UNIVERSITÀ POLITECNICA DELLE MARCHE

Engineering Faculty

Master Degree in Biomedical Engineering

CE Marking for Medical Devices: Technical Documentation for Annex XVI Devices according to Regulation (EU) 2017/745

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Abstract

From the publication of the new Medical Device Regulation 2017/745 manufacturers are forced to comply with the new requirements. MDR imposes obligations related to the risk management procedure, clinical evaluation, traceability of MD and many other requirements. A correct classification of the MD is necessary to identify the path to follow for the conformity assessment procedure in order to obtain the CE mark.

The publication of the common specifications (CS) established that the products without an intended medical purpose listed in Annex XVI are also covered under the MDR. Thus, the scope of this thesis is to develop the Technical Documentation necessary to complete the certification procedure for aesthetic devices of Annex XVI .

The Technical Documentation was developed for a family of devices used for photoepilation treatments of the company Elits Group. The Technical documentation was developed following Annex II of the MDR and includes the risk management, the biocompatibility, the usability test and the clinical evaluation report (CER).

From the Technical documentation the main properties of the devices under study are described. They are active electrical devices which exploit laser radiation and selection phototermolysis for hair removal purposes. There are two variants of the device. The first uses 808nm diode laser radiation, while the other is available in three configurations: Single Band (808nm), Dual Band (808 & 1064nm) and Trial Band (755, 808 and 1084nm).

The risk management was performed according to ISO 14971:2019 and many electrical, thermal, mechanical and biological risks were analysed. Moreover, risks associated to operating instructions, error of use and those specific of the technology are discussed too. Suitable control measures were adopted to minimize these risks.

All the materials directly in contact with the consumer or with the operator are biocompatible according to the ISO 10993-1:2018. strong rationals have been used in order to avoid biocompatibility testing.

The devices have performed usability tests to prove that the products have been implemented in a correct and functional manner. The devices capable of fulfilling all their functions.

The clinical evaluation takes data primarily from equivalent MD in the literature in order to confirm the safety and performance of the devices under study.

In conclusion, this Technical Documentation, developed for Annex XVI devices, was carried out with the aim to complete as soon as possible the certification procedure.

Contents

Introduction

The application of the new Medical Device Regulation 2017/745 brings novelties with respect to the previous Directive 93/42/EEC. Among these, with the publication of Common Specifications (CS), also the products listed in Annex XVI of the MDR are covered under the MDR.

Manufacturers who wants to place their device on the European market have to be compliant with the new requirements in order to obtain the CE mark. To do this, it is necessary to follow a conformity assessment procedure according to the risk class of the device.

The current work applies to Epil family devices of the company Elits Group. They are aesthetic devices which exploits laser radiation for hair removal purposes. Epil family is composed by Epil808 and EpilSmart models. This last one is available in three different configurations.

The scope of this thesis is to develop the technical documentation for Annex XVI devices for the certification procedure under MDR. It was developed following Annex II of the MDR and includes also the risk management, the biocompatibily, usability test and the clinical evaluation report (CER).

Chapter 1

Medical Device Regulation 2017/745

1.1 Scope of the new Medical Device Regulation 2017/745

The new **EU Medical Device Regulation 2017/745** (MDR) is a set of regulations that governs the production and distribution of medical devices in Europe. It was introduced in 2017 to *increase the safety and quality of medical devices* in the European Union (EU)[1].

Due to a growing number of serious safety issues in medical devices, they proved to be dangerous to patients' health in the EU, making the implementation of MDR necessary. The MDR replaces the Directive 93/42/EEC (*Medical Device Directive, MDD*) and the Directive 90/385/EEC (*Active Implantable Medical Device Directive, AIMDD*) [2]. Regulations, unlike directives, are binding legal acts, therefore they are immediately applicable and have immediate effect in all EU member states without having to be transcribed into national law. [2].

MDR applies primarily to medical devices and its accessories, as well as devices intended for clinical investigations. A **medical device** (MD) is defined as any instrument intended to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- *diagnosis and monitoring* of diseases, injury or disability;
- *replacement or modification* of the anatomy;
- providing information by means of in vitro examination of specimens derived from the human body [3].

In the definition of MD are also included those devices for the control or support of conception and the products specifically intended for the cleaning, disinfection or sterilisation. However, this Regulation does not apply to in vitro diagnostic medical devices, medicinal products, advanced therapy medicinal products, human blood, blood products, plasma or blood cells of human origin or devices which incorporate such products, cosmetics and food. It neither apply to human nor animal tissues and cells. Finally, it does not apply to bacteria, fungi, and viruses [3].

The previous directive for medical devices, which was in effect since 1993, was considered outdated and inadequate in the regard of the limited control mechanisms. Thus, the MDR was created to guarantee that all medical devices licensed for use in the European market adhere to strict safety and quality requirements, thereby reducing patient health risks. In addition to the overarching goal of ensuring a high level of patient protection, harmonization and strengthening of the European internal market for medical devices, the European Community also pursues the objective of facilitating innovation and ensuring the competitiveness of the medical device industry in the EU[1]. With a much broader scope, the MDR addresses the entire lifecycle of a medical device. For all stakeholders in the medical device industry, this inevitably means change; this is due to:

- the extended scope of the MDR;
- incresead requirement for clinical evaluation and clinical investigations;
- mandatory implementation of a system for identification and traceability of medical devices: the Unique Device Identification (UDI) system;
- entering information into the EUDAMED database;
- enhanced specifications for post market surveillance and post market clinical follow-up [2].

Manufacturers, hospitals, and regulators will face significant challenges as a result of the new regulatory requirements. In addition to conducting additional clinical testing and data collection for new devices, manufacturers are required to re-evaluate and re-certify many existing medical equipment. Manufacturers may find it more costly and challenging to create and release new MD due to the additional regulatory requirements, particularly if they must redirect their resources toward re-certifying their existing range of products. This could lead to a reduction in innovation and a slower pace of progress in the industry. Comprehensive technical documentation, on the other hand, can also contribute to improving patient safety by enhancing the quality and safety of medical devices. [1].

1.2 Medical Device nomenclature and identification

Among the innovation that have been introduced with the MDR there is the obligation to implement two system for the identification and traceability of MDs. These are the Unique Device Identification (UDI) system and the European Database on Medical Devices (EUDAMED).

1.2.1 Unique Device Identification system

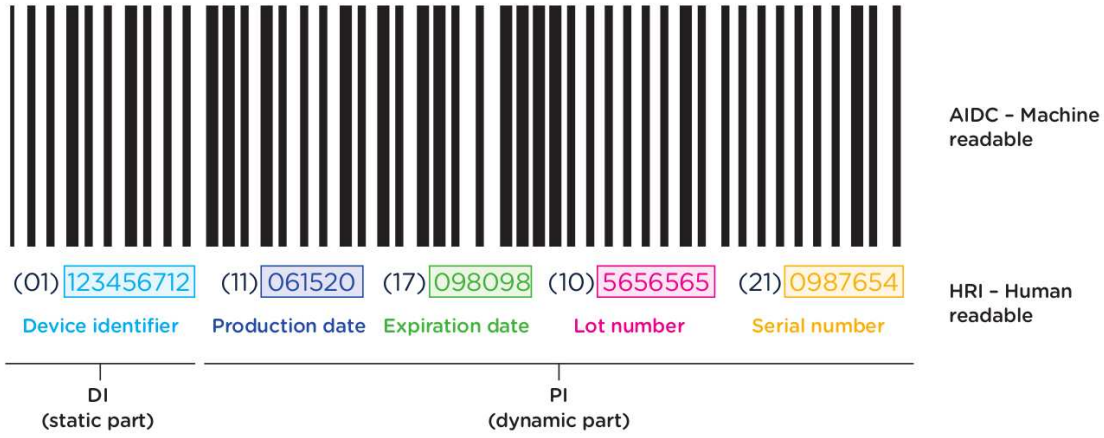


Figure 1.1: Example of a UDI

The UDI system allows the *identification* and facilitate the *traceability* of devices, except custom-made or investigational devices [3]. It was introduced also to improve incident reporting and supervision by national competent authorities [4]. UDI is characterised by a series of numeric or alphanumeric characters and it is created through internationally accepted device coding standards which allow unambiguous identification of specific devices on the market facilitating their traceability [5].

A UDI code is composed of two parts: a UDI-DI and a UDI-PI (Fig.1.1). The **UDI-DI** refers to a *model of device* and it is also used as the access key to information stored in a UDI database. The **UDI-PI** identifies the *unit of device production* and it may include one or more of the following parts: serial number, lot number, software identification, manufacturing date, expiry date [3].

UDI carriers need to be placed on the label and on all higher levels of packaging [3].

1.2.2 European Database on Medical Devices

To meet the objectives of the new regulations, it is important the creation of EUDAMED that must incorporate different electronic systems to gather data about devices on the market, relevant economic operators, as well as certain aspects of conformity assessment, notified bodies, certificates, clinical investigations, vigilance and market surveillance [5].

The goals of EUDAMED include *improving public and healthcare professional access to information*, improving coordination among member states and facilitating information flow between economic operators, notified bodies or sponsors, and member states as well as between member states and the Commission. [5].

EUDAMED is structured around 6 interconnected modules and a public website:

- Actors registration;
- UDI/Devices registration;
- Notified Bodies and Certificates;
- Clinical Investigations and performance studies;
- Vigilance and post-market surveillance;
- Market Surveillance;
- EUDAMED public;

Some of these modules are already available, in particular:

- Actor registration module is available since December 2020;
- The module on UDI/device registration is available since October 2021;
- Notified Bodies and Certificates module is available since October 2021 except for some mechanisms [6].

The remaining modules are under development and will be released when they are declared functional and become mandatory to use (Fig.1.2).

In accordance with the transitional provisions set out in *Regulation (EU) 2024/1860* amending the medical devices regulations, the mandatory use of each module will start **6 months after** it is declared functional [6].

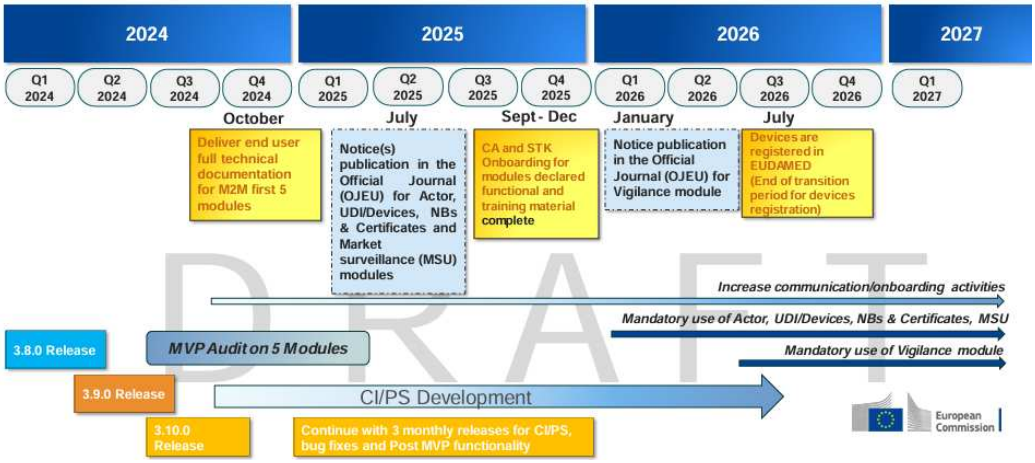


Figure 1.2: Current planning for gradual roll out and modules' functionality view [6]

1.3 Annex I: General Safety and Performance Requirements

Annex I of the MDR regards the General Safety and Performance Requirements (GSPR). Devices must follow strict design and production rules in order to achieve the performance intended by the manufacturer and be suitable for their intended use. This means that devices have to be *safe and effective* without compromising the clinical condition of the subjects [3].

Any risk or hazardous situation associated with the device shall be reduced as far as possible and manufacturers must implement a **risk management system** which has to be updated throughout the entire lifecycle of the product. The majority of GSPR apply to all the devices whereas some dispositions are specific for certain categories of devices, such as active ones, implantable ones, devices with a diagnostic function, sterile ones and also software [3].

In order to fulfill the requirements regarding design and manufacturing many aspects are analyzed such as *chemical, physical, and biological characteristics* of the materials, which have to satisfy the compatibility with body tissues, body liquids, and cells. Moreover, manufacturers have to consider possible medicines and substances that could be introduced into the human body, as well as the presence of those substances considered carcinogenic, mutagenic, or toxic to reproduction (CMR) and endocrine-disrupting (ED). Manufacturers shall also examine if the materials are of biological origin and the eventual presence of nanoparticles [3]. Special attention is given to protection against radiation. In general, the exposure of patients to radiations

has to be reduced as far as possible with different cautions based on whether the radiation is ionizing or not. Furthermore, devices shall be manufactured in order to protect patients from mechanical and thermal risk [3].

This Annex gives also information about **labelling** and the **instruction for use** (IFU). In general each device must be embedded by the information necessary to identify the device itself, the manufacturer and any other relevant information to the user like safety and performance data. These contents may appear on the device, on the packaging or in the IFU [3]. Regarding the labelling, it must contain mainly data about the device (UDI, trade name), the identification of the manufacturer, the time limit for use (or the date of manufacture) and warnings that need to be brought to the immediate attention of the user [3]. If the intended use of the device is not obvious, also this specification must be reported on the label.

The IFU contains the same information that are reported in the label with an higher degree of specification together with additional information such as:

- performance characteristics of the device;
- contraindications and any undesirable side-effect;
- specification to the user for using the device properly;
- the necessity of special training or particular qualifications of the user;
- indications about procedures to be performed before the use (calibration, cleaning and sterilization) [3];

Given all the essential information present in the IFU, they have to be easily understood by the users [3].

1.4 Annex VIII: Classification Rules

The classification of medical devices in use by the EU medical device legislation is a **risk-based system** taking into account the vulnerability of the human body and the potential risks associated with the devices. This approach uses a set of criteria that can be combined in various ways in order to determine classification such as duration of contact with the body, degree of invasiveness, potential toxicity, the part of the body affected by the use of the device and if the device is active or not. The criteria that are applied are referred to as the '*classification rules*' and are set out in Annex VIII of MDR [7]; according to them, devices can be classifies as Class I, IIa, IIb and III.

The *duration of use* of the device is an important aspect that is considered in the classification and it can be:

- **transient**: means continuous use for less than 60 minutes;
- **short term**: continuous use for between 60 minutes and 30 days;
- **long term**: continuous use for more than 30 days [3].

The manufacturer must take into consideration all the rules in order to establish the proper classification for its device. The strictest rule resulting in the highest classification determines the class [7].

Non invasive devices: Rules 1,2,3,4 (Fig. 1.3):
All non-invasive devices are classified as *Class I* according to the Rules 1,2,3 and 4 (Fig. 1.3). Higher risk classes are for devices containing body fluids, entering in contact with mucosal membrane or wounds, or modifying the chemical and biological composition of human cells and tissues [3].

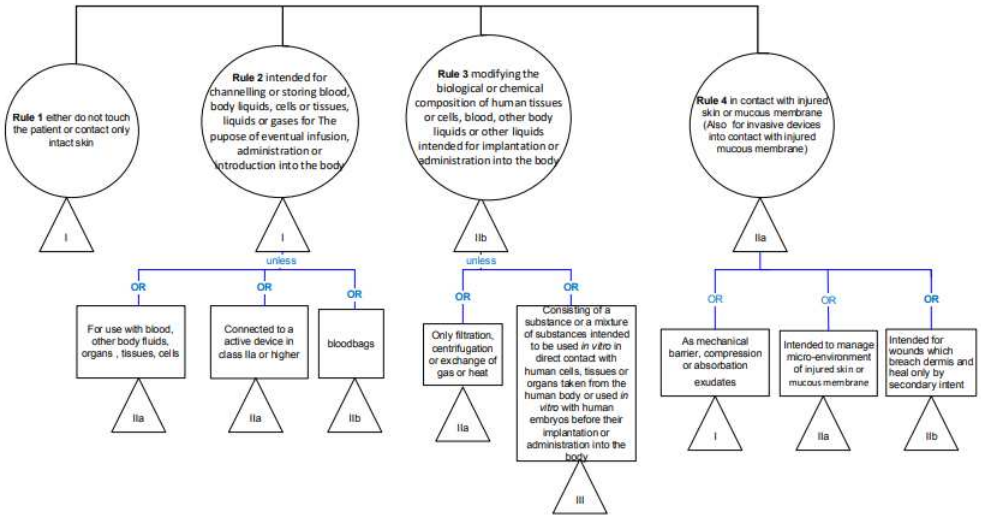


Figure 1.3: The figure shows the blocks containing rules for non-invasive devices [7]. From the blocks, it is possible to see how non-invasive devices are divided into different classes.

Invasive devices: Rule 5 (Fig. 1.4), Rule 6 (Fig. 1.5), Rule 7 (Fig. 1.6) and Rule 8 (Fig. 1.7) :
These rules apply to invasive devices. An invasive device is defined as *any device which, in whole or in part, penetrates inside the body, either through a*

body orifice or through the surface of the body. A device that administers energy to the body should not be considered as invasive if only energy penetrates the body and not the device itself [3]. Each rule is specific for a particular kind of invasive device as is shown by the Table 1.1.

Rule number	Characterization
Rule 5	Invasive devices with respect to body orifices
Rule 6	Surgically invasive devices intended for transient use
Rule 7	Surgically invasive devices intended for short-term use
Rule 8	Implantable devices and long-term surgically invasive devices

Table 1.1: Rules for invasive devices.

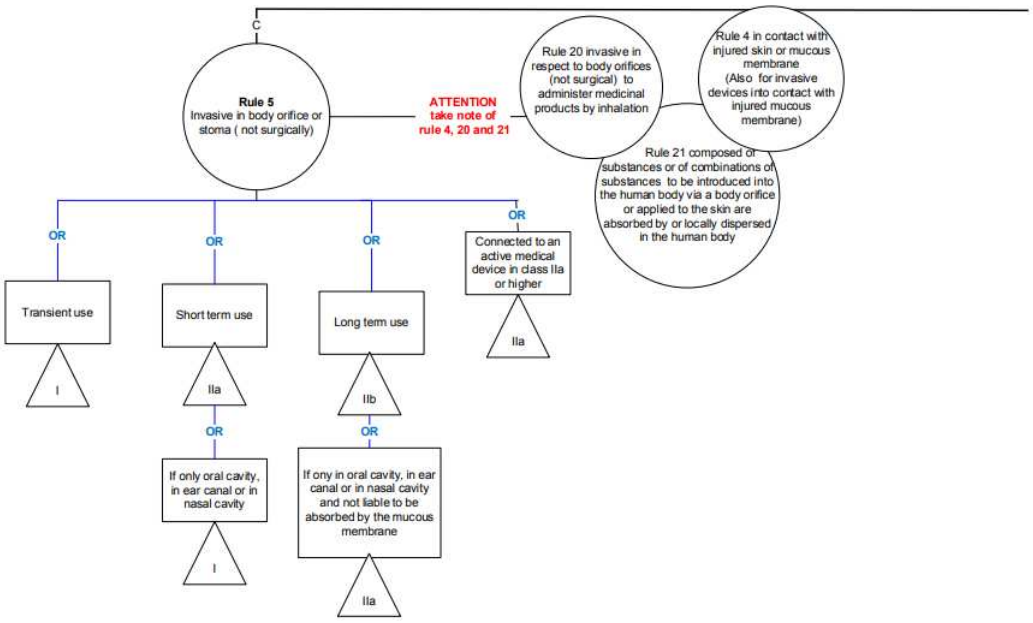


Figure 1.4: The figure shows the blocks containing rule 5 for invasive devices with respect to body orifices [7]. From the blocks, it is possible to see how these invasive devices are divided into different classes.

Devices belonging to the Rule 5 are classified according to the duration of use (Fig. 1.4):

- class I if they are intended for transient use;

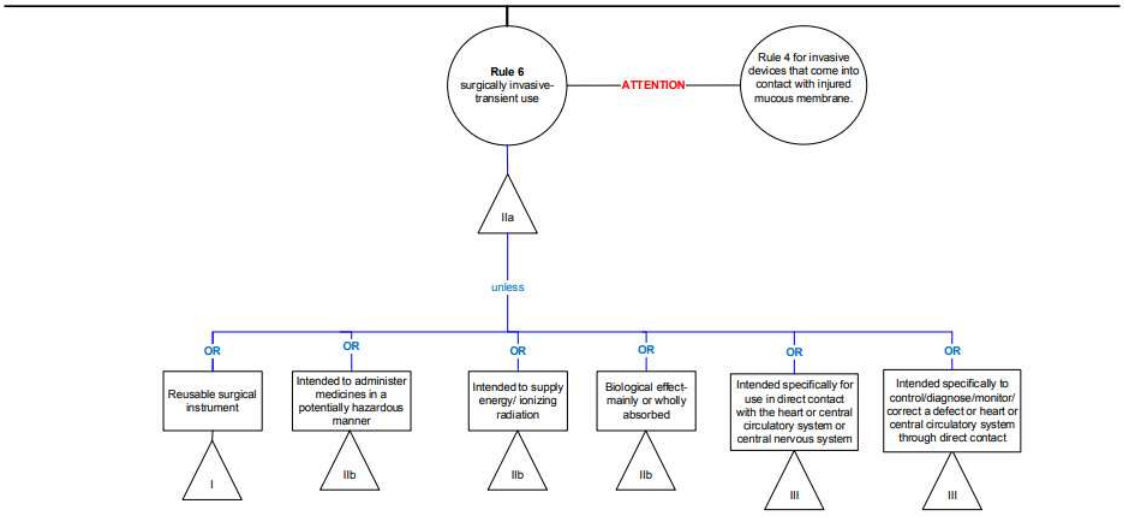


Figure 1.5: The figure shows the blocks containing rule 6 for surgically invasive devices for transient use [7]. From the blocks, it is possible to see how these invasive devices are divided into different classes.

- class IIa if they are intended for short-term use, except if they are used in the oral, ear or cavity in which case they are classified as Class I;
- class IIb if they are intended for long-term use, except if they are used in the oral, ear or nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are classified as class IIa [3].

Devices falling under Rule 6 and 7 are classified as IIa, with some exceptions as shown in the figures (Fig. 1.5, 1.6). All implantable devices and long-term surgically invasive devices are classified as class IIb [3] with the exception shown in the figure (Fig. 1.7)

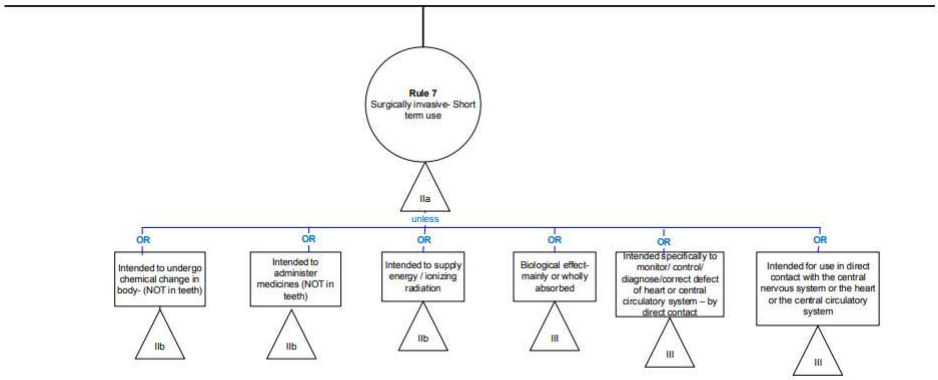


Figure 1.6: The figure shows the blocks containing rule 7 for surgically invasive devices for short term use [7]. From the blocks, it is possible to see how these invasive devices are divided into different classes.

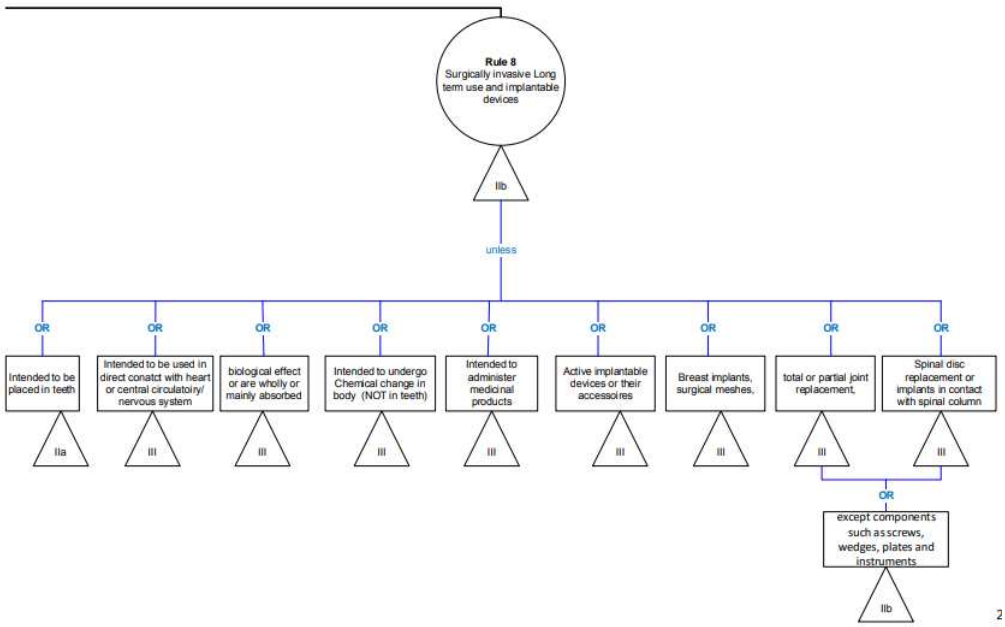


Figure 1.7: The figure shows the blocks containing rule 8 for surgically invasive devices for long term use and implantable devices [7]. From the blocks, it is possible to see how these invasive and implantable devices are divided into different classes.

Active devices: Rules 9-10 (Fig.1.8), 11-13 (Fig.1.9)

An active device means *any device, the operation of which depends on a source of energy other than that generated by the human body for that purpose,*

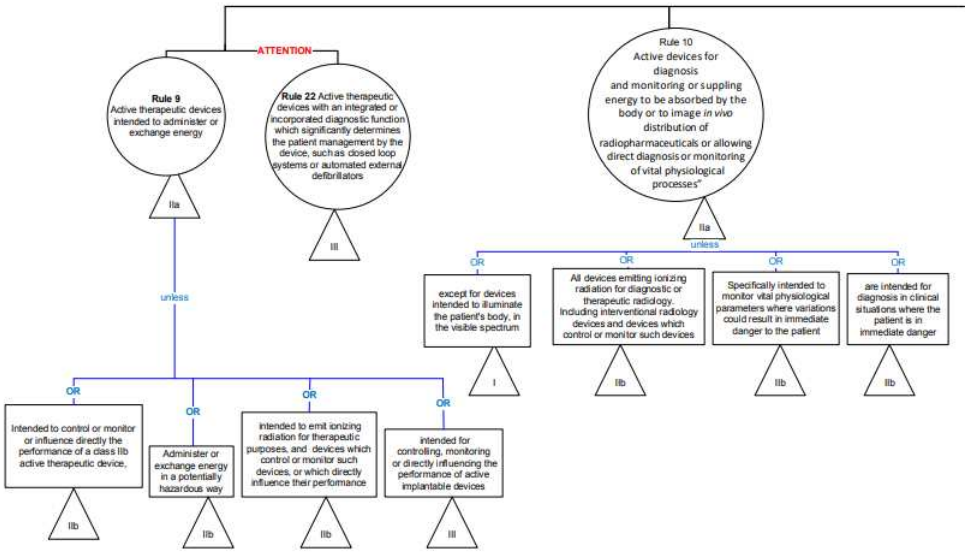


Figure 1.8: The figure shows the blocks containing rules 9 and 10 for active devices [7]. From the blocks,it is possible to see how these active devices are divided into different classes.

or by gravity, and which acts by changing the density of or converting that energy [3].

All active therapeutic devices (Fig. 1.8) intended to administer or exchange energy are classified as class IIa unless their characteristics are such that they may administer energy with the human body in a potentially hazardous way in which case they are classified as class IIb [3]. Devices falling under the Rule 10 are classified as IIa with the exception presented in the figure (Fig.1.8). Rule 11 (Fig. 1.9) refers to software intended to provide information for taking decisions with diagnostic or therapeutic purposes; they are generally classified as IIa, such as those software intended to monitor physiological processes. Exceptions are present in the case in which:

- the decision taken by the software may cause death or an irreversible deterioration; in that case it is classified as Class III;
- the decision taken by the software may cause a serious deterioration of a person's state health; in this case it is classified as IIb;
- the software is intended to monitor vital physiological parameters; in this case it belongs to Class IIb [3].

In all the other cases the software belong to Class I [3].

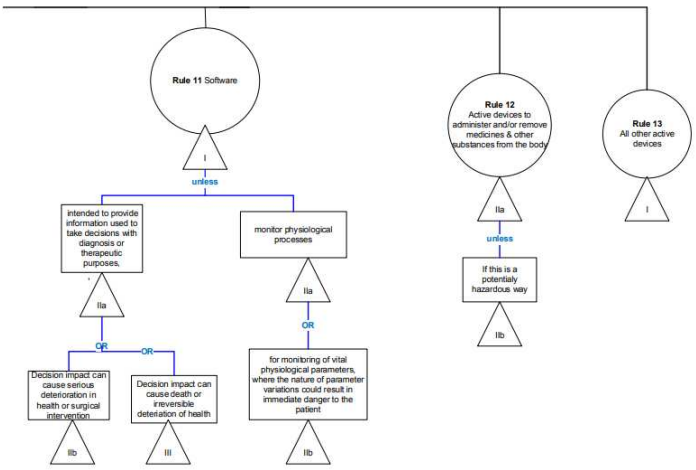


Figure 1.9: The figure shows the blocks containing rules 11, 12, and 13 for active devices [7]. From the blocks, it is possible to see how these active devices are divided into different classes.

Special Rules: 14-18 (Fig. 1.10), 18-22 (Fig.1.11)

Special rules are reported in Tab.1.2. Devices falling under the special rules are classified as shown by the Figures 1.10, 1.11.

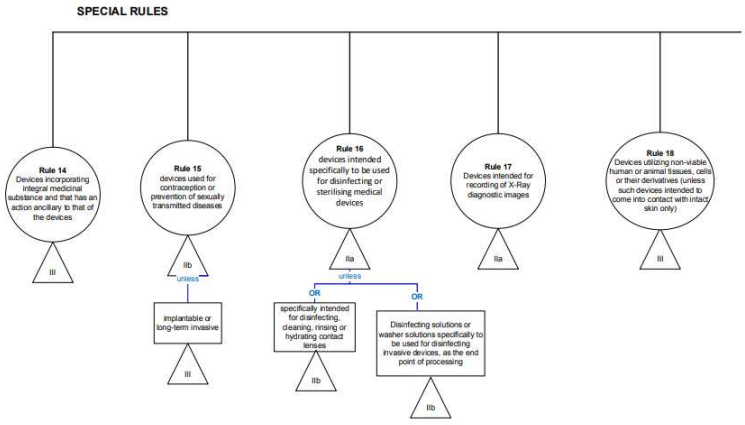


Figure 1.10: The figure shows the blocks containing special rules number 14, 15, 16, 17, and 18 [7]. From the blocks, it is possible to see how medical devices are divided into different classes.

Table 1.2: Special rules for medical devices [3].

Rule number	Characterization
Rule 14	Devices incorporating a medicinal product
Rule 15	Devices used for contraception
Rule 16	Devices for disinfecting, cleaning, or sterilising medical devices
Rule 17	Devices for recording images generated by X-ray radiation
Rule 18	Devices manufactured with non viable human/animal tissue
Rule 19	Devices incorporating or consisting of nanomaterial
Rule 20	Invasive devices for administrating medicinal products by inhalation
Rule 21	Devices composed of substances to be introduced via a body orifice
Rule 22	Active therapeutic devices with an integrated diagnostic function

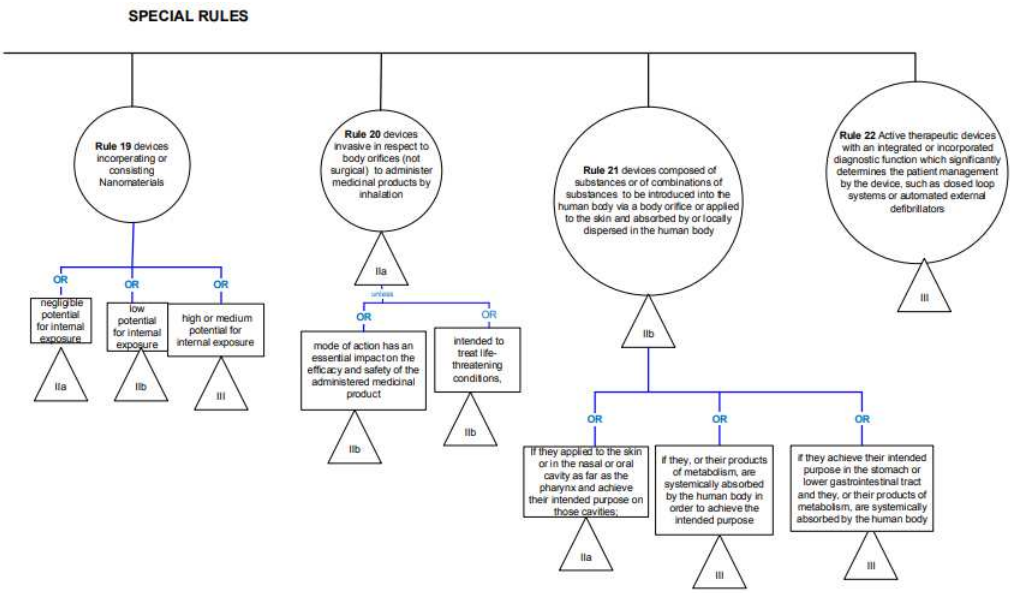


Figure 1.11: The figure shows the blocks containing special rules number 19, 20, 21, and 22 [7]. From the blocks, it is possible to see how medical devices are divided into different classes.

1.5 Annex XIV-XV: Clinical Evaluation and Clinical Investigation

Clinical Evaluation and **Clinical Investigation** represent two distinct processes with the same purpose *to assess and verify the safety and perfor-*

mance of a device. In particular, clinical evaluation refers to a theoretical assessment of collecting and generating clinical data, while the clinical investigation regards the involvement of a group of humans [3]. According to MDR, clinical evidence provided according to Article 61 and Annex XIV is necessary to demonstrate compliance with the relevant general safety and performance requirements [8]. To conduct a clinical evaluation, a specific and methodologically sound procedure should be followed based on the following points:

- the device's safety, performance, design characteristics, and intended purpose need to be evaluated critically in the relevant, currently available scientific literature;
- a thorough evaluation of all clinical investigation results;
- examining the available alternative treatment options for that purpose, if there are any [8].

Updating the clinical evaluation and its documentation is necessary throughout the device's life cycle and it must be implemented in a manner that its inputs and outputs can be utilized for various related activities.

Clinical evaluation may be made using clinical data related to a device that demonstrates equivalence to the device in question [3]; to establish equivalence, every device must meet all technical, biological, and clinical characteristics as descripted in Figure 1.12.

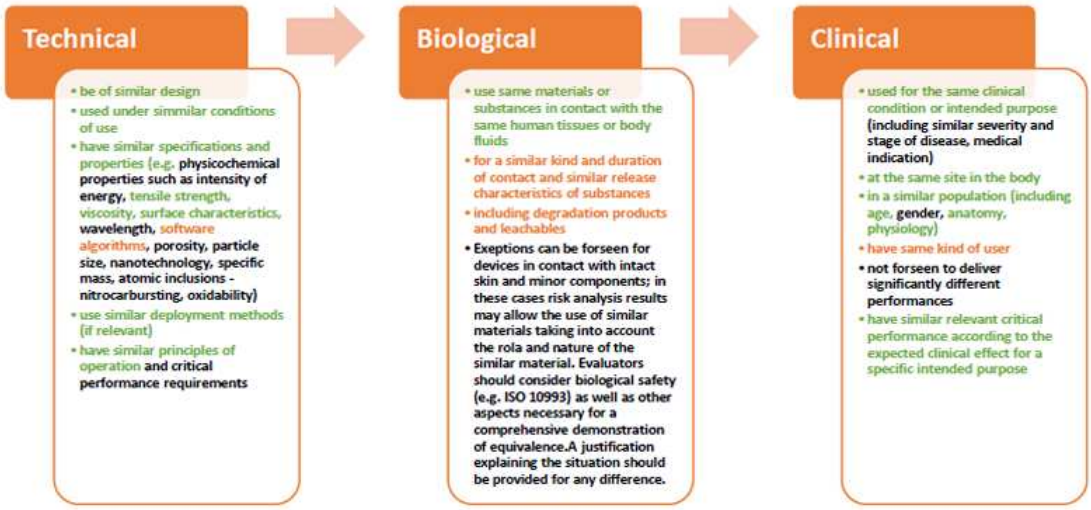


Figure 1.12: Technical, biological and clinical characteristics for demonstration of equivalence [8].

In the case of the products without an intended medical purpose listed in Annex XVI, the requirement to demonstrate a clinical benefit means to demonstrate the performance of the device [3].

The clinical evaluation, its results and the clinical evidence derived from it shall be documented in a **clinical evaluation report** (CER) for each device, except for custom-made devices [3]. Clinical evaluation must be performed for all the device.

Clinical investigations are mandatory for implantable and Class III devices, unless:

- it is equivalent to a device already marketed by the same manufacturer and the clinical evaluation of the latter is adequate to demonstrate the conformity of the new one;
- class III devices already marketed under MDD and for implantable devices listed in paragraph 6 of the Article 61 (like sutures), that have sufficient clinical data to demonstrate their conformity [8].

It means that in all the cases in which the clinical investigation is not mandatory, if the manufacturer is able to demonstrate that its device is equivalent to another one already CE marked and compliant with MDR, the clinical investigation is not necessary. Anyway, it is important to note that, in the absence of clinical data, a low-risk MD requires a clinical investigation [8].

Clinical investigation requires a sponsor which is responsible for its initiation, management and setting up of the financing. This sponsor shall submit an application to the Member State in which the clinical investigation is to be conducted by means of an electronic system and it has to report any adverse event or device deficiency encountered during the examination [3].

The investigator is a person qualified for the role of investigator and having the necessary scientific knowledge and experience in patient care. Other personnel involved in conducting a clinical investigation shall be suitably trained [3]. Moreover, all the subjects performed the interview must give their informed consent [3].

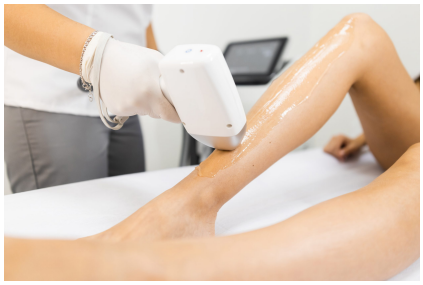
1.6 Products without an intended medical purpose

Annex XVI refers to those products covered under the MDR without an intended medical purpose.

This is a new category of products, and the MDR introduces requirements for their manufacture and surveillance because they are similar to medical devices in terms of function and risk profile. These products are divided in six groups:

1. Contact lenses or other items intended to be introduced into the eye (Fig. 1.13a);
2. Products introduced into the human body through surgically invasive means to modify the anatomy or fix body parts (except tattoos and piercings);
3. Substances or items for facial or other dermal or mucous membrane filling;
4. Equipment for removing adipose tissue (equipment for liposuction, lipolysis or lipoplasty);
5. Products emitting high intensity electromagnetic radiation such as lasers and intense pulsed light equipment for skin treatment
6. Devices for brain stimulation that apply electromagnetic fields which penetrate the cranium [3].

(a) *Contact Lenses*



(b) *Laser for epilation*

Figure 1.13: Examples of products without an intended medical purpose

While there are definitions for a "medical device" and an "accessory for a medical device" that determine the meaning of the two terms, for Annex XVI products the Regulation does not provide any definition. Therefore, to determine if a product is covered by the MDR, the descriptions of the groups must be used [9]. Moreover, for these products, Regulation (EU) 2017/745 established the need to define common specifications (CS) and a period of six months from the date of their entry into force (22 December 2022), to allow manufacturers to comply with the new requirements.

Therefore, from 22 June 2023, Regulation (EU) 2017/745 is also applicable to products without a medical use for which common specifications have been defined.

Manufacturers must follow certain guidelines to guarantee that these products comply with EU regulations and these include:

- **Common specifications**: propose requirements for risk management, labeling, and instructions for use, as well as clinical evaluation [10];
- **Risk reclassification**: certain active products without medical purposes have been reclassified according to Regulation (EU) 2022/2347 [11];
- **Technical documentation**: manufacturers must provide evidence of meeting relevant GSPRs and common specifications;
- **Conformity Assessment**: manufacturers must choose the appropriate conformity assessment route and involve a Notified Body where necessary.

Regulation (EU) 2022/2347 of 1 December 2022 lays down reclassification of groups of certain active products without an intended medical purpose, in particular:

- devices emitting high intensity electromagnetic radiation for skin treatment are reclassified as class IIb, unless they are intended for hair removal only in which case it is reclassified as class IIa;
- products for reducing or removing adipose tissue are reclassified as class IIb;
- equipment intended for brain stimulation that apply electromagnetic fields is reclassified as class III [11].

1.6.1 Common specifications for the groups of products listed in Annex XVI

Common Specifications (CS) have been released by the European Commission with the Implementing Regulation (EU) 2022/2346 of 1 December 2022 and are applicable form 22 June 2023. It means that from that date, the rules estabilished by MDR becomes mandatory also for the products listed in Annex XVI [10]. CS represent a set of technical and clinical requirements, other than a standard, that provide a means of complying with the legal obligations [10]. It contains seven Annexes, the first of which propose CS for all the products without an intended medical purpose and the remaining ones each refer to one group of products listed in Annex XVI.

Regulation 2022/2346 explains risk management requirements for the product to which it relates. They involve:

- risk management planning;
- identification of hazards;
- risk evaluation;
- risk evaluation and control of residual risks;
- risk management review;
- production and post- production activities [10].

Moreover, according to Annex I of the CS, for these products the label must contain the words "*non-medical purpose*" followed by a description of this purpose [10]. Addiotionally, the IFU shall include information regarding categories of users and consumers, the expected performance of the device, its residual risk and the expected lifetime [10].

CS also introduce transitional provisions to allow devices to remain on the market waiting for MDR compliance. These give manufacturers time to carry out the requirements of clinical trials and conformity assessment procedures [12].

Chapter 2

Social Environment around MDR

2.1 Economic Operators

With the adoption of the MDR and IVDR the regulations for medical devices and in vitro medical devices have changed dramatically.

For example, with the new MDR the figures of the importer and the distributor, which were not regulated in the MDD, have also been regulated.

2.1.1 Manufacturers

Manufacturer refers to a legal person who manufactures and markets a device under its name or trademark [3]. Given that both the device and the manufacturer must comply with the MDR, the manufacturer has the main role in complying with the Regulation and holds the largest part of responsibility. According to *Article 10* of the MDR, manufacturers shall:

- have systems for **risk management** and q**uality management**;
- conduct **clinical evaluations**;
- compile **technical documentation** and apply a **conformity assessment procedure** [3], [13].

Moreover, manufacturers are also responsible for their devices once they are on the market and need systems in place to cover their financial responsibility for harm caused by defective devices [13]. Every manufacturer shall have a named person responsible for regulatory compliance. Once they have completed all these obligations, manufacturers have to execute a *declaration of conformity* and apply CE marking to their devices [13].

Manufacturers outside the EU who wants to place its device on the European market shall have a contract with a sole **authorised representative** [3]. The authorized representative's tasks are agreed upon with the manufacturer and documented in the mandate. The duties concern checking the technical documentation, the certificates of conformity, the EU declaration of conformity, and the registration to Eudamed.

The authorized representative can be changed; in this case, the terms of the cessation of the outgoing representative's mandate are agreed with the manufacturers [3].

2.1.2 Importers and Distributors

An **importer** is defined as any natural or legal person established in the EU that places a device from a third country on the EU market [14]. *Article 13* of the MDR outlines several general obligations for importers. These include ensuring that the device placed on the market comes with the CE marking, is labeled in accordance with the MDR, have assigned a UDI and is registered in EUDAMED [14].

A **distributor** performs similar tasks of an importer and he is the one that makes a device available on the market, up until the point of putting it into service. Distributors' responsibilities are described in *Article 14* of MDR [14].

Importers shall indicate on the device or its packaging their registered place of business and the address at which they can be contacted [15]; then, the distributor checks if the importer's name is indicated on each device. Both importers and distributors shall inform the manufacturer and the authorised representative if the a device is not compliant with the Regulation, if there is a suspicion that a device has been falsified or that there is a serious risk to health. According to this, they have to keep a register of complaints, non-conforming devices, recalls and withdrawals [15].

Sometimes obligations for the manufacturers apply to importers and distributors. This happens when importers or distributors:

- place a product on the market with their name;
- change the intended purpose of a device already on the market;
- modify some characteristics of the device so that its compliance has to be proved again [3].

2.2 Medical Device Coordination Group

The Medical Device Coordination Group (MDCG) is an expert committee composed of people appointed by the Member States according to their expertise in the field of medical devices. Its role is to *give support and advices to the Commission* and assist the Commission and the Member States in ensuring a harmonised implementation of the Regulation. Each Member State appoint **one member and one alternate** with expertise in the field of *medical devices* and one member and one alternate with expertise in the field of *in vitro* diagnostic medical devices. The alternates are those that represents and vote for the members in their absence [3]. Among the tasks performed by the MDCG there are:

- the *assessment of the Notified Bodies* who did application;
- *development of standards* or CS related to MD;
- contribution to the *implementation of MDR*;
- possible *modifications to general requirements*;
- *collaboration with the competent authorities* in important decisions, such as classification, clinical investigation, vigilance, and Post-Market Surveillance [3].

The MDCG members cover their role for **three years**, then the designation has to be renewed [3].

2.3 Notified Bodies

A **Notified Body** (NB) is an organisation designated by an EU country to *assess the conformity* of certain products before being placed on the market. These bodies carry out tasks related to conformity assessment procedures set out in the applicable legislation, when a third party is required [3]. In particular, NB:

- are free to offer their conformity assessment services to any economic operator inside or outside the EU;
- these activities may be carried out on the territory of other EU countries or non-EU countries;

- must operate in a *non-discriminatory, transparent, neutral, independent, and impartial manner*;
- must employ the necessary personnel, with sufficient knowledge and experience to carry out the conformity assessment;
- must take the necessary precautions to ensure the confidentiality of the information;
- must be adequately insured to cover their professional activities;
- must provide information to their notifying authority, the market surveillance authorities, and other notified bodies [3]

In order to carry out the conformity assessment procedure, the manufactures are free to choose any NB that has been legally designated. Lists of NB are available on the **NANDO** website (New Approach Notified and Designated Organisations). The list is regularly updated and each notified body is *identified by a number and associated with a description* of its role.

NB take responsibilities in areas of public interest and, therefore, must remain accountable to the competent national authorities. They shall inform the competent authorities about their activities and must report all the certificate that have been refused or suspended due to non-conformities [16].

The NB applies to the authorities responsible for them, specifying the activities they would like to perform and the devices they would like to work with. Then, this application is checked by those authorities together with the joint assessment team, who is appointed by the Commission and the MDCG and composed of experts for this assessment. The NB will have time to apply corrective actions in case of non-conformities. Once the application's compliance is confirmed, an electronic notification regarding the NB's designation is sent by the Member State.
The designation becomes valid the day after the notification when the NB shall start to perform their conformity assessment activity [3].

2.4 Expert panels

MDR contains important improvements including stricter control for high-risk devices via a new pre-market scrutiny mechanism, reinforcement of the rules on clinical evidence and increased transparency. To this end, they require the establishment of scientific bodies, namely expert panels, expert laboratories and EU Reference Laboratories (EURLs). Their roles, described

in *Article 106* of the MDR, are to provide the European Commission, Member States, notified bodies and manufactures with scientific and technical advice, contribute to guidance and other relevant documents, and to identify emerging issues of concern regarding medical devices.

The expert panels have the following tasks, depending on needs:

- providing an opinion on the notified bodies' assessments of clinical evaluation of certain high-risk medical devices and the performance evaluation of certain in vitro diagnostic medical devices;
- providing advice to the MDCG and the European Commission concerning safety and performance of medical devices and in vitro diagnostic medical devices;
- providing advice to manufacturers on their clinical development strategy and proposals for clinical investigations;
- providing advice to EU countries, manufacturers and notified bodies on various scientific and technical matters;
- contributing to the development and maintenance of relevant guidance documents, common specifications and international standards;
- providing opinions in response to consultations from manufacturers, EU countries and notified bodies;

Panel members are top-notch experts in their own field appointed by the European Commission on the basis of their scientific, clinical and technical expertise following a call for expression of interests. The selection is made by the European Commission and the appointment in consultation with the MDCG. The experts must have:

- full rights as a citizen of a Member State of the EU;
- a university degree in a relevant medical or scientific areas;
- at least 10 years of relevant professional experience;
- good knowledge of the English language allowing active participation in the work of the panels;

Experts are appointed for a term of three years, with the possibility of renewal.

Chapter 3

European Certification procedures

3.1 From Device Manufacturing to CE Marking

Commercializing medical devices in the EU requires a CE marking demonstrating compliance with MDR. Prior to CE marking a medical device, it is important that it is designed following GSPR and to define its risk class. The manufacturers have also to carry out a clinical evaluation or a clinical investigation to demonstrate that the device's clinical benefits overcome possible harmful situations and side effects.

Manufacturers planning to sell the products in the EU should have a **Quality Management System** (QMS) that complies with the requirements of Annex IX of MDR. One of the most common way to create it is through the implementation of *ISO 13485:2018*; this standard is fully harmonized according to the requirements of the Regulations and permits verification of the QMS used by the manufacturer.

The manufacturer prepares the **technical documentation** which scope, structure and contents are determined by the *Annex II and III* of the MDR. During the preparation of this technical file, the manufacturer should perform all the required trials on the MD. Among these, there are technical testing, testing for biocompatibility and clinical trials [3].

Then, the procedure depends on the risk class of the device. For **Class I** devices (non sterile and without measuring functions) the process is simplified and *does not required the involvement of a NB*. Thus, the procedure is resolved with a **self-conformity assessment**, declaring that the device is compliant with MDR requirements; the CE mark is put on the device and it

is placed on the market [3]. Otherwise, if the devices fall within **class IIa, IIb and III**, the conformity assessment requires a NB and takes longer time. This procedure includes the *evaluation of the QMS and the technical documentation*. When the NB declares the **non-conformity** of the device, the manufacturers must make corrections or modify the intended use. Once the conformity assessment is passed, the ND released the certificate to the manufacturer, who affix the CE mark and can release the device on the market [3]. Finally, the last step is represented by the **Post-Market Surveillance** (PMS) which guarantees the safety of the device after the commercialization. When a major incidence is verified, manufacturers take corrective actions. In the worst-case scenario, non-compliant devices may be withdrawn until they meet MDR requirements again.

3.2 EU Declaration of Conformity

EU declaration of conformity is a mandatory document that the manufacturer need to sign to declare that the device under examination complies with the EU requirements. It shall be translated into the language required by the EU country in which the product is sold [3]. It must include the following information:

- *name and address of the manufacturer* or his authorised representative;
- the product's *serial number*, model or type identification;
- means of identification of product allowing *traceability*;
- the details of the NB which carries out the conformity assessment procedure, if applicable;
- the relevant legislation with which the product complies, as well as any harmonised standards or other means used to prove compliance [3].

Sometimes, additional information for the unambiguous identification of the product is reported, such as a photograph or a product code.

3.3 Conformity Assessment Procedure

A conformity assessment procedure must be undertaken by the manufacturer before the device is put in service or in the market [3]. The specific procedure to follow depends on the risk class of the device and it is described

in the scheme (Fig. 3.1). It shows that only **Class I** devices can be placed on the market without the action of a NB. If devices fall within *Class Is, Im or Ir* the involvement of a NB is required in any case [17].

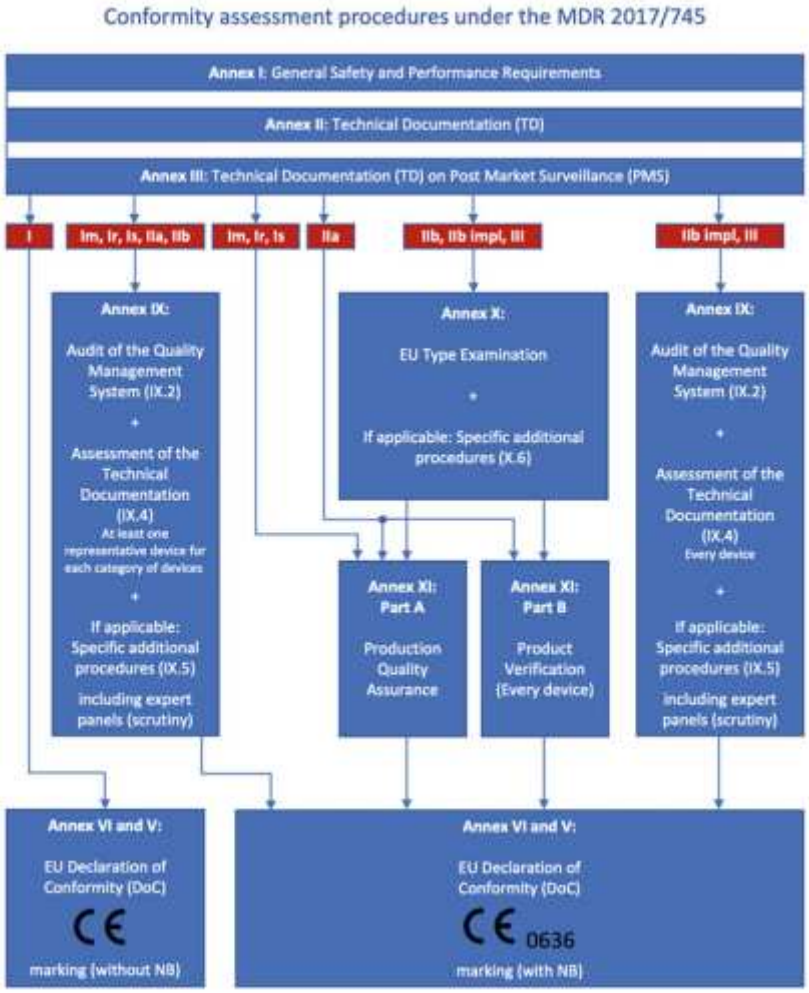


Figure 3.1: Conformity assessment procedures for medical devices under MDR [17]

For **Class IIa, IIb and III** devices the conformity assessment procedure is carried out according to *Annex IX, X and XI* of MDR (Fig. 3.1). Exceptions are represented by the custom-made devices whose procedure is performed according to Annex XIII and investigational products whose requirements to be observed are those for devices under clinical investigation [3].

The NB carries out the conformity assessment activities according to the specific procedure. This includes the quality management system auditing,

product testing, review of the technical documentation, preclinical evaluation assessment, clinical or performance evaluation assessment and special procedures if applicable. Depending on the particular characteristics of the product sometimes the NB needs to performs additional procedures; this happens when the device under examination is:

- class III implantable device;
- class IIb active devices administering a medicinal product;
- devices incorporating a medicinal substance;
- devices consisting of animal or human origin, or their derivatives [3].

3.4 CE Marking of Conformity

CE marking means a marking by which a manufacturer indicates that a device is in conformity with the applicable MDR requirements [3].

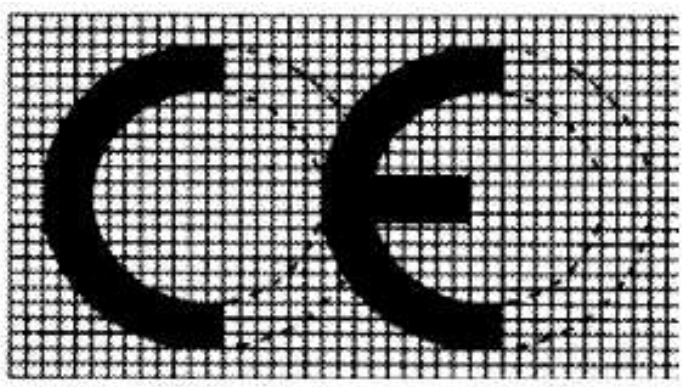


Figure 3.2: The CE marking is affixed on devices compliant with requirements of Regulation 2017/745 [3]

The letters 'CE' have to appear as shown in the Figure 3.2. The components must have the *same vertical dimension* and if the mark is reduced or enlarged the same proportion must be maintained [3]. The minimum vertical length is set at 5mm, but exceptions can be done for small- scale devices [3].

The CE marking must be affixed on the device in a visibly, legibly and indelibly way. If for the nature of the device the affixing is not possible, it must be placed on the packaging. If the conformity assessment has required the involvement of a NB, the CE marking shall be followed by the identification number of the NB [3].

3.5 Implementing Regulation 2023/1194

Implementing Regulation (EU) 2023/1194 modify the Regulation (EU) 2022/2346 about the transitional provisions for the products listed in Annex XVI [18].

In particular, a product which is already in compliance with the general safety and performance requirements and for which the manufacturer *intends to conduct clinical investigations*, may be placed on the market until **31 December 2029**, provided that:

- the product was already *legally marketed* in the Union before **22 June 2023** and continues to comply with the requirements;
- there are *no significant changes* in the design and intended use of the product [18].

Considering the conditions described before, a product may be placed on the market or put into service:

- **from 22 June 2024 until 22 December 2024**, only if the sponsor has received notification from the Member State concerned, confirming that *the clinical investigation application for the product is complete*;
- **from 23 December 2024 until 31 December 2027**, if the sponsor *has started the clinical investigation*;
- **from 1 January 2028 to 31 December 2029**, if the notified body and the manufacturer *have signed a written agreement* for carrying out the conformity assessment [18].

Products for which the manufacturer *does not intend to perform clinical investigations* can be put on the market until **31 December 2028** but from 1 January 2027 the notified body and the manufacturer must have signed a written agreement for the assessment of conformity [18].

For the products covered by a certificate issued by a notified body in accordance with MDD, the certificates valid on 26 May 2021 and not revoked remain valid after the expiry of the certificate:

- **until 31 December 2027** for *Class III and implantable IIb* devices with the exception of suture materials, orthodontic appliances and wires;
- **until 31 December 2028** for devices of *Class IIb* other than those above, for devices of *Class IIa*, for devices of *Classes Im, Is* and for devices for which the MDD did not require intervention by a NB [18].

During the extension period, devices may be placed on the market or put into service only under the following conditions:

- continue to comply with MDD;
- there are no significant changes in the design and intended use of the product
- the devices do not present an unacceptable risk to health or safety;
- **by 26 May 2024** the manufacturer has established a QMS in accordance with the MDR;
- **by 26 May 2024**, the manufacturer has formally applied for MDR certification of the device benefiting from the extension or a replacement device, and **by 26 September 2024** the NB and the manufacturer have signed a written agreement [18].

Chapter 4

Materials and Methods

4.1 Experimental study

The current work proposes the technical documentation necessary to perform the conformity assessment for aesthetic devices belonging to Annex XVI of MDR. The experimental study is applied to Epil family devices which are designed, produced and manufactured by the company Elits Group. The Epil family devices are composed by two laser products: **Epil808** (Fig. 4.1a) and **Epil Smart** (Fig. 4.1b). The devices exploit laser energy for aesthetic photoepilation purposes. In addition the model EpilSmart is available in three different configurations according to the wavelength that it exploits: *EpilSmart Single Band*, *EpilSmart Dual Band* and *Epil Smart Trial Band*.

4.2 Technical Documentation according to the MDR (Annex II)

A single technical documentation was generated for the Epil Family devices where all the models and variants have been included. The technical documentation was prepared according to *Annex II* of the MDR. It must contain:

- the identification of the device and its intended use;
- the risk class of the device;
- the intended users and consumers;
- the description of the materials and of their interaction with the human body;

Epil 808 *Epil Smart*

(a) **(b)**

Figure 4.1: Epil family devices

- the technical specifications of the device;
- the labels and the IFU;
- information about design and manufacturing;
- results of validation tests, such as biocompatibility, elctrical safety, electromagnetic compatibility and software validation [3].

Moreover, the risk management file, the biocompatibility and usability assessment and the CER are also part of the technical documentation.

4.2.1 Risk management file

The Risk Management File (RMF) is a document that is part of the technical documentation and it was developed according to the standard **ISO 14971:2019**. The risk management follow a specific procedure which is shown in the Figure 4.2; the procedure have to be implemented throughout the lifecycle of the product.

The first step is represented by the **risk analysis** which involves the identification of the possible hazards and hazardous situations both in a normal condition and after a single fault condition. A single fault condition refers to a device defect or malfunction, but also in the case in which the IFU are not properly followed. The **risk evaluation** was performed considering two

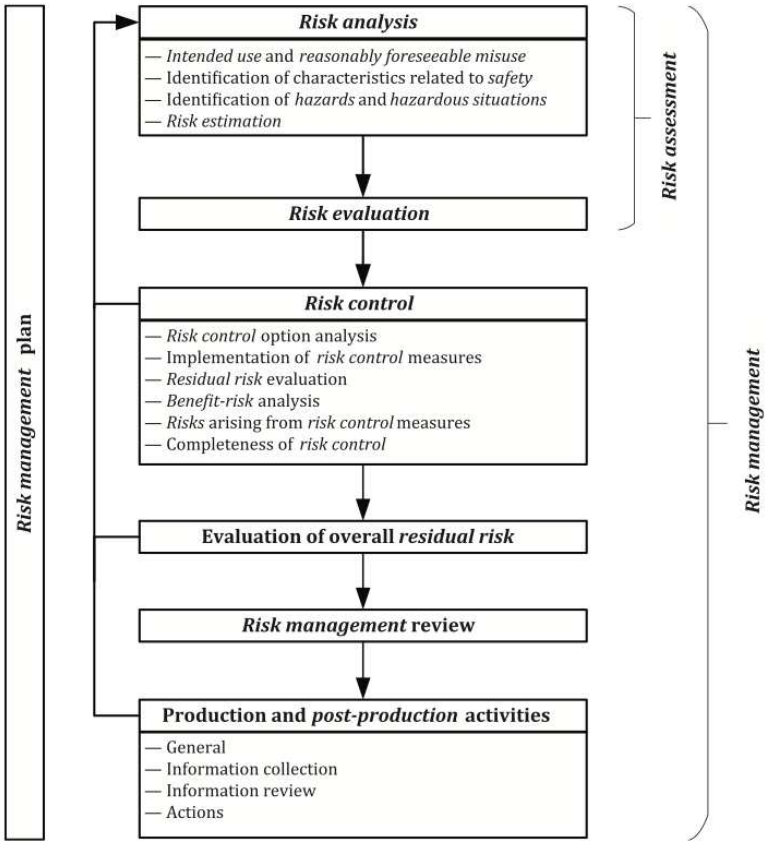


Figure 4.2: Schematic representation of the Risk Management Process with the main steps: risk analysis, risk evaluation, risk control, and risk management review [19]

indexes: the *severity* and *probability* index. A score from 0 to 6 was assigned to each of them according to the magnitude of the harm considered and their probability of occurrence [19].

IG= Index of Gravity
0 = **Non applicable** (NA) (no harm)
1 = **Negligible** (scare)
2 = **Minor** (discomfort)
3 = **Marginal** (lesion with no medical intervention)
4 = **Severe** (lesion with medical intervention)
5 = **Critical** (permanent lesion)
6 = **Catastrophic** (patient and/or user's death

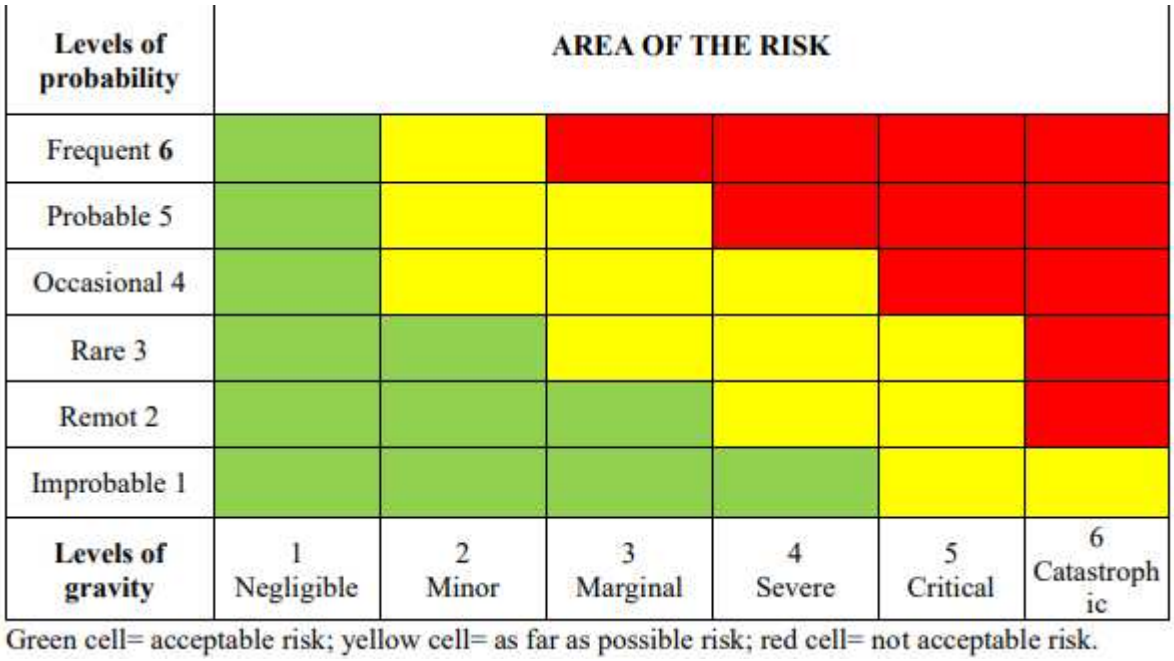


Figure 4.3: Risk Estimation

IP = Index of Probability
0 = **NA** (No harm at all)
1 = **Improbable**: P = 1/1.000.000 (almost impossible event)
2 = **Remot**: P = 1/100.000 (extremely low probability)
3 = **Rare**: P = 1/10.000 (low probability)
4 = **Occasional**: P = 1/1.000 (medium/high probability)
5 = **Probable**: P = 1/100 (high probability)
6 = **Frequent**: P = 1/10 (extremely high probability)

The **risk estimation** was carried out through the combination of the two indexes as shown in the Figure 4.3. Thus, the risk can result to be:

- **Acceptable**: both IG and IP are low;
- **As far as possible**: the risk could be further reduced by adopting control measures;
- **Unacceptable**: the risk cannot be accepted and the manufacturer has to implement control measures to reach the acceptable area of the risk [19].

Everytime that the risk was not acceptable the manufacturer shall adopt *control measures* in order to reduce it. These control measures include:

- safe design and manufacturing;
- protective measures in the design or in the manufacturing process;
- information for safety and training for users [19].

After this phase, the **residual risk** (RR) was estimated. If the risk was still unacceptable a risks/benefits analysis was performed: the benefits have to overcome the risks.

Lastly, the overall residual risk was evaluated. This one had to result acceptable to pass the risk analysis, otherwise, manufacturers had to make corrections or change the intended use of the device [19].

According to the CS additional risks need to be considered. Annex VI of Regulation 2022/2346 presents **specific risks** for lasers and intense pulsed light equipment. Thus, the following features and related risks were considered:

- various skin types and their degree of tanning;
- presence of any skin abnormality;
- age of the consumer;
- use of photosensitizing medicines or any other concurrent medical treatment;
- exposure to other light sources [10].

As consequence, it was required to reduce as much as possible risks related to burns, allergic skin reaction, overexposure, unintended release of radiation and explosions.

4.2.2 Biocompatibility

Biocompatibility assessment was carried out according to the standard **ISO 10993-1:2018**. Its goal is to assess the compatibility of devices with biological tissue and thus to study the interaction between the product and the skin. The tests that were necessary to perform regard the type of contact between the device and the skin.

The biocompatibility conformity was conducted only for parts produced by the manufacturer or for parts which did not have an appropriate certification.

4.2.3 Usability

The usability process has the scope to analyze, design, and verify the usability of medical devices with regard to safety. Firstly, the specifications for the device were identified, considering both the physical part and the software (SW). Usability verification involved the implementation of all these specifications and their subsequent validation. The usability validation consists in two assessment:

- a **formative assessment** which is performed by technical experts in the company where the prototype was developed ;
- a **summative assessment** with the partecipation of potential users, beauticians in this case.

These two tests are quite similar. The user need to use all the functions the device is able to do and the evaluation is done through a specific questionnaire with multiple answer with the possibility to add comments. To each question the user gives a score from 0 to 4:
0= Inappropriate: Result that requires improvement
1= Acceptable: Result that should be improved as soon as possible
2=Sufficient= Result that implies a widely implemented solution
3= Good: Result that implies a solution implemented in a workmanlike manner
4= Amazing: Result that implies a solution that has never been seen before
The questions regards different aspects of the device, such as:

- unpackaging and installation of the device;
- ignition and general set-up;
- visual and acoustic interface;
- handling, transport and storage;
- software interface;
- interaction with IFU;
- operability in the execution of the treatment.

Only answers with a score of at least 2 is considered; otherwise additional justifications are needed.

Another part is dedicated to the **SW development** documentation. It started with the identification of all the requirements that are specific for the

SW and then the definition of the architecture required to implement them. Before releasing the SW, each requirement had to be verified and evaluated with suitable tests, taking into account all the possible risks associated with it.

4.2.4 Clinical Evaluation Report

Clinical Evaluation was performed to assess the safety and performance of the devices under study and the CER is compiled following *Annex XIV* of the MDR. Data for this CER come mainly from literature studies of equivalent MD, but for the Epil808 model also a high-level survey on the legacy device has been carried out. Legacy devices are those products which are covered by a valid certificate under MDD and that continue to be placed on the market after the date of application of the MDR [20].

Clinical literature was used to assess the performance and safety of the Epil Family devices but also to demonstrate the equivalence of the EpilSmart TrialBand with another product that has similar characteristics. The different steps for collecting clinical data were shown in the Fig. 4.4 and explained below:

- STEP 1: search all the potential articles containing clinical data using primarily PUBMED research engine;
- STEP 2: analyze the articles in order to found out the following features:
  - Technical and performance characteristics to assess the equivalence;
  - Appropriate device application and consumer group;
  - Acceptable report data.
- STEP 3: the evaluation of the equivalence with other MD is carried out considering:
  - the appropriate design of the study;
  - measures of results appropriate to the intended use of the device;
  - sufficient follow-up to assess treatment effects and/or complications;
  - the statistical significance of the measured results;
  - the clinical significance of the outcomes.

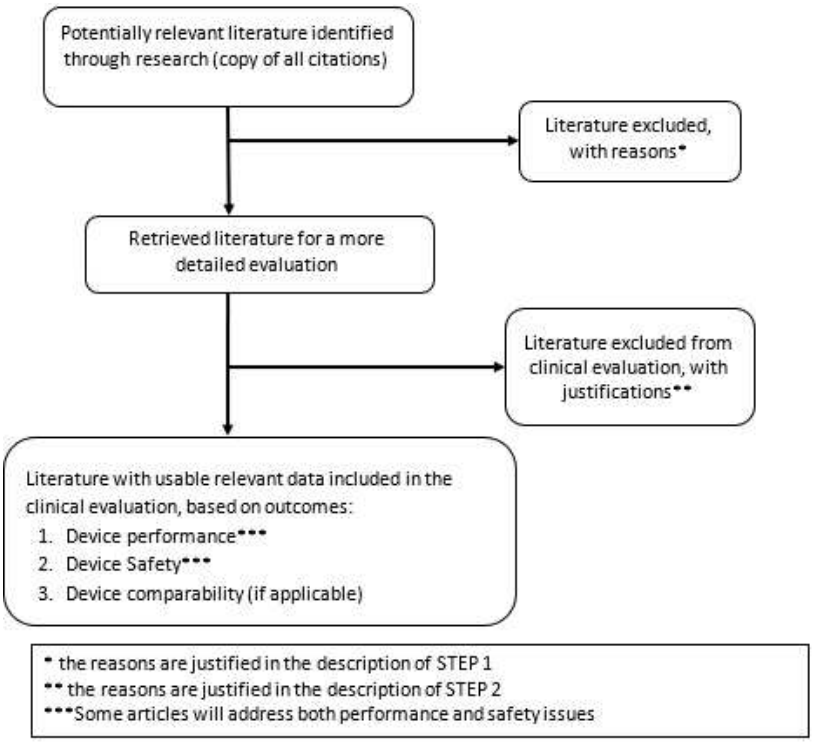


Figure 4.4: Search strategy to gather sufficient clinical data to demonstrate safety and performance of the devices under evaluation

To assess the safety and performance of the EpilFamily model these articles were considered: [21],[22],[23],[24], [25], [26], [27], [28], [29]. The device described in the article [30] was used to demonstrate its equivalence with EpilSmart Trial Band.

The **high-level survey** was conducted by doctors who used the Legacy device and the following features were considered:

- *identification of the operator*: name and address of the study/clinic;
- *type of device*;
- *patient characterization*: patient code, phototype, hair thickness, gender and age;
- *treatment parameters*: number of treatment, start and end date
- *density of the hair*: calculated before the treatment and after 3 and 6 months from the first one. The area involved in the study were the axillae, the chest and the thigh.

- *report of the adverse effects*: they are classified in unexpected, solved in hours and expected.
- *level of satisfaction of the patient*: defined by a score ranging between 0 and 5

In order to consider the clinical data coming from the high-level survey, it was previously necessary to assess the equivalence between Epil808 and its legacy device taking into account technical and performance characteristics.

Chapter 5

Results

5.1 Technical Documentation

GENERAL DESCRIPTION OF THE DEVICE

Epil Family devices are *electrical active* products used for hair removal. More in detail, Epil808 is embedded with a handpiece containing a laser diode which emits laser energy at 808nm. EpilSmart is instead available in three different configurations according to the laser energy emitted:

- *EpilSmart Single Band* at 808nm;
- *EpilSmart Dual Band* at 808 and 1064 nm;
- *EpilSmart Trial Band* at 755, 808 and 1064nm.

They are **non-invasive** and **non-sterile** devices with an expected lifetime of 5 years.

INTENDED USE

The devices use laser diode technology for aesthetic purpose of hair removal.

CONSUMER CHARACTERIZATION

The consumers should not be in the paediatric age; if they are less than 18 years old, an authorization from the parents is necessary. Moreover, treatments are not suitable in these cases:

- Pacemaker and internal defibrillator wearers;
- Subjects with acute inflammation;
- Subjects with severe arterial hypertension;

- Subjects with neurological disorders;
- Subjects with particularly severe cardiac conditions;
- Subjects with renal insufficiency;
- Subjects with 'infected' or 'traumatised' dermis;
- Subjects with epilepsy;
- Subjects with diabetes;
- Subjects with significant allergic diseases;
- Subjects with severe contagious diseases (e.g. tuberculosis);
- Subjects with febrile states;
- Subjects with immunodeficiency syndromes or diseases;
- Women who are known or suspected to be pregnant and breastfeeding.

PRECAUTIONS FOR USE AND WARNINGS

The equipment cannot be used near the eyeball, the brain region and the heart but even in orifices, on genital organs and near the eyes and ears. It is not recommended to treat areas with tattoos and moles. If this is the case, it is recommended to isolate the area with a white pencil and in any case not to operate the laser over such areas.

SIDE EFFECTS

Excessive power can cause *skin irritation, crusting or burns.* In addition, signs of folliculitis may occur after a hair removal treatment.

INTENDED USER

These devices are developed for professional aesthetic use not intended for medical services. Their use is intended for **qualified operators** such as professional beauticians or medical personnel like dermatologists who have been instructed in the use of the devices by an appropriate training course.

DURATION OF USE OF THE DEVICE

The device can be used for a working day of 8 hours performing many different treatment on several consumers (it can be used more times a day) but on the same consumer the treatment can be applied on the same area of the

body at most twice a month.

PRINCIPLE OF OPERATION

During the treatment the operator applies on the skin the handpiece with a diode emitting monochromatic, coherent, and unidirectional light energy. The specific wavelength emitted depends on the specific variant of the device used. The operator sets the output parameters according to the phototype and hair type of the consumer being treated. The principle of function is based on the theory of selective photothermolysis for which laser and light-based devices target melanin in the hair bulb and outer areas of the root sheath of the hair follicle, to cause permanent damage to hair stem cells, while limiting thermal damage to adjacent structures [23].

TECHNICAL CHARACTERISTICS

Technical characteristics are described in the Tab. 5.1.

Table 5.1: Technical specifications of the laser technology.

Laser	Class 4 laser enclosured in a 1C Class
Power source	230 Vac/50-60 Hz
Spot size	12 x 16 mm
Energy density	1 – 40 J/cm^2
Pulse duration	5 – 200 ms
Spot frequency	1 – 10 Hz
Maximum output power of the laser	1200 W
Fast axis divergence (FWHM)	32°
Slow axis divergence (FWHM)	8°
Handpiece cooling	0°C-7°C

BLOCK SCHEME

The functional elements are reported in the scheme below (Fig.5.1). Precisely, it refers to the EpilSmart model, but there are no significant changes for the Epil808 device:

- the **display** is an 8" TFT LCD with a resolution of 800 x 600 pixels with a resistive touch function, powered by 12Vdc and driven by a 115,200 Kbit bidirectional RS232 serial line;
- the electrical and electronic **control unit** contains power supplies, the driver for the laser diode and the CPU for the control of the display and programs of the machine;

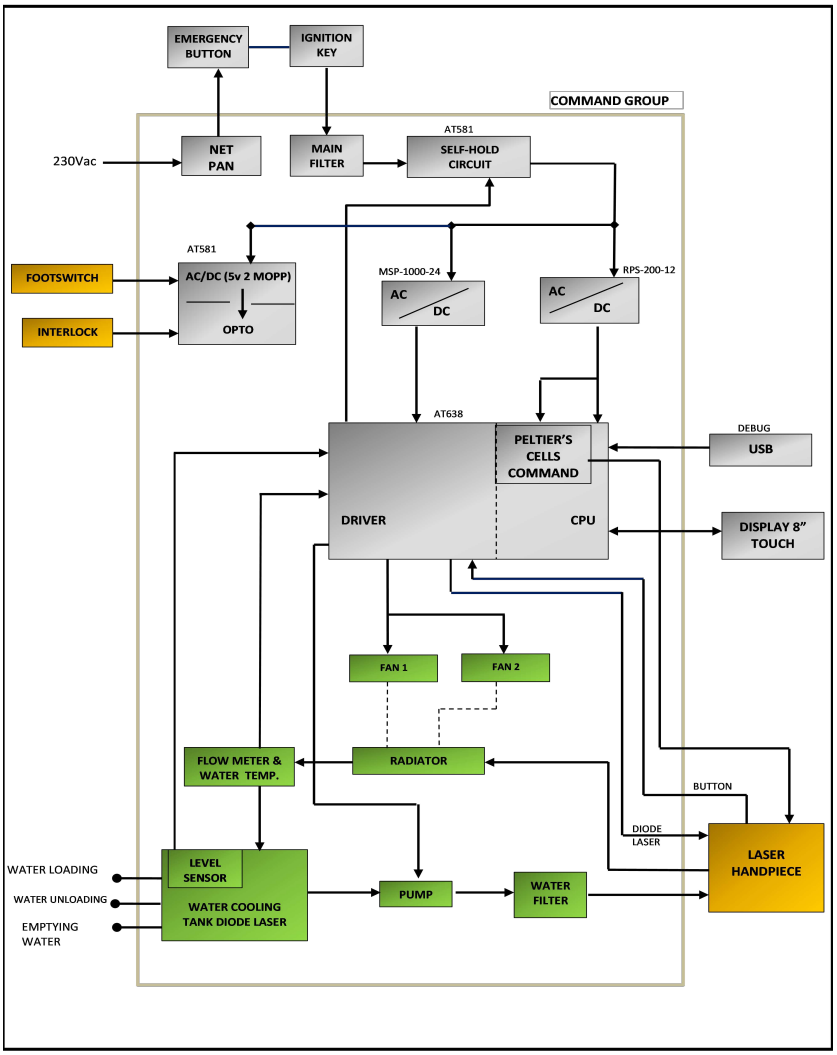


Figure 5.1: Block scheme of the functional elements of EpilSmart.

- the **pedal** has the function of double consent to the output of the laser beam in combination with the button on the handpiece. In order to perform the treatment, after enabling the "start" on the touch screen of the machine, it is necessary to press both devices (button + pedal);
- the **interlock** is a connector to which an external, additional, environmental safety device must be connected. This device is intended to keep the working environment, operators and patient safe. The interlock connector must be connected to the safety devices (switches and

signal lamps) present in the entrances of the room (doors, windows) in order to enable or not the laser operation only under safe conditions (all closed accesses).

COMPONENTS

Epil family devices are constituted by the following components:

- **functional parts**:
  - funnel for the water emptying/filling;
- **operative parts**:
  - footswtich;
  - ignition key;
  - interlock connector;
- **applied part**: characterized by the handpiece available in different configurations:
  - handpiece with 808 nm diode laser;
  - handpiece with 808 and 1064 nm diode laser;
  - handpiece with 755,808 and 1064 nm diode laser;
- **personal protective equipment**:
  - googles for the operator (Fig. 5.2a);
  - googles for the patient (Fig. 5.2b);
- **accessories**:
  - handpiece holder;

Googles for the operator  *Googles for the patient* 

(a) **(b)**

Figure 5.2: Personal protective equipment needed to use Epil Family devices.

ASSOCIATION WITH OTHER DEVICES

There is no association with other devices.

RISK CLASS
The Epil family devices are classified as Class IIa, according to Regulation (EU) 2017/745 Rule 9 and according to Commission Implementing Regulation (EU) 2022/2347, Article 1, section a [3], [11].

5.2 Risk Management

The main risks that have been analyzed are represented in the Figures 5.3, 5.4 and 5.5. More in detail, Fig.5.3 analysed the hazards related to electromagnetic, thermal and mechanical energy; Fig.5.4 considers hazards connected to the use chemists, the funtioning of the device and common errors of use; lastly, Fig.5.5 relates to operating instructions, warnings and maintenance risks, while the last three hazards analysed are specific for the laser technology under study.

For each hazard values for the IG and IP are assigned and the resulting area of risk is identified. In the last column of Fig.5.3 are inserted the IG and IP values after the implementation of the control measures and the subsequent evaliuation of the overall RR.

5.2.1 Conclusion of the risk analysis

The following considerations can be done about the risk analysis:

- RR in the acceptable area: all risks are in the acceptable area;
- RR in the afap area: no risk;
- RR in the unacceptable area: no risk;

The risk analysis has a positive evaluation and the overall RR is acceptable.

Figure 5.3: Hazards regarding electromagnetic, thermal, and mechanical energy.

H	Hazard	IG	IP	Control measures	IG	IP
1	**Main voltage**	6	3	The device has performed all the electrical safety tests.	2	1
		IR: unacc.			**IRR: acc.**	
2	**Leakage current:** **- in the casing** **- to earth** **- in the consumer**	6	2	Use of conform power supplies	2	1
		IR: unacc.			**IRR: acc.**	
3	**Electric fields**	4	2.	Other electromagnetic devices have to stay at least 30cm away from the device	1	2
		IR: afap			**IRR: acc.**	
4	**Magnetic fields**	4	1	Other electromagnetic devices have to stay at least 30cm away from the device	2	1
		IR: afap			**IRR: acc.**	
5	**Non-ionizing radiation**	5	1	The output is delivered according to the input parameters	2	1
		IR: afap			**IRR: acc.**	
6	**Ionizing radiation**	N.A.	N.A.	The device is not intended to deliver ionizing radiation.	N.A.	N.A.
		IR: N.A.			**IRR=N.A.**	
7	**High temperature**	5	3	Maximum level energy are set in the device	2	1
		IR: afap			**IRR: acc.**	
8	**Low temperature**	2	1	The device is designed with a suitable cooling systems	1	1
		IR: acc			**IRR: acc.**	
9	**Gravity:** **- falls** **-suspended masses**	2	1	Device shall be transported in a correct way by qualified personnel	1	1
		IR: acc.			**IRR: acc.**	
10	**Vibrations, stored energy and moving parts**	N.A.	N.A..	The device does not vibrate or contains moving parts. It is not intended to store energy.	N.A.	N.A.
		IR: N.A.			**IRR: N.A.**	
11	**Acoustic energy**	2	1	The emitting sounds are not annoying	1	1
		IR: afap			**IRR: acc.**	

Figure 5.4: Hazards regarding chemists, functioning of the device and error of use.

H	Hazard	IG	IP	Control measures	IG	IP
12	**- Acid or alkaline - Residues -Contaminants -Additives**	N.A.	N.A.	These chemists are not involved in the use of the device	N.A.	N.A.
		IR: N.A.			**IRR: acc.**	
13	**Cleaning, disinfecting or testing agents**	1	2	Operator must follow maintenance instructions	1	1
		IR: acc.			**IRR: acc.**	
14	**- Degradation products - Medical gases - Anaesthetic products**	N.A.	N.A.	These products are not involved in the use of the device	N.A.	N.A.
		IR: N.A.			**IRR: N.A.**	
15	**Toxicity or chemical constituents, for example: - allergenicity - pyrogenicity**	3	2	The materials in contact with the skin are biocompatible	1	1
		IR: afap			**IRR: acc.**	
16	**Incorrect functionality**	4	2	Usability test	1	1
		IR: afap			**IRR: acc.**	
17	**Incorrect measurement and/or data transfer**	N.A.	N.A.	The device is not intended to measure or to transfer data	N.A.	N.A.
		IR: N.A.			**IRR=N.A.**	
18	**Attention error**	4	3	Prescriptions about use by qualified personnel	1	1
		IR: afap			**IRR: acc.**	
19	**Error related to competency or violation of procedure**	4	3	The operator is suitably qualified and trained	2	1
		IR: afap			**IRR: acc.**	

Figure 5.5: Hazards regarding operating instructions, warnings, maintenance and specific risks.

H	Hazard	IG	IP	Control measures	IG	IP
20	Inadequate specification of accessories for use with the device	2	2	Usability test	1	1
		IR: acc			**IRR: acc.**	
21	Overly complicated operating instructions	2	2	Usability test	1	1
		IR: acc.			**IRR: acc.**	
22	Warnings of side effects	2	2.	Warning about contraindications and side effects	2	1
		IR: acc.			**IRR: acc.**	
23	Maintenance specification	3	2	The operator must follow the maintenance procedure	1	1
		IR: afap			**IRR: acc.**	
24	Consideration of the various skin types and their degree of tanning	2	2	The operator is qualified and suitably trained	1	1
		IR: acc			**IRR: acc.**	
25	Presence of any skin abnormality	3	3	Warnings about consumer characterization	2	1
		IR: afap			**IRR=N.A.**	
26	Concurrent medical treatments or use of photosensing medicines	3	3	Warnings about consumer characterization	1	1
		IR: afap			**IRR: acc.**	

5.3 Biocompatibility

Although the handpiece is available in three different configuration, the external part is always the same for each of them. It is consituted by the following materials:

- *polymer PA12*;
- *alluminium 2017A*;
- *glass N-BK7*;
- *two tips of gold connected with the contact sensor.*

The polymer is the material of the external part of the handpiece and it is contact with the operator, while the other materials are those directly in contact with the skin of the consumer.

The **glass** and the **polymer** are provided with their own certification, thus a biocompatibility assessment is not required. The test to be performed for the other materials depend on the type and duration of the contact between the device and the human body.

The handpiece is hold by the operator for all the duration of the treatment and the nature of the contact is similar to that of any household object; however, it is recommended to use gloves. When the handpiece is used on the consumer, it is moved very quickly on the treated area and the operator does not remain for more than an instant on the same skin area even if the operator pass over it often during the treatment.

Considering that both the **gold** and the **alluminium** have been placed on the market since years (2018 for the gold and 2020 for the alluminium), adequate information about material safety are available. Taking into account also the *transient nature of the contact*, according to the standard ISO 10993-1:2018, biocompatibility tests are not necessary.

Moreover, the biocompatibility prorperties of gold are also demonstrated by data coming from literature ([31], [32]). Such invasive applications demonstrate the high degree of biocompatibility of the material as these procedures represents more risky cases with respect to the use of the applied parts under study.

5.4 Usability

The usability specifications for the physical part of the product are presented in Tab.5.2. These take into account different aspects:

- manoeuvrability of the device body;
- manoeuvrability of the treatment delivery accessories;
- enclosure protection.

Table 5.2: Usability specifications for the physical part of the product.

Specific	How
Manoeuvrability of the device body	
Grap easily	Prehensile edges of the casing
Easily movable	Weight of 10 kg
Manoeuvrability of the treatment delivery accessories	
Not bulky cables	Light and flexible cables
Easily grip handpieces and allow for easy operation	Ergonomic design both for the operator's handle and for use on the patient
Delivery method that allows the hand holding the handpiece to work more easily	Pedal for the initiation/interruption of the delivery of the treatment
Enclosure protection	
The case can only be opened by tools by the mainteinance operator	Closed by screws. Opening limited to ventilation.
Protection from the penetration of substances used during sanitation can only be dismantled using tools by the specialized mainteinance operator	The assembled parts must be equipped with adequate protection systems. Fixing by screws or threads.

The specifications related to the SW are shown in Tab.5.3. The requirements that are considered involve:

- user friendly interface;
- setting of the physical treatment parameters;
- recognition of connections by the SW
- the safety of the SW with respect tot he human error.

Table 5.3: Usability specifications for the SW.

Specific	How
User friendly	
Touch screen interface	Display-colour touch screen
Sequence of the screens	Hierarchy/tree-like graph
Intuitive communication Machine ->Operator	Commonly recognized symbols of use are used for visual messaging information.
Intuitive communication Operator ->Machine	Screen selection by typing in labelled buttons.
Start / Stop treatment	Green "START" button for start which becomes red "STOP" for stopping treatment
Setting of the physical treatment parameters	
Storage of physical therapy output parameters for specific pathologies	Dedicated space in memory to insert specific parameters for each treatment protocol
Recognition of connections by the SW	
Connection of the handpieces	Reading of the internal calibrated resistance of the handpiece.
Pedal connection	Recognition of the presence of the pedal
Safety with respect to Human error	
Parameter selection	At the time of choosing the critical parameters for the therapy a double confirmation is requested to the operator

Formative assessment

The result of the formative assessment has been reported in Tab.5.4. The technical experts performing it have been identified with an ID: F1, F2 and F3. All the questions reported a score equal to 3.

Conclusion about the formative assessment No scores below the predetermined threshold value have occurred, thus the test is considered passed

Summative assessment

The results of the summative assessment are reported in Tab. 5.5.
It was performed by 4 beauticians (users) (S1, S2, S3 and S4). All the

Table 5.4: Formative assessment

#	Question	Result	
		Used ID	**Answer**
1	**Unpacking and installing the device**		
1.a	When opening the packaging, the device is easily grippersile and transportable in relation to weight and gripping points?	F.1 F.2 F.3	3 3 3
1.b	Are the separable parts properly protected in the packaging?	F.1 F.2 F.3	3 3 3
2	**Power on/off and general set-up of the device**		
2.a	Do separable parts have the necessary identification labeling also in relation to their connections to the device?	F.1 F.2 F.3	3 3 3
2.b	Is the on and off button well identified and placed in such a position that it cannot be activated if you accidentally leave on the device?	F.1 F.2 F.3	3 3 3
3	**Visual Interface**		
3.a	Is the size of the symbols in the label at least 1 cm in its smallest size?	F.1 F.2 F.3	3 3 3
4	**Acoustic interface**		
4.a	Are the acoustic signals when selecting the buttons of the SW interface clearly distinguished?	F.1 F.2 F.3	3 3 3
5	**Touch interface, transport and maintenance**		
5.a	Does the touch of the device have sharp surfaces or difficult to prehensile?	F.1 F.2 F.3	3 3 3
5.b	Is the weight in relation to the volume of the device adequately sized in order to make the device transportable?	F.1 F.2 F.3	3 3 3
5.c	Maintenance operations: resistance of mechanical parts to sanitation substances.	F.1 F.2 F.3	3 3 3
6	**Software Interface**		
6.a	Speed of SW commands: does the opening of the selected page last less than a second when the command is selected?	F.1 F.2 F.3	3 3 3
6.b	Once treatment has started, is it possible to stop and resume treatment?	F.1 F.2 F.3	3 3 3
7	**Interaction with the IFU**		
7.a	Are the IFU easily clear to be read by the user who is the clinician?	F.1 F.2 F.3	3 3 3

Table 5.5: Summative assessment

#	Question	Result	
		Used ID	**Answer**
1	**Unpacking and installing the device**		
1.a	When the packaging was opened, was the device stored in an orderly and composed manner?	S.1	3
		S.2	3
		S.3	3
		S.4	3
1.b	Was the removal of all parts of the package carried out easily?	S.1	3
		S.2	3
		S.3	3
		S.4	3
2	**Power on/off and general set-up of the device**		
2.a	Are separable parts easily identifiable with their connections to the device?	S.1	3
		S.2	3
		S.3	3
		S.4	3
3	**Visual and Acoustic**		
3.a	Is the information on the menu screens easy to read?	S.1	3
		S.2	3
		S.3	3
		S.4	3
3.b	Are noises tolerable?	S.1	3
		S.2	3
		S.3	3
		S.4	3
4	**Transport and maintenance**		
4.a	Is there a perception of robustness of the materials used?	S.1	3
		S.2	3
		S.3	3
		S.4	3
4.b	Are maintenance operations clear and easy to perform?	S.1	3
		S.2	3
		S.3	3
		S.4	3
5	**Software Interface**		
5.a	Are the interactions with the SW application easy to interpret?	S.1	3
		S.2	3
		S.3	3
		S.4	3
6	**Interaction with the IFU**		
6.a	Is specific information on IFUs easy to find?	S.1	3
		S.2	3
		S.3	3
		S.4	3

questions reported a score equal to 3.

Conclusion about the summative assessment No scores below the predetermined threshold value have occurred, thus the test is considered passed.

Conclusions on usability test

The usability checks did not reveal any problems and/or observations either by technical experts or by beauticians for each configuration of accessories used. The usability test is considered passed.

SW development

ID	Requirement	Result to be verified	Test	Result
R.SW.1	Graphical interface with simple and intuitive navigation (Reachability of all screens)	All selectable screens must be reachable	Selection of the navigation keys of the various "menus" and "submenus".	All address keys pressed led to the indicated destination.
R.SW.2	Identify the presence of the handpiece	Show an on-screen message if the handpiece is not connected.	Activation of the machine when the handpiece is not connected.	Display on the monitor of the presence of a fault. When the fault was restored, the device continued to work properly.
R.SW.3	Liquid temperature detection	If the liquid temperature is too high or too low the SW must interrupt its functions and warn with an on-screen message.	Activate the machine when the temperature of the liquid is too low or too high with respect to the expected value.	Display on the monitor of the presence of a fault. When the fault was restored, the device continued to work properly.
R.SW.4	Handpiece current detection	If there is an abnormality in the emission of the current of the handpiece it has to be detected and warn with an on-screen message	The output current is altered in order to obtain a higher output value through the alteration of the operational gain U6.2 with the adding of another resistance of 10k in parallel with R179.	Display on the monitor of the presence of a fault. When the fault was restored, the device continued to work properly.
R.SW.5	Failed test	When there is an abnormality in the machine the SW must interrupt its functions and warn with an on-screen message.	The sensing of the power supply 24V is disconnected.	Display on the monitor of the presence of a fault. When the fault was restored, the device continued to work properly.
R.SW.6	Password for the access	The access to the home screen display is possible only through a password	The device is turned on and the access to the treatment screen is tried.	You are prompted to enter a Password.

Figure 5.6: The figure show the requirements for the SW, the relative test to be performed and the results of these test.

The Fig.5.6 shows the main requirements for the SW development. Each requirement identified is associated with the result to be verified and how the test will be performed. Lastly, the outcome of the trials are reported.

5.5 Clinical Evaluation

The results of the comparison between Epil808 model and the legacy device are shown in Fig.5.8 and 5.7. In particular, Tab.5.7 refers to the

1) The device has the same condition or purpose, including similar severity and stage of disease	
Device in question	**Device compared**
Device intended for aesthetic purposes for the removal of unwanted hair and provide a long-term hair reduction.	Device intended for medical purposes for the treatment of hirsutism diseases.
Conclusions: The devices employ the same technology for similar clinical purposes	
2) Similar population, including as regards age, anatomy and physiology	
Device in question	**Device compared**
There are no restrictions for the consumers except the requirements presented in the contraindications.	There are no restrictions for the patients except the requirements presented in the contraindications
Conclusions: The devices have the same population contraindications related to the same technology employed	
3) Same kind of user	
Device in question	**Device compared**
It can be used only by qualified personnel, such as professional beauticians and medical personnel like dermatologists, for photoepilation treatment.	It can be used only by qualified medical personnel for photoepilation treatment.
Conclusions: The devices have the similar kind of user	

Figure 5.7: Performance characteristics considered to assess the equivalence between Epil808 and the legacy device.

performance characteristics where are analysed similar purposes, population and users. Technical specifications are described in Tab.5.8; they involve the analysis of design, specifications, deployment methods and principles of operation.

(1T) The Device is of similar design	
Device in question	**Device compared**
Device powered by mains (230Vac, 50÷60 Hz) with a control console and software interface that implements	Medical device powered by mains (230Vac, 50÷60 Hz) with a control console and software interface that implements.
Conclusions (1T): The devices have the same design specifications	
(3T) It has similar specifications and properties including physiochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and software algorithms	
Device in question	**Device compared**
Handpiece with Diode laser wavelength 808 nm; energy density 1 – 40 J/cm^2 ; pulse duration 5 – 200 ms; spot frequency 1 – 10 Hz; spot size 12x16mm.	Handpiece with Diode laser wavelength 808 nm; energy density 1 – 40 J/cm^2 ; pulse duration 5 – 200 ms; spot frequency 1 – 10 Hz; spot size 12x16mm.
Conclusions (3T): The devices have the same output parameters	
(4T) It uses similar deployment methods where relevant	
Device in question	**Device compared**
The device delivers laser energy through a handpiece.	The device delivers laser energy through a handpiece.
Conclusions (4T): The devices use the same deployment method	
(5T) It has similar principles of operation and critical performance requirements	
Device in question	**Device compared**
The energy is delivered through a handpiece which is in contact with the skin. The output parameters are set via a control console.	The energy is delivered through a handpiece which is in contact with the skin. The output parameters are set via a control console.
Conclusions (5T): The devices have the same principles of operation	

Figure 5.8: Technical characteristics considered to assess the equivalence between Epil808 and the legacy device.

High-level survey: The results of clinical surveys conducted on Legacy devices are shown in the Fig.5.9.
The survey involved the participation of 50 consumers (33 females and 17 males) between 17 and 49 years old with an average age of 32.5 years. The consumers participate to a minimum of 3 to a maximum of 12 treatments with an average of 7.6 total sessions. The treated areas were the thigh (for both males and females), the axillae (only for females) and the chest (only for males).

The performance of the device was assessed by considering the percentual reduction of the hair density by counting the number of hairs in a square area of 1 cm^2.
The first count was performed before the first treatment was delivered and

Technology: Diode Laser						
Type of treatment:	Photoepilation					
Total Number of consumers:	50	**Females:**	33	**Males:**	17	
Average Age of consumers:	32.5	**The Youngest:**	17	**The Oldest**	49	
Average of total sessions per consumer:	7.6	**Minimum n° of sessions:**	3	**Maximum n°of sessions:**	12	
During the treatments						
Average trend of the hair density	**Before the First Treatment**			**At the Last Treatment**		
	Axillae	**Chest**	**Thigh**	**Axillae**	**Chest**	**Thigh**
Value [n° of hair in a square centimeter]	31.79	31.65	27.66	8	8.88	7.72
Improvement [%]				74.78	71.9	77.0
Follow-up						
Average trend of the hair density	**At 3 months**			**At 6 months**		
	Axillae	**Chest**	**Thigh**	**Axillae**	**Chest**	**Thigh**
Value	6	9.88	8,72	10.45	10.88	9.72
Improvement* [%]	81.6	68.8	74.0	67.1	65.6	71.0
IG maximum on Expected Adverse Events:	2	**Maximum resolution time:**	2 h	**IG maximum on NOT Expected Adverse Events:**	0	**Maximum resolution time:** N.A.
IG maximum on Incidents:	0	**Maximum resolution time:**	N.A.	**Average consumer Satisfaction [from 1 to 5]:**	4.15	

Figure 5.9: High-level survey summary

all the successive counts were compared with the first one. Before the treatments the average number of hairs per area were: 31.79 for the axillae, 31.65 for the chest and 27.66 for the thigh. After the last session performed the count shows 8 average hairs for the axillae, 8.88 for the chest and 7.72 for the thigh; this corresponds to a reduction of 74.78%, 71.9% and 77.0% respectively.
The follow up was performed two times: the first after 3 months and the second after 6 months; both of them are related to the first treatment delivered. The first follow up shows a reduction of 81.6% for the axillae, 68.8% for the chest and 74.0% for the thigh. The second follow up shows a reduction of 67.1% for the axillae, 65.6% for the chest and 71.0% for the thigh.
About the expected adverse effects the maximum grade of severity index was 2, which corresponds to a temporary discomfort; the maximum resolution time was of 2 hours.
No unexpected effects or incidents were registered.
The average consumer satisfaction was 4.15.
In conclusion, the data reported in the survey show that the device is efficient and safe for its intended use.

5.5.1 Clinical literature

Literature to assess the equivalence: The comparison between EpilSmart Trial Band and the device coming from [30] from a technical and performance point of view is shown in Fig. 5.10, 5.11, where the same aspects of the comparison between Epil808 and the legacy device are considered.

Supportive literature The tables below (tab. 5.6 - 5.14) show a summary of the articles considered to assess the safety and performance of the Epil family devices. For each one the following features were analysed:

- target population and Fitzpatrick photoytpe;
- the treatment protocol;
- evidence and outcomes;
- conclusion of the authors.

The Fitzpatrick photoytpe is a classification method to distinguish different skin types according to the amount of melanin present in the skin. The Fitzpatrick scale goes from I (pale white skin) to VI (dark brown).

1) The Device is of similar design	
Device in question	**Device compared**
Diode laser device powered by mains with a control console and software interface that implements.	Diode laser device powered by mains with a control console and software interface that implements.
Conclusions: The devices have the same design specifications	
2) It is used under similar conditions of use	
Device in question	**Device compared**
It can be used only by qualified personnel for photoepilation treatment.	It can be used only by qualified personnel for photoepilation treatment.
Conclusions : The devices are used under similar conditions of use	
3) It has similar specifications and properties including physiochemical properties such as intensity of energy, tensile strength, viscosity, surface characteristics, wavelength and software algorithms	
Device in question	**Device compared**
Handpiece with triple Diode laser wavelength 755nm, 808 nm & 1064 nm (EpilSmart Trial Band); energy density 1 – 40 J/cm^2 ; pulse duration 5 – 200 ms; spot frequency 1 – 10 Hz; spot size 12x16mm	Handpiece with triple Diode laser wavelength 755nm, 810nm & 1064nm (Soprano Ice Platinum); fluence up to 60 cm^2, a pulse repetition frequency up to 10Hz and a 2cm^2 spot size.
Conclusions : The devices have similar output parameters	
4) It uses similar deployment methods where relevant	
Device in question	**Device compared**
The device delivers laser energy through a handpiece.	The device delivers laser energy through a handpiece.
Conclusions : The devices use similar deployment method	
5) It has similar principles of operation and critical performance requirements	
Device in question	**Device compared**
The energy is delivered through a handpiece which is in contact with the skin. The output parameters are set via a control console.	The energy is delivered through a handpiece which is in contact with the skin. The output parameters are set via a control console.
Conclusions : The devices have the same principles of operation	

Figure 5.10: Technical characteristics considered for the assesment of the equivalence between EprilSmart Trial Band and the device studied in [30]

1) The device has the same condition or purpose, including similar severity and stage of disease	
Device in question	**Device compared**
Device intended for aesthetic purposes for the removal of unwanted hair and provide a long term hair reduction.	Device intended for aesthetic purposes for the removal of unwanted hair and provide a long term hair reduction.
Conclusions: The devices employ the same technology for the same clinical purposes	
2) Same site in the body	
Device in question	**Device compared**
On any part of the body except of the ocular area.	Treatment areas included: face, beard, neck, chest, axilla, upper and lower limbs, suprapubic, and bikini line.
Conclusions: The devices can be used on similar sites in the body	
3) Similar population, including as regards age, anatomy and physiology	
Device in question	**Device compared**
There are no restrictions for the patients except the requirements presented in the contraindications.	Subjects excluded were those who were lactating or pregnant, having skin injuries in the area to be treated, had used other hair removal methods within the last 6 months, history of photosensitivity, or on any photosensitive drugs.
Conclusions: The devices have the similar population contraindications.	
4) Same kind of user	
Device in question	**Device compared**
Device used only by qualified personnel for aesthetic purposes.	It can be used only by qualified personnel for photoepilation treatment.
Conclusions: The devices have the similar kind of user	
5) Similar relevant critical performance in view of the expected clinical effect for a specific intended purpose	
Device in question	**Device compared**
Excessive power can cause skin irritation, crusting or burns. In addition, signs of folliculitis may occur after a hair removal treatment. These probable side effects generally do not require medical intervention.	No adverse events were recorded throughout the study.
Conclusions: The devices have the similar "critical performance" in view of the expected clinical effects	

Figure 5.11: Performance characteristics considered for the assesment of the equivalence between EprilSmart Trial Band and the device studied in [30]

A1 [21]: analyses the effects of a 810nm diode laser on the skin after a single session on the axillae. The study founds out a hair growth of almost 50% after two weeks until arriving to a hair growth of 48% after 6 weeks (Tab. 5.6). No significant side effects were recorded.

Table 5.6: Effects of the 810-nm diode laser on hair and on the biophysical properties of skin [21].

Target Population and Fitzpatrick phototype	35 women between 18 and 45 years of age with phototype II, III and IV.
Treatment protocol	Single-session diode laser therapy at 810nm: - fluence: $25 \div 30\ J/cm^2$ - spot size: 12mm. Treated areas: axillae.
Evidence	Hair growth with the diode laser was determined as 49.68% in 2 weeks, 46.01% in 4 weeks and 48.15% in 6 weeks.
Side Effects	None.
Conclusions of the authors	The diode laser can perform a significant reduction in the hair amount without significant epidermal damage, at least for a short period.

Table 5.7: Six-month follow-up multicenter prospective study of 368 patients, phototypes III to V, on epilation efficacy using an 810-nm diode laser at low fluence [22].

Target Population and Fitzpatrick phototype	368 patients between males and females with phototype II, IV and V
Treatment protocol	Fluence: $5 \div 10$ J/cm^2 Repetition rate: 10Hz Pulse interval range: of $10 \div 20$ ms. Spot size: 12x10mm. Treated areas: axillae, bikini line, lower abdomen, pubis, thorax
Evidence	Percentage of clearance of hair density 6 months after the fifth session: 0-24% 29 patient, 25_49% 102 patient, 50-74% 219 patient, 75-100% 18 patient.
Side Effects	Intense erythema in most patients but these signs were transient.
Conclusions of the authors	The results show efficacy without hair re-growth for a longer period than that of hair growth, being a safe, convenient therapeutic resource for patients of high skin phototypes

A2 [22]: exploits 810nm diode laser to verify the efficacy of this technology on dark skin types on different parts of the body. The efficacy was

demonstrated in percentage of clearance of hair density and the most of the patients have experienced a performance between 50-74%. Most of the patients undergo intense erythema after the session but the effects were transient.

A3 [23]: 810nm diode laser was used in this case study considering all the Fitzpatrick skin types. The results show a hair reduction of 48.15% 6 months after the first treatment. Slight erythema were recorded after the session but these disappear in 48 hours.

Table 5.8: Low Fluence–High Repetition Rate Diode Laser Hair Removal 12-Month Evaluation: Reducing Pain and Risks While Keeping Clinical Efficacy [23].

Target Population and Fitzpatrick phototype	17 patients aged between 18 and 70 years with phototype I, II, III, IV and V.
Treatment protocol	Patients were treated four times at 1-month intervals with a 810nm diode laser. Fluence energy: 15 J/cm^2 Spot size: 7mm Treated areas: upper back (males) and posterior thigh (females).
Evidence	The mean percent reduction was 48.15% 6 months following the last treatment session.
Side Effects	Most patients presented slight erythema disappeared within 48 hours
Conclusions of the authors	Low fluence 810 nm laser diode therapy can lead to progressive hair loss with minimal discomfort

A4 [24]: it proposes a clinical assessment of a 755nm diode laser exploiting three different techniques: conventional, in-motion and stacking technique. The efficacy was proved for all the three cases, in particular the results shows an average clearance of 75.5% for the conventional one. No significant side effects were recorded.

A5 [25]: the articles proposes a comparison between two 1060 nm diode lasers with different spot size in order to confirm the efficacy and safety of this technology. Different area of the body were considered and the efficacy of these products were recorded considering a percentage age reduction; a reduction of 81% has been observed in the arm. Only one subject reported a little burn after the second session.

A6 [26]: the study compares the use of a 755nm (on the right axilla) and a 810nm (on the left axilla) diode lasers exploiting different parameters. The performance was demonstrated with the percentage hair reduction in both sides with values of 72.16% and 71.30% in the left and right axilla

Table 5.9: Clinical Assessment of a New 755 nm Diode Laser for Hair Removal: Efficacy, Safety, and Practicality in 56 Patients [24]

Target Population and Fitzpatrick phototype	56 subjects with Fitzpatrick phototypes between II and V.
Treatment protocol	A 755-nm diode laser was used with a spot size of 1.5 cm^2. Treated areas: chest, abdomen, arms, back, bikini line.
Evidence	The average clearance achieved were 75.5%.
Side Effects	None
Conclusions of the authors	755-nm diode laser may be a highly efficacious, versatile, and efficient tool for medical hair removal.

Table 5.10: Long-Term Clinical Evaluation of Hair Clearance in Darkly Pigmented Individuals Using a Novel Diode1060 nm Wavelength With Multiple Treatment Handpieces: A Prospective Analysis With Modeling and Histological Findings [25].

Target Population and Fitzpatrick phototype	16 subjects age 33 ± 10.9 years were treated with the chilled sapphire tip 26 subjects age 36.3 ± 7.67 years were treated with the large spot size vacuum-assisted handpiece. Skin type between I-VI.
Treatment protocol	The treated areas were axillae, shin, and arm. Spot size: 9x9 mm and 22z35mm. Pulse duration: 30ms or 30, 60,100,400ms.
Evidence	With chilled sapphire treatment a mean 67.0%, 77.9%, and 81.0% a reduction in hair counts was obtained in the axillary, shin, and arm, after two treatment sessions.
Side Effects	A single subject reported a mild treatment-related burn in the right axillae after the second treatment session.
Conclusions of the authors	The clinical findings demonstrate the safety and efficacy of the 1060 nm diode laser system. Long-term hair reduction was achieved in all skin types.

Table 5.11: Long-Term Efficacy of Linear-Scanning 808 nm Diode Laser for Hair Removal Compared to a Scanned Alexandrite Laser [26].

Target Population and Fitzpatrick phototype	28 adult women (mean age 31.2± 9.3 years) and three adult men (mean age 30.3± 4.9 years) with skin types I-IV.
Treatment protocol	The right axilla was treated with the 755 nm alexandrite laser: - fluence: 25–30 J/cm^2 - pulse duration: 30–40 ms - spot size:10x10 mm The left axilla was treated with the 808 nm linear-scanning diode laser: - fluence: 24–30 J/cm^2 - pulse duration:12 ms -spot size: 50 mm x 12 mm.
Evidence	There was a significant reduction in axillary hair after the 6th treatment on both sites: left axilla: hair clearance of 72.16%; right axilla: hair clearance of 71.30%
Side Effects	None
Conclusions of the authors	Significant but comparable hair reduction among individuals with skin types I–IV that persists at least for 18 months after the termination of treatment.

respectively. No side effects were recorded.

A7 [27]: this comparison between a home use and a 810nm diode laser confirms the performance of diode laser technology in terms of percentage hair reduction (88%) on skin types III and IV. In addition, no significant side effects were reported 5.12.

A8 [28]: it makes a comparison between a 755nm diode laser and a 755nm alexandrite laser with the scope to prove the safety and performance of the diode laser on dark skin types. The study shows a hair reduction between 26-50% with the diode laser e no side effects were reported.

A9 [29]: here the subjects involved in the study were treated with a triplewavelength (810 nm, 940 nm, 1060 nm) diode laser on the right side of the body and with a 810nm diode laser on the left. The results show a reduction between 58% and 93% on the right side and on the left side ranging in between 39% and 81%.

Table 5.12: Evaluating the effectiveness of laser hair reduction using a home use laser in comparison to a Diode laser [27].

Target Population and Fitzpatrick phototype	15 females aged between 20 to 30 years and within the Fitzpatrick skin types III and IV.
Treatment protocol	Spot size: 24x38mm Fluence: 6 or 8 Jcm^2 Treated areas: axillae
Evidence	The overall reduction of hair on the right axilla was estimated to be 85% and 88% on the left axilla
Side Effects	None
Conclusions of the authors	Performance and safety of diode laser for photoepilation treatments are confirmed. In addition, no severe undesirable effects in follow-up are shown.

Table 5.13: Comparison of efficacy and safety of a novel 755-nm diode laser with conventional 755-nm alexandrite laser in reduction of axillary hairs [28]

Target Population and Fitzpatrick phototype	20 healthy female volunteers with ages ranging between 18 and 50 years old and skin type III–IV
Treatment protocol	Each subject received a total of six treatments at 1-month intervals in the axilla area. Fluence:up to 34.25 J/cm^2 Spot size: 120 mm^2
Evidence	Percentage hair reduction between 26–50%
Side Effects	None
Conclusions of the authors	This study showed that the 755-nm diode laser is suitable for hair removal procedures and it is as effective and safe as the conventional 755 -alexandrite laser in darker white and light brown skin types.

Table 5.14: Triple Wavelength and 810 nm Diode Lasers for Hair Removal: A Clinical and in Silico Comparative Study on Indian Skin [29].

Target Population and Fitzpatrick phototype	3 subjects (2 males and 1 female) aged between 21 and 27 years with skin type IV.
Treatment protocol	One subject was treated on the abdominal area, one on the back, and the other on the arms. The right side was treated with a triple-wavelength diode laser: - fluence: 20J/cm^2 - pulse duration: 30ms - frequency: 1Hz The left side was treated with 810nm diode laser: - fluence 8 J/cm^2 - pulse duration: 16ms - frequency: 6Hz
Evidence	Hair reduction of between 58% and 93% was achieved with the triple-wavelength diode laser, while the 810 nm diode laser achieved hair reduction of between 39% and 81%.
Side Effects	None
Conclusions of the authors	On darker skin types, the triple-wavelength diode laser (810 nm, 940 nm, 1060 nm) has been found to be more effective for permanent hair reduction compared to the 810 nm diode laser.

Conclusion about data found in literature

Data coming from the literature research are useful to assess the high performance of the diode lasers, especially for the wavelength considered: 755, 808 and 1064 nm. The laser epilation is a well-established technology for aesthetic purposes. Also, if the usage of this technology may be accompanied by the presence of side effects, these disappear in a short time. Thus, the benefits of diode laser technology for hair removal outweighs risks.

Chapter 6

Discussion

6.1 Technical Documentation

Technical documentation compiled according to Annex II of the MDR, provides the information to be supplied by the manufacturer to carry out the conformity assessment procedure. As the Epil family devices do not belong to the Class I risk, the documentation need to be submitted to NB together with the documentation of the QMS in order to obtain the certificate of conformity.

The technical documentation contains importants information related to the device such as the scope, the intended users, the target consumer and the technical specifications. The devices under study are active electrical products which exploits laser energy at different wavelength for aesthetic hair removal purposes. The principle of operation is that of the selective phototermolisis that allow laser to target melanin in the hair bulb while avoiding damages to the outer areas.

Epilsmart variant has a smaller case with respect to Epil808. In addition, with respect to the previous generation of the device, new power supplies and electronic board have been implemented.

Considering that we are dealing with active devices, electromagnetic interferences should be avoided. For this reason, consumer that are pacemaker or internal defibrillator wearers are not predisposed for the treatment. In general, consumers affected by acute disease or characterized by skin abnormality should not undergo the treatment. However, side effects such as skin irritations or burns need to be considered, also if a correct use of the products

shall guarantee that these harms are minimized as much as possible. The operator is responsible in ensuring that the consumer is appropriate for the treatment. Infact, the operator must be properly qualified and trained before the use of these devices.

The technical characteristics described in Tab.5.2 contains important parameters and some of them (spot frequency and energy density) should be taken into account also during the choice of the literature for the clinical evaluation.

Epil family devices are characterized by a display with a CPU and the other applicators necessary for the functioning of the device. the presence of the pedal guarantees an additional safety measure because the output of the laser is ensured only if the both the pedal and the button on the handpiece are pressed contemporary. the products are provided with their accessories. The use of personal protective equipment, such as the googles, are indicated to avoid the contact with scattered radiation. About this scattered radiation, it is important to say that according to the CS the handpiece is embedded with a contact sensor. This means that the laser emission is possible only if the handpiece is put directly in contact with the skin, otherwise no emission occurs. This represents an additional safety measure in the device but anyway the use of google is highly recommended.

The risk class of the device represents a key point for the definition of the procedure to follow for the conformity assessment. Epil family devices belong to risk Class IIa according to Rule 9 of the Annex VIII of the MDR because they are active electrical products that provide energy to the human body [3]. Regulation 2022/2347, moreover, reclassified devices emitting high-intensity radiation for only photoepilation purposes as class IIa [11].

6.2 Risk Management

The risk analysis focused on different kind of hazards including those related to:

- electromagnetic, thermal and mechanical energy (tab.5.3);
- chemists, functioning of the device, error of use (tab.5.4);
- operating instructions, warnings, maintenance (Tab.5.5);
- specific risks (Tab.5.5).

Rationales for hazards proposed in section 5.2 are provided in the following paragraph. However, an objective and quantitative evaluation was not possible because many hazards were not actually experienced, but just foreseen.

Electromagnetic energy
1&2: the hazards which show a higher degree of risk are those related to the main voltage and the leakage currents. This happens because they are connected with the consumer risks of electric shock (IG=6).
3&4: considering that the devices under study are active electrical devices they are asscoiated with types of harms which requires a medical intervention (IG=4).

These types of hazards are controlled by adopting electrical components that are compliant with CEI EN 60601-1 [33]. Moreover, to avoid electromagnetic interferences other electromagnetic devices shall stay away from these products.

Radiation
5: these devices emit high-intensity radiation which if it is not controlled may cause permanent lesions (IG=5).
6: the radiation emitted by the devices is non-ionizing, thus no risk is associated with ionizing radiation.

The laser radiation emitted is controlled according to the input parameters; limit value of emission are imposed.

Thermal energy
7: if too energy is delivered to the consumer, risks of burns may occur (IG=5) in the case of overexposure.
8: on the other hand, the handpiece is cooled with a suitable cooling systems. Problems may achieve in case of fault of this system.

Mechanical energy
9: problems of falls may occur if the handpiece accidentally falls from the hand of the operator or if the machine is not transported in a correct manner.
10: the devices have no moving parts and are not intended to store energy.
11: alarms in the machines are used during the correct functioning or in case of warnings but they are not annoying.

Chemists

12: no acid, residues, contaminants or additives are used with the devices.
13: if incorrect cleaning agents are used, this may lead to malfucntions in the machines. The operator is required to follow the cleaning prescritions in the IFU.
14: degradation products, medical gases or anaesthetic products are not used with the devices.
15: allergies may occur after the contact between the handpiece and the skin. The materials under study are biocompatible.

Functioning of the device
16: the incorrect functionality is primarily related to alarms. This hazards is reduced thanks to safety measure implemented in the device and verified through usability tests.
17: the devices are not intended to have a measuring function.

Error of use
18: it depends on the user attention and may the cause the operator to point the laser towards the eyes (IG=4).
19: this kind of error is connected to experience and violation of procedures; the same consideration of the hazard 18 can be done.

Operating instructions
20: if the intended use of the accessory is not specified clearly damage to the machine may occur.
21: the IFU must be written in a way that is easily understood by the operator. If they are too complicated the operator may use the device without the necessary knowledge of the functioning.

Warnings and maintenance
22: the risk is connected to the fact that the contraindications specified in the IFU are not considered and thus relevant side-effects can be experienced.
23: if the operator does not follow the maintenance prescription some problems in the devices may occur.

Specific risks
24: it is important to define suitable input parameters according to the skin type of the consumer. For this reason, it is preferable that the operator uses the standard parameter proposed for each skin type.
25: the problem arises when the operator does not consider the contraindications about consumer presented in the IFU.
26: the same considerations of the hazard 25 can be done.

Finally, after implementing the control measures, the overall RR results acceptable. It means that the risk analysis got a positive evaluation.

6.3 Biocompatibility

The materials that constitute the handpiece are discussed in section 5.3. Particular attention is given to those materials that are put directly in contact with the skin of the consumer: alluminium, glass and gold. The glass is provided with its own biocompatibility certification, while strong rationals have been used for the other materials for not performing the tests.

Primarily, the nature of the contact is transient, which means that the handpiece is moved very quickly on the area to be treated and it does not stay for more than an instant on the same point. Then, the materials under study have been placed on the market since years and their safety has been highly proved. In addition, for gold material, data coming from the literature give more proof of its higher degree of biocompatibility [31],[32]. In these studies the material is applied in invasive surgical operations, thus it implies that gold is used for more risky cases with respect to the one implied in the handpiece of the Epil family. Considering all these aspects, according to the ISO10993:2018, there is no need to perform biocompatibility tests.

6.4 Usability

The usability specifications regards both the physical part and the SW. For the physical part the aspects that are considered are specified in Tab.5.2.

Manoeuvrability of the device body
The device is designed to be with prehensile edges of the casing in such way to be grapped easily. Moreover, the light weight of the devices under study makes them easily movable.

Manoeuvrability of the treatment delivery accessories
The use of the devices is operator friendly thanks to the handpiece design which allows an easily grip during the treatment. The use of the pedal for the initiation and interruption of the treatment simplify the work of the operator.

Enclosure protection
The case of the devices is closed by screws so it cannot be opened by the operator but only the personal dedicated to the maintenance. The case is designed and assembled in such way that external substances used during sanitation do not enter in the machines.

Different considerations are made for the SW specifications and these are listed in Tab.5.3.

User friendly interface
The communication between the operator and the machine is performd through the dislpay. It is implemented using commonly recognized symbols that allow the user to clearly identify messaging information. Common coloured buttons are used for the start and stop of the session.

Setting of the physical treatment parameters and recognition of connections by the SW
The SW has a dedicated space in memory that allows to insert specific parameters for each treatment protocol.

The recognition of the handpiece by the SW is done by reading the internal calibrated resistance of the handpiece. A recognition of the pedal is also implemented.

Safety with respect to human error
The protection toward the human error is implement with a double request of confirmation when the critical parameters are selected.

Formative and Summative Assessments The results of the formative and summative assessments are presented in Tab.5.4,5.5. The tests have been performed on a prototype that had to be fully functional and provided with the IFU in order to let the experts and the users to evaluate its functioning. The test takes into account different aspects of the device that are described below.

Starting from the opening of the packaging, a primarily evaluation of the packaging itself and the labelling of the accessories was carried out. This last aspect is fundamental for a correct connection of all the parts to the device. During the use of the device, particular attention is given to the sounds level of the acoustic alarms and the intuitive user interface. The sounds of the warnings need to be enough to let the operator to catch it but not too high

to bother the operator and the potential consumer. A user-friendly interface should be implemented to reduce as much as possible errors related to the input of the parameters. Anyway, the use of the products implies consulting the IFU that are delivered with the device; these should be written in a comprehensive way.

In both the test, each question obtained a score of 3 that means that the device has been implemented in a workmanlike manner. Thus, considering that there is no answer with a score under the threshold, the usability test is considered passed.

SW development

For the SW development the requirements considered are shown in Fig.5.6 and in this section will be discussed.

REACHABILITY OF ALL THE SCREENS
All the screens that are available must be reachable. To verify it all the menus available have been selected and the destination has always been reached.

IDENTIFY THE PRESENCE OF THE HANDPIECE
If the handpiece is not properly connected, the machine is not able to deliver the treatment. The SW detects the fault and a warning error appears on the screen.

LIQUID TEMPERATURE DETECTION
When the liquid temperature reaches levels that are too high or too low, the machine must interrupt its functions in order to avoid further damages. The test performed provides for activation of the device when the liquid temperature outsides the acceptable range and demonstrates that in case of fault the machine stops to work and advise with an error message on the display. When the fault is restored the device continues to work properly.

HANDPIECE CURRENT DETECTION
If the current passing in the handpiece outsides the acceptable range, this have to be detected and an error message must be displayed. This problem is verified with the use of a voluntary altered current which is obtained by altering the operational gain U6.2 with the adding of an additonal resistance in parallel with R179. During the trial the SW detected the fault and stops to work.

FAILED TEST
This error must appear when there is an abnormality in the machine. For this test the sensing of the power supply is disconnected and the display shows an error message followed by the interruption of the functioning.

CONTROL FOR THE ACCESS
The access to the machine should be possible only through a password. To verify this, it is simply necessary to turn on the machine because when this happens the operator is prompted to enter a password.

6.5 Clinical Evaluation

This clinical evaluation aims to demonstrate the **safety** and **performance** of the Epil family. Clinical data are taken from the literature for this scope but also for demonstrating the equivalence between EpilSmart Trial Band and another device already present on the market. Moreover, for the Epil808 model a high-level survey of the legacy device is available.

Before considering the data coming from the high-level survey, the equivalence between Epil808 and the legacy device must be demonstrated. The Tab. 5.7,5.8 include the technical and performance characteristics evaluatede to assess this equivalence.

Performance characteristics: A slight difference is represented by the fact that Epil808 is intended for *non-medical aesthetic purposes* for the removal of unwanted hair, while the legacy device was intended for *medical purposes* for the treatment of *hirsutism diseases*. As consequence of this condition of use, the legacy device can be used only by medical personnel, while Epil808 is intended for qualified operators, which include both professional beauticians and medical personnel. Anyway the two devices employ the same technology and are used on the same kind of population, thus the products have similar performance characteristics.

Technical characteristics: There are no changes in the technical parameters between Epil808 and the legacy device. They are powered with the same supply mains and the same technical specification for the laser emission are maintained. Thus, the two products are equal from a technical point of view.

Since the equivalence between Epil808 and the legacy device has been demonstrated, clinical data from the high-level survey can be exploited. The results are explained in section 5.3 of this work and summarized in Fig.5.9. The efficay of the legacy device is evident. At each follow-up high percentage values of hair reduction are registered. Generally, higher values are found just after the last treatment but also after six months the performance is still high (67.1% for the axillae, 65.6% for the chest and 71% for the thigh). Moreover, no significant side effects were reported and the score satisfaction of the consumer is very high with an average of 4.14 out of 5.

Clinical data for the evaluation of the equivalence between EpilSmart Trial Band and another similar device are taken from [30]. As for the legacy device, technical and performance characteristics were compared.

The equivalent device is characterized by a handpiece with triple diode laser wavelength 755nm, 810nm & 1064nm. It exploits an energy density which is a little bit higher with respect to the one of the EpilSmart (60 J/cm^2 vs $40J/cm^2$), but same frequency and spot size are used. Considering the information taken out from the study [30], there are no significant changes in other technical or performance characteristics, thus the equivalence between the devices can be assessed and the safety and performance of the EpilSmart Trial Band is confirmed.

All the others literature studies are used to demonstrate the safety and performance of all the Epil family, considering all the wavelength that can be exploited with the different models: 755nm, 808nm & 1064nm.

Last part of the section 5.3.1 is dedicated to the summary of the studies that have been included in the clinical evaluation. From these articles can be concluded that the Epil family devices are safe and performing, in particular:

- 810nm diode laser is efficient already from the first session [21] on all the different types of skin, including also dark skin types [22][23];
- 755nm diode laser efficacy is proved to be higher of an alexandrite laser [28];
- a triple wavelength (810nm, 940nm & 1060nm) diode laser has been shown to be more efficient with respect to a 810nm diode laser [29].

Although the wavelength exploited in the literature studies sometimes are quite different with respect to those implemented in the Epil family, these differences are so small that are no significant.

A the end, it can be concluded that the diode laser epilation is a well established technology which founds a high degree of performance for aesthetic

purposes. Only negligible and transitory adverse effects can be experienced, which cannot compromise the person health status and, for this reason, they can be accepted.

Conclusions

In conclusion, this work developed the Technical documentation for Annex XVI devices, according to Annex II of the MDR. It contains also the risk management, the biocompatibility, the usability tests and the clinical evaluation report.

Specifically this study applies to Epil family devices for hair removal purposes. These products are designed, manufactured and produced by the company Elits Group, which is still working to conclude this certification procedure.

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