procedure"*	***Article 52*** *"Conformity assessment procedures"*
Article 11 (1)	Article 52 (3)
Article 11 (2)	Article 52 (6)
Article 11 (3)	Article 52 (4) and (5)
Article 11 (4)	–
Article 11 (5)	Article 52 (7)
Article 11 (6)	Article 52 (8)
Article 11 (8)	Article 11 (3)
Article 11 (12)	Article 52 (12)
Article 11 (7)	–
Article 11 (9)	Article 53 (1)
Article 11 (10)	Article 53 (4)
Article 11 (11)	Article 56 (2)
Article 11 (13)	Article 59

Article 11 (14)	Article 4 (5) and Article 122 third paragraph
Article 12 *"Particular procedure for systems and procedure packs and procedure for sterilisation"*	***Article 22*** *"Systems and procedure packs"*
Article 12, letter a (a)	***Article 17*** *"Single-use devices and their reprocessing"*
Article 13 *"Decision with regard to classification and derogation clause"*	—
Article 13 (1) (c)	—
Article 13 (1) (a)	Article 51 (3)(a) and Article 51 (6)
Article 13 (1) (b)	Article 51 (3)(b) and Article 51 (6)
Article 15 *"Clinical Investigations"*	***Article 61*** *" Clinical evaluation "* to ***Article 82*** *" Requirements regarding other clinical investigations"*
Article 14 *"Registration of persons responsible for placing devices on the market"*	Article 30
Article 14 (1,2,3)	Articles 29(4), 30 and 31
Article 14 (2)	Article 11 (1)
Article 14 (a)	***Articles 33*** *"European database on medical devices"* and ***Article 34*** *"Functionality of Eudamed"*
Article 14 (b)	***Article 98*** *"Preventive health protection measures"*
Article 16 *"Notified Bodies"*	***Chapter IV*** *"Notified Bodies"*
Article 16 (1)	Articles 42 and 43
Article 16 (2)	Article 36
Article 16 (3)	Article 46 (4)
Article 16 (4)	—
Article 16 (5)	Article 56 (5)
Article 16 (6)	Article 56 (4)
Article 16 (7)	Articles 38 (2) and 44 (2)
Article 17 *"CE marking"*	***Article 20*** *"CE marking of conformity"*

Article 18 *"Wrongly affixed CE marking"*	***Article 94*** *"Evaluation of devices suspected of presenting an unacceptable risk or other non-compliance"* ***Article 97*** *"Other non-compliance"*
Article 19 *"Decision in respect of refusal or restriction"*	***Article 99*** *"Good administration practice"*
Article 20 *"Confidentiality"*	***Article 109*** *"Confidentiality"*
Article 20 (a)	***Article 102*** *"Cooperation"*
Article 22 *"Implementation, transitional provisions"*	—
Article 23	—
Article 21 *"Repeal and amendment of Directives"*	—

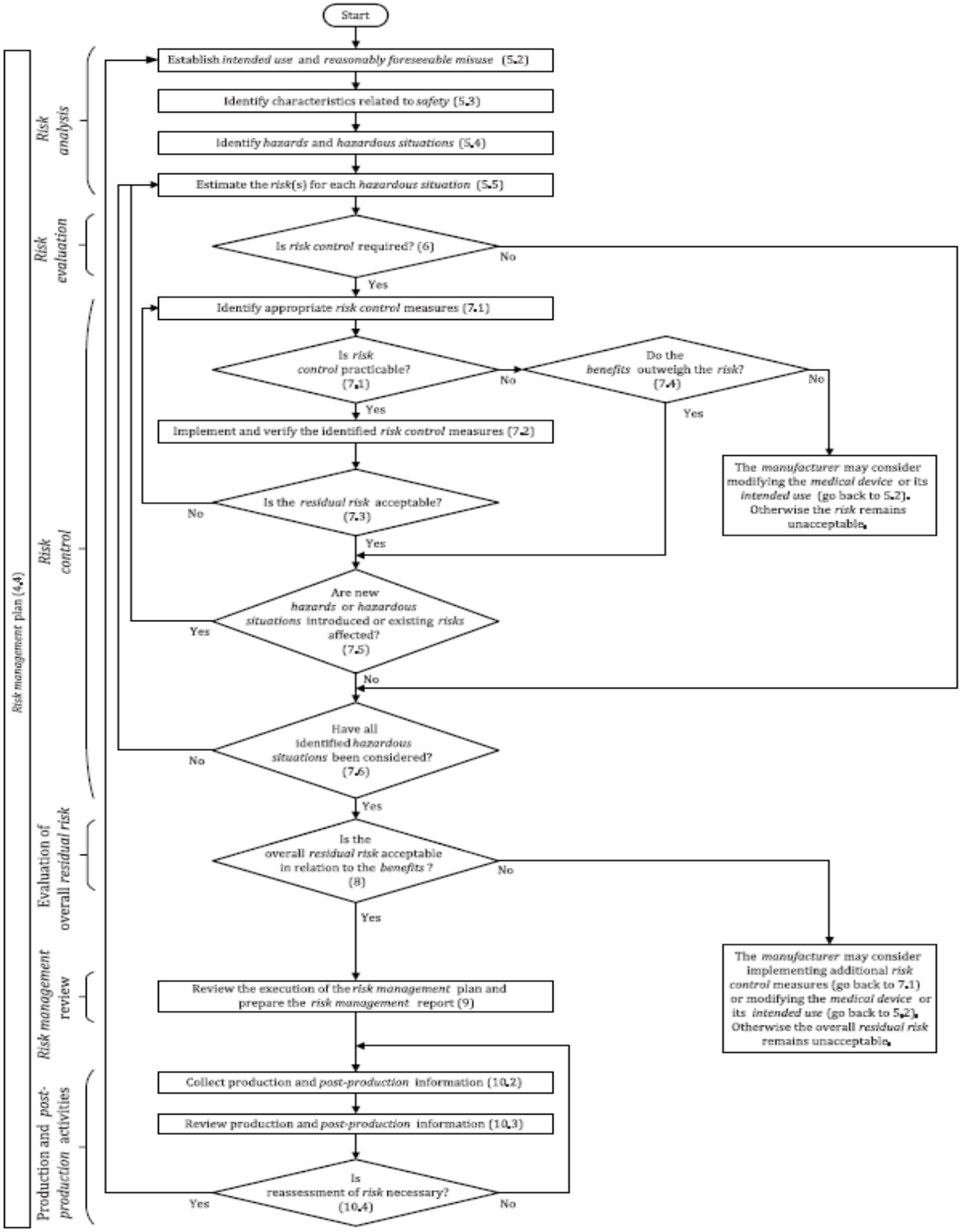
Annex 3

Correlation table of the Annexes between 93/42/EEC Directive and the Medical Device Regulation (UE) 2017/745

Topic of the Annexes	Council Directive 93/42/EEC	Regulation 2017/745
Essential Requirements	Annex I	Annex I
Declaration of Conformity	Annex II Annex III Annex IV Annex V Annex VI Annex VII Annex VIII	Annex IV Annex IX Annex X Annex XI
Classification	Annex IX	Annex VIII
Clinical Evaluation	Annex X	Annex XIV Annex XV
Notified Bodies	Annex XI	Annex VII Annex XII
CE Marking	Annex XII	Annex V
Technical Documentation	–	Annex II
Technical Documentation on post-market surveillance	–	Annex III
Information to be submitted upon the registration of devices and economic operators, UDI database	–	Annex VI
Performance evaluation, performance studies and post-market performance follow-up	–	Annex XIII
Correlation table	–	Annex XVII

Annex 4

Overview of risk management activities as applied to medical devices



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Ringraziamenti

È giunta la conclusione di questo percorso e mi sento di dover ringraziare tutte le persone che mi hanno affiancata, supportata e sopportata.

Innanzitutto, desidero ringraziare la Consultek Group e la Professoressa Laura Burattini per avermi dato l'opportunità di realizzare questo lavoro di tesi. Un ringraziamento va al prezioso aiuto, la disponibilità e cordialità dell'Ing. Andrea Zampa e di Luca Paolini per avermi saputo guidare nella creazione di questo lavoro di tesi.

Un doveroso ringraziamento va alla mia famiglia. A mamma, babbo e Chiara, che in questi anni hanno sempre sostenuto e appoggiato ogni mia decisione. Con il loro instancabile sostegno, sia morale che economico, mi hanno permesso di arrivare fin qui, contribuendo alla mia formazione personale.

Vorrei ringraziare i miei compagni di questo viaggio durato due anni. Siete stati il mio punto di riferimento, non solo a livello universitario, ma soprattutto umano. Un ringraziamento speciale va a Veronica e Claudia, ci siamo trovate a condividere ogni istante di questo percorso, condividendo ansie, mille progetti ma anche tante soddisfazioni. Gli infiniti audio, il loro supporto, la loro determinazione sono stati fattori essenziali del mio percorso.

Ringrazio Stefano. Grazie per aver appoggiato le mie scelte, senza mai ostacolarle. Grazie per aver gioito con me e per aver avuto sempre una parola di conforto. Grazie della tua immensa pazienza e la tua straordinaria comprensione. Grazie per credere e tenere tanto al mio futuro.

Infine, ringrazio me stessa. Per aver creduto tanto in questo percorso e per non aver ceduto al pensiero di non sentirsi abbastanza, per aver stretto i denti ed iniziato la salita. Questa è la prima sosta del mio lungo cammino ed è arrivato il momento di scoprire com'è fatto il mondo vero.

Grazie ad ognuno di voi, avete reso il raggiungimento di questo traguardo unico e speciale.

GRAZIE!