# Deliverable 4.1.

# Reduced Version*

## Regulations and legal issues at European Union to be fulfilled to the purposed pilot service

*Note: this is a REDUCED VERSION of the original document.
Please refer to the complete report for a detailed information on the standards.

**02-2014-25**

diagnoptics

# Deliverable 4.1. Reduced Version* - Regulations and legal issues at European Union to be fulfilled to the purposed pilot service

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# INTRODUCTION

This document covers the regulations and standards affecting the prototypes and processes to be realised on Diagnoptics project. The main purpose is to provide to all project partners, a common framework for the understanding and application of the legislation and recommendations related to each project stage, to build prototypes (and later products) that meet EU regulation and international standards.

Terms used in this document, as for example, company(ies), project partner(s), designer(s), developer(s) are referring to the organisations and responsible persons involved. Other terms used like medical device(s), prototype(s), pilot(s), product(s) are to be understood as per their correspondent development phase.

The Annex and Formularies provided will be used through the whole project and will be labelled accordingly as per its status of review (with an indicative letter or date).

This document is therefore a preliminary over-view of the regulations and standards at the level of technology specs provided. Upcoming deliverable nr 4.2 (month 12 of the project) must provide the detailed standardization report as far as the technology designs will be further developed.

# UNE-EN ISO 13485:2013 Medical devices - Quality management systems - Requirements for regulatory purposes - Design Control

According ISO 13485 (and ISO 9001), design must be done according to several rules. These rules are:

## Design and development planning

The project partners will plan and control the design and development of prototypes. During the design and development planning, the partners will determine:

The design and development stages, the review, verification, validation and design transfer activities that are appropriate at each design and development stage, and the responsibilities and authorities for design and development.

The project partners will manage the interfaces between different groups involved in design and development to ensure effective communication and clear assignment of responsibilities.

Planning output shall be documented, and updated as appropriate, as the design and development progresses.

Design transfer activities during the design and development process ensure that design and development outputs are verified as suitable for manufacturing before becoming final production specifications.

## Design and development inputs

Inputs relating to product requirements shall be determined and records maintained. These inputs shall include

a) functional, performance and safety requirements, according to the intended use,
b) applicable statutory and regulatory requirements
c) where applicable, information derived from previous similar designs,
d) other requirements essential for design and development, and
e) output(s) of risk management .

These inputs shall be reviewed for adequacy and approved.

Requirements shall be complete, unambiguous and not in conflict with each other.

## Design and development outputs

The outputs of design and development shall be provided in a form that enables verification against the design and development input and shall be approved prior to release.

Design and development outputs shall:

a) meet the input requirements for design and development,
b) provide appropriate information for purchasing, production and for service provision,
c) contain or reference product acceptance criteria, and
d) specify the characteristics of the product that are essential for its safe and proper use.

Records of the design and development outputs shall be maintained. Records of design and development outputs can include specifications, manufacturing procedures, engineering drawings, and engineering or research logbooks.

### Design and development review

At suitable stages, systematic reviews of design and development shall be performed in accordance with planned arrangements to evaluate the ability of the results of design and development to meet requirements, and to identify any problems and propose necessary actions.

Participants in such reviews shall include representatives of functions concerned with the design and development stage(s) being reviewed, as well as other specialist personnel.

Records of the results of the reviews and any necessary actions shall be maintained.

### Design and development verification

Verification shall be performed in accordance with planned arrangements to ensure that the design and development outputs have met the design and development input requirements. Records of the results of the verification and any necessary actions shall be maintained.

### Design and development validation

Design and development validation shall be performed in accordance with planned arrangements to ensure that the resulting product is capable of meeting the requirements for the specified application or intended use. Validation shall be completed prior to the delivery or implementation of the product. Records of the results of validation and any necessary actions shall be maintained.

As part of design and development validation, the project partners shall perform clinical evaluations and/or evaluation of performance of the medical device, as required by national or regional regulations.

### Control of design and development changes

Design and development changes shall be identified and records maintained. Changes shall be reviewed, verified and validated, as appropriate, and approved before implementation. The review of design and development changes shall include evaluation of the effect of the changes on constituent parts and product already delivered.

Records of the results of the review of changes and any necessary actions shall be maintained.

## FORMULARIES

In a quality management system all activities affecting product quality must be registered. We provide two forms:

### FORM DC-001 (Design Control form)

This form can be used for a main project or for the small projects which together form a main project. In this form the project partners must define a series of inputs for the project: some functional, performance and safety requirements, according to the intended use, and regulations applicable (mandatory). Also is mandatory compliance with directive 93/42/MDD as input.

In order to know if the project meets with each input requirement a validation protocol is used.

As results of the design control are the documents needed to manufacture the product (drawings, manufacturing procedures, protocols, bill of materials, control plans, protocols, and so on).

### FORM DR-001 (Design Review form)

At the different stages of a project design reviews are needed. This form is used to ensure registration for the activities in such reviews. By one hand the state in which the project is located and the other conclusions of the meeting, which may include new tasks assigned to different persons. Also are recorded the names of the people attending the review.

## CONCLUSIONS

ISO 13485 defines the requirements for the design process of a medical product.

- Defines inputs, which are the design specifications (requirements to be met by design), implies that these inputs are met by protocols.
- This part applies to all sub-projects.
- Compliance with this procedure provides a formal structure for any type of design.
- Provides consistency in developing projects.
- Provides traceability for the different parts that make up the project.

# Medical Device Directive 93/42/CEE of 14 June 1993

Directive 93/42/MDD modified by 2007/47/MDD is the main document which defines the requirements that must meet a medical device.

Medical device means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its company to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the company to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.

Before to put in the market a medical device, it is mandatory that the company demonstrates that the device meets with the provisions of the annex I of this directive. And also provide a Clinical Evaluation

It is convenient remember here the mentioned annex, due to the high importance in the regulations field.

**ANNEX I. ESSENTIAL REQUIREMENTS**

**ANNEX X. CLINICAL EVALUATION**

**FORMULARIES**

**ER-001 (Essential Requirements MDD 93/42/MDD modified by 2007/47/MDD)**

The first part of this form is designed to ensure that the company complies with the essential requirements. To do this, in the first two columns on the left are the paragraphs of Annex I to the Directive 93/42/MDD. In the right column the company defines the conclusion for the paragraph, and finally in the right the location in the technical file where is the evidence that supports that conclusion indicated.

The second part of this form is designed to ensure that the company meets with the requirements for clinical evaluation. To do this, in the first two columns on the left are the paragraphs of Annex X to the Directive 93/42/MDD. In the column to the right the company writes if this paragraph is applicable or not and finally the location in the technical file where is the evidence that the company meets the paragraph if applicable.

**CONCLUSIONS**

The mentioned directive 93/42/MDD amended by 2007/47/MDD is the basic document for the regulation of medical devices.

- All the sub-projects must meet with the requirements of this main standard.
- Each of the project partners can demonstrate compliance with this general directive ensuring compliance with the various paragraphs of the document ER-001.
- The document ER-001 is built like a check-list, to facilitate the understanding of compliance with this directive.

# UNE-EN ISO 14971:2012 - Application of risk management to medical devices

The requirements contained in this standard give to the companies and designers a framework in which experience, intuition and review systematically apply for managing the risks associated with the use of medical devices.

This standard deals with the processes for risk management, which mainly affect the patient, but also the operator, other people, other devices and the environment.

It is accepted that the concept of risk has two components:

a) the probability of occurrence of harm;
b) the consequences of such damage, that is, how severe it may be.

Highlighted terms and definitions

- Damage: Injury or physical damage to the health of people or damage to property or the environment.
- Danger: Potential source of harm
- Severity: Measure the potential consequences of a hazard.
- Risk: Combination of the likelihood of such harm and the severity of that harm.
- Dangerous situation: Circumstance in which people, property or the environment are exposed to a hazard.
- Residual risk: Risk that remains after you have taken the risk control measures.
- Risk Control: Process in which decisions are made and actions for which the risks are reduced or kept within specified levels are implemented. Is equivalent to mitigation.
- Risk estimation: Process used to assign values to the probability of occurrence of harm and the severity of that harm.
- Risk assessment: Process of comparing the estimated risk against risk criteria to determine the acceptability of the same.
- Risk Management: Systematic application of policies, procedures and management practices of the tasks of analyzing, evaluating, controlling and monitoring risk.
- Risk management file: Set of records and other documents generated by risk management.
- Security: Absence of unacceptable risk.
- Lifecycle: All phases in the life of a medical device from initial conception to decommissioning and waste. These phases are:
    - design,
    - production,
    - transport,
    - post-production,
    - when the medical device becomes waste.

**FORMULARIES**

**RA-001 (Risk Analysis form)**

This form can be used each phase of the Lifecycle of the product.

This form is an “Excel” document with a page for each stage of the analysis.

Page 1

The usefulness of this page is to remember the map of the various risks that are analyzed and its place in the intolerable, undesirable and tolerable areas, depending on the severity and likelihood of the risks.

Page 2

This page is for list the risks detected.
In the left column there is a number that will identify the risk for traceability and further operations.
The column “RISK” is for describe the risk.
The column “EFFECT” is for describe the effect that the risk will cause.
The column “CAUSE” is for describe the cause that can produce the risk.
The column “P” is for write the estimated probability of occurrence of the risk.
The column “S” is for write the severity of the risk.
The column “RPN” is the risk product number. Is the value P*S.
Is a good practise to define the risks which are related with security.

Page 3

This page is for risks evaluation before mitigation.
We must place the number of the risk mentioned in Page 2 depending on the number P and S in the same page.

Page 4

This page is for list the risks after mitigation.
In the left column there is again a number that identify the risk
The column “RISK” is for describe the risk again.
The column “Initial level” is for write the “RPN” calculated in Page 2.
The column “RISK MITIGATION ACTION” is for describe the action for mitigate the risk.
The column “New Risks?” is for write if a new risk has appeared after mitigation.
The column “P final” is for write the estimated probability of occurrence of the risk after mitigation.
The column “S” is for write the severity of the risk after mitigation.
The column “RPN” is the risk mitigated product number. Is the value P final *S final.

Page 5

This page is for risks evaluation after mitigation.
We must place the number of the risk mentioned in Page 5 depending on the number P final and S final in the same page.

Page 6

This page is for list the risks after mitigation by the same cause.

In the left column there is again a number that identify the risk
The column “RISK” is for describe the risk again.
The column “New Risk number” is for define a new number for the grouped risks.
The column “RISK MITIGATION ACTION” is for describe the action for mitigate the grouped risks.
The column “New Risk?” is for write if a new risk has appeared after risks grouped risks.
The column “P final” is for write the estimated probability of occurrence of the risk after grouping. It will be the highest probability for the initial risks that form the group.
The column “S” is for write the severity of the risk after grouping. It will be the highest probability for the initial risks that form the group.
The column “RPN” is the risk mitigated product number. Is the value P final * S final.

Page 7

This page is for make a global analysis for residual risks.
We must place the number of the risk mentioned in Page 6 depending on the number P final and S final in the same page.

Page 8

Acceptability assessment of global residual risk.
This page is for write the conclusions of the risk analysis.
In this page we will write:
- Situation in the assessment table for all individual risks after mitigation:
- Number of individual risks.
- Maximum severity.
- Maximum Probability.
- Conclusions about the global risk.
- Number of risks by different cause.
- Maximum severity.
- Maximum Probability.
- Additional Comments.

**CONCLUSIONS**

- Risk analysis in a medical device is a key part of its design, as it is not acceptable that the medical device could endanger the patient, other people, other devices or the environment.
- All the sub-projects must meet with the requirements of this main standard.
- Risk management is not only applicable to risks in general; also is applicable to other standards, such as biological risks, usability, etc.
- To ensure that the process of risk management is carried out, the project partners can fulfill the Form AR-001, identifying the various risks, assigning for each risk their likelihood and severity. Once done this should proceed with mitigation measures for each risk, when the process is completed, all risks must be in the tolerable zone. If any of the risks is not ultimately in that area should get a risk-benefit assessment of that risk

# UNE-EN ISO 10993-1:2010 Biological evaluation of medical devices

The main objective of this part of the 10993 is the protection of potential biologic hazards arising from the use of medical devices.

## HIGHLIGHTED TERMS AND DEFINITIONS

Materials:
Any synthetic or natural polymer, metal, alloy, ceramic material, or other substance, used as a medical device or any part thereof.

Final product:
Medical device in its "as used" as defined by the specification or company labels.

Chemical constituent:
Any natural or synthetic substance that is used in a process for manufacturing materials and / or health, such as additives and processing aids processes.

## GENERAL PRINCIPLES OF BIOLOGICAL EVALUATION OF MEDICAL DEVICES

The biological evaluation of any material or device intended to be used in humans should be part of a biological assessment program within a structured risk management process in accordance with the standard 14971. The biological assessment should be planned, completed and documented by knowledgeable and experienced professionals.

In the selection of materials used in the manufacture of the product, the first consideration should be the suitability for purpose considering the characteristics and material properties, including their chemical, toxicological, physical, electrical, morphological and mechanical properties.

The choice of tests and data required in a biological assessment and interpretation must take into account the chemical composition of materials, including exposure conditions, and the nature, extent, frequency and duration of exposure the medical device or its constituents to the body, allowing the categorization of products to facilitate the selection of appropriate tests.

Selecting any trial must be based on the end use applications.

## RATING OF MEDICAL DEVICES

Medical devices should be categorized according to the nature and duration of contact corpora.

Categorization by the nature of body contact

Products that come into contact with the surface (due to the characteristics of the Diagnoptics project, this is the type of contact we are interested)

a) Skin. Products that come into contact only with intact skin surfaces.
b) Mucous Membranes. Products that come into contact with intact mucous membranes
c) Surfaces torn or compromised. Product in contact with surfaces of the body torn or otherwise compromised form.

**Categorization according to the duration of contact**

Medical devices should be categorized according to the anticipated duration of contact as follows:

a) limited exposure (A) products which cumulative or single contact, multiple or repeated is not more than 24 h;
b) prolonged exposure (B) or products which contact a cumulative, multiple or repeated long term can only be expected to exceed 24 h but not 30 days.
c) permanent (C) or products which contact a cumulative, multiple or repeated single term exceeds 30 days.

If a material or product can be ascribed to more than one category by duration of contact, should apply the tests and / or considerations of a more rigorous evaluation.

**CONSIDER EVALUATION TESTS**

Once we have categorized the type of contact and the duration of it, in order to determine the tests to be performed on the part of the product in contact with the patient. We refer to Table A.1. (evaluation tests to consider) on Annex A of the standard.

This table shows the nature of body contact listed in category and contact. Then the duration of contact and on the right the tests required for the particular categorization. To the right of these columns appear necessary tests.

In the Diagnopitcs project would be to contact surface or torn or compromised skin surface. The duration of contact would be less than 24 hours, which corresponds to Category A.

Consequently the tests to be applied will be:

- Cytotoxicity (ISO 10993-5).
- Hypersensitization (ISO 10993-10).
- Irritation or intracutaneous reactivity (ISO 10993-10).

## FORMULARIES

### BR-001 (Biological Risk Management form)

The object of this form is to record the various arguments and tests to ensure that the device is safe related to biohazards.

RISK ANALYSIS PRODUCT:

-In this paragraph will we written the name of the medical device under test.

Intended use of product characteristics.

-Materials that make up the product and which of them may represent a biological risk are described in this paragraph.

Identification of the biohazard.

-Here are described as manifest in the patient different biological risks.

Determination of exposure.

-Here is described depending on the time of exposure of the patient if that time is of the class A, B or C as defined in ISO 10993-1.

Risk Estimation.

-Are redefined materials forming the product and being in contact with the patient and the exposure time.

Risk Assessment.

-The type of disease that the patient may suffer from the use of the product are defined.

Risk Control

-The way to reduce or eliminate the risk. Possibly contracting the services of external laboratories for testing the testing set.

Risk assessment / global residual benefit.

-Determining the outcome of external testing. If the final risk of any of these tests were not void a benefit / risk assessment be conducted.

Report of the biological assessment.

-Writing where they are located in the technical file the reports for the external tests and a final conclusion on whether the biological risk is zero or not.

Information on post-production.

-Describing how the company will track the risk control measures if they are effective.

**CONCLUSIONS**

- The sub-projects that have parts in contact with the patient must ensure that this part conforms with EN 10993-1.

- For the "In-vivo Confocal Microscopy" and "Exvivo Confocal microscopy" with EC Certificate nr 7602 rev 1, because at the time of writing this document is not defined what new components will incorporate these sub-projects, we can not evaluate at this moment the application of this standard in them.
- The "3D Topography" sub-project includes with the information available at his moment the following components:
    - Ring window in contact with patient
    - Power supply
    - 2 scientific cameras
    - 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision
    - 2 imaging lenses
    - A linear motion guide driven by a step motor
    - CMOS Color camera
    - Personal computer with USB supplying electric power

  From all the components mentioned above only the "Ring window in contact with patient" must meet with EN 10993-1. For this reason this component must be purchased with its biocompatibility certificate. If the designer considers that another of the mentioned components may come into contact with the patient, that component must be purchased as biocompatible.
- The "Multispecral" sub-project includes with the information available at his moment the following components:
    - Ring window in contact with patient
    - Power supply
    - Scientific camera
    - Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670)
    - 1 imaging lens and two polarizers
    - Personal computer with USB supplying electric power

  For all the components mentioned above only the "Ring window in contact with patient" must meet with EN 10993-1. For this reason this component must be purchased with its biocompatibility certificate. If the designer considers that another of the mentioned components may come into contact with the patient, that component must be purchased as biocompatible.
- The "OFI" sub-project, with the information we have currently, has no parts in contact with the patient. If the sub- project finally has parts with patient contact, these parts should be biocompatible.
    - Laser (pending class)
    - Power supply
    - Personal computer with USB supplying electric power

  Any of the components mentioned seems that will have contact with the patient. If the designer considers that another of the mentioned components may come into contact with the patient, that component must be purchased as biocompatible.

# UNE-EN 60601-1:2008 - Medical electrical equipment - Part 1: General requirements for basic safety and essential performance

## SCOPE

This international standard applies to the basic safety and essential performance of medical electrical equipment and medical electrical systems referred to as ME equipment and ME systems.

## OBJECT

The object of this standard is to specify general requirements and serve as a basis for special rules.

## HIGHLIGHTED TERMS AND DEFINITIONS

Access cover:
Part of an enclosure or guard that provides the ability to access parts of electrical equipment in order to adjustment, inspection, replacement or repair.

Accessible part:
Different part of the electrical equipment of an applicable part you can play through a standard test finger.

Accessory:

- Additional part for use with equipment in order to:
- Achieve the intended use;
- Adapted to a special use;
- Ease of use;
- Improve their performance, or
- Enable functions to be integrated with other equipment.

Distance in air:
Shortest path between two conductive parts.

Applicable part:
Part of the ME that in normal use necessarily comes into physical contact with the patient for a ME equipment or ME system to perform its function.

Main insulation:
Insulation that provides basic protection against electric shock

Basic safety:
Free of unacceptable risk directly caused by physical hazards when the ME equipment is used in normal condition and in single fault condition.

AP category:
Class of ME equipment or ME part of an equipment that meets the specified requirements of construction, marking and documentation in order to avoid sources of ignition in a flammable anaesthetic mixture with air.

APG category:
Class of ME equipment or ME part of an equipment that meets the specified requirements of construction, marking and documentation in order to avoid sources of ignition in a flammable anaesthetic mixture with oxygen or nitrous oxide.

Class I:
A term referring to a ME in which protection against electric shock does not lie solely on the main insulation, but includes an extra measure of safety in which means are provided to accessible metal parts or metal internal parts may be protective earthing.

Class II:
A term referring to a ME in which protection against electric shock does not lie solely on the main insulation, but includes an extra measure of safety and additional double insulation or reinforced insulation double, there being no provision for protective earthing or depend on the conditions of the installation.

Leakage line:
The shortest distance along the surface of the insulation distance between two conductive parts.

Double insulation:
Insulation comprising both basic insulation and supplementary insulation.

Duty cycle:
Maximum activation time followed by the minimum off time necessary for the safe operation of the ME.

Earth leakage current:
Current flowing from the network portions through or along the ground conductor insulation protection.

Envelope:
Outer surface of the equipment or parts thereof.

Essential performance:
Necessary operation for freedom of unacceptable risks.

Applicable Part isolated type F (Floating):
Applicable part where patient connections are isolated from other parts of the equipment ME to an extent that does not flow higher than the leakage current patient allowable current if a voltage desired not caused by an external source is connected to the patient, and therefore applied between the patient and earth connection.

Functional connection:
Connection, electrical or otherwise, including those provided to transmit data, signals, energy, or substances.

Functional earth conductor:
Conductor to be connected to a functional ground terminal.

Functional ground terminal:
Terminal, directly connected to a circuit or a shielded part, which is intended to be grounded for functional purposes.

Dangerous situation:
Circumstances in which people, property or the environment are exposed to a hazard.

Insulation coordination:
Interrelationship of insulation characteristics of electrical equipment in view of the expected environment micro-overload and other influences.

Leakage:
Current that is not functional.

Terminal device main supply:
Terminal device by which the electrical connection to the mains supply is done.

Transient voltage:
Highest peak voltage expected at the input power of electrical equipment, arising from external transients on the power supply.

High voltage power:
Voltage used for testing purposes on the supply voltage and connected to certain parts of the ME equipment.

Maximum allowable working pressure:
Maximum allowable pressure on a component according to the company declaration of the component.

Means of operator protection, MOOP:
Means of protection for risk reduction due to electric shock to persons other than the patient.

Means of patient protection, MOPP:
Means of protection for risk reduction due to electric shock for patients.

Means of protection, MOP:
Means for reducing the risk due to electric shock in accordance with the requirements of this standard.

Model or type reference:
Configuring figures, letters or both used to identify a particular model of equipment or accessories

Coupling network / data:
Any means to transmit or receive information to or from other equipment in accordance with company specifications

Nominal (value):

Value indicated by reference that is subject to agreed tolerances

Normal condition:
Condition in which all means provided for protection against hazards are intact.

Normal use:
Operation, including routine inspection and adjustments for any operator and standby, according to the instructions

Patient auxiliary current:
Current flowing in the patient in normal use any connection between the patient and the other patient connections and is not intended for producing or physiological effect.

Connecting patient:
Single point on the applicable part that current can flow between the patient and the ME computer in normal condition or in single fault condition.

Patient leakage current:
Or which is caused by the sudden appearance of a voltage from an external source to the patient and from the patient flowing through the connections of a relevant part of the patient which flows from the patient connections through the patient to earth current type F to ground.

Voltage peak:
Highest peak value or D.C. a voltage work including repetitive peak impulses generated in the electrical equipment, but they do not include external transients.

Conductor equipotential:
Driver other than the protective ground conductor or neutral conductor, which provides a direct connection between the electrical equipment and the equipotential bar wiring

Programmable Electronic System PEMS:
ME equipment or system that contains one or more programmable electronic systems (PESS)

Programmable electronic subsystem, PESS:
Based on one or more central processing units, including its system software and interface

Protective earth conductor:
Conductor to be connected between the ground terminal and protective ground system external protection

Protective earth connection:
Connection to protective earth terminal provided for the purpose of protecting and fulfilling the purpose of this standard

Protective earth terminal:
Connected to the conductive terminal equipment class I parts security purposes. This post is intended to be connected to an external ground system protection through a protective earth conductor.

Grounded protection:

Connected to the protective earth terminal for protection by meeting the requirements of this standard
Reinforced insulation

Safe Working Load:
High external mechanical load (mass) on the computer or a piece of equipment that is allowed in normal use

Secondary circuit:
Circuit which is separate from the network portions by at least one means of protection and power comes from a transformer, converter or equivalent, or an internal power supply isolating device.

Part I / O signal:
ME Part of the equipment that is not as relevant, expected to deliver or receive signals from other electrical equipment, for example, to show record or process data.

Single fault condition:
A condition in which a single means of risk reduction is defective or is present in a single abnormal condition

First fault insurance:
Characteristic of ME equipment or parts through which remains free of unacceptable risk during their expected life cycle under single fault conditions have

Supplementary insulation:
Independent insulation applied in addition to basic insulation in order to provide protection against electrical shock in case of a failure of basic insulation

Terminal device:
Part of the electrical equipment through which electrical connection is made

Thermal stability:
Condition under which the temperature of an object does not increase more than 2 ° C over a period of one hour

Contact current:
Current flowing from the enclosure or parts thereof, excluding patient connections accessible to any operator or patient in normal use, to ground or another part of the enclosure through a different path to the protective earth conductor leakage

Entrapment zone:
Location accessible on or inside the equipment ME computer or computer environment where a human body or a part of the human body is exposed to a risk of entrapment, crushing, shearing, impact, shearing, entanglement, stretching, pinching or abrasion

Type B applied part:
Applicable part that meets the specified requirements of this standard to provide protection against electric shock, particularly regarding allowable leakage current values of patient and patient auxiliary current

Type BF applied part:
Part F applicable rate that meets the requirements of this standard to provide a degree of protection against electric shock, higher than that provided by the applicable parts B type parts

Type CF applied part:
Part F applicable rate that meets the requirements of this standard to provide a degree of protection against electric shock, higher than that provided by the applicable parts BF type parts

Type test:
Essay on a representative sample of the equipment in order to determine whether the equipment as it is designed and manufactured, can meet the requirements of this standard

**GENERAL REQUIREMENTS**

Unless otherwise indicated, the requirements of this standard should be applied in normal use and reasonably foreseeable misuse one.

It should conduct a risk management process that complies with EN 14971.

The company must identify which functions of ME equipment and ME system are essential performance.

The company should establish the expected service life in the ME equipment or ME system in the risk management file.

The risk management process should include an assessment of whether the parties that may come into contact with the patient, but are outside the definition of applicable parts shall be subjected to the requirements of applicable parts.

Equipment must be designed so as to continue first fault insurance or risk should be acceptable.

All components, including wiring, whose failure could result in a hazardous situation should be used in accordance with their specified ranges unless a specific exception is made in this standard through the process of risk management.

You must use a component of high integrity should be used when a component failure can generate an unacceptable risk.

Equipment ME must be suitable for connection to the mains supply must be specified for connection to a separate power supply must be supplied or an internal power supply. Alternatively you can use a combination of these sources.

The average entry into stable ME equipment or ME system at rated voltage and performance settings indicated in the instructions for use must not exceed the range marked by more than 10% state.

## GENERAL REQUIREMENTS FOR TESTING ME

The tests described in this standard are type tests. The tests to be performed are determined taking into account the general requirements.

Type tests are performed on a representative sample of the item being tested.

After the ME equipment to be tested has been adjusted for normal use tests are performed within the range of environment conditions specified in the technical description.

Unless otherwise specified in this standard, the ME equipment shall be tested under the least favourable conditions of work as specified in the instructions that are identified during the risk analysis.

When the test results will be influenced by deviations from the supply voltage of the rated value, the effect of such deviation must be considered.

Unless otherwise stated, the tests are performed in an order that the results of any test not influence the results of the next test.

The applicable parts are identified by inspection and by reference to the accompanying documents.

ME equipment parts to be considered as accessible parts are identified by inspection and if necessary by testing. If in doubt, accessibility is determined by a standardized test with artificial finger.

ME equipment openings are mechanically tested by through the test if the hook can be inserted hook

## CLASSIFICATION OF EQUIPMENT AND SYSTEMS ME

ME equipment fed from a source external power equipment should be classified as Class I or ME Class II equipment. All other equipment must be classified as internally powered ME equipment.

The ME internally powered equipment having means for connection to a mains supply must meet the requirements for ME Class I equipment or ME Class II equipment while connected, and ME requirements for internally powered equipment when not connected.

The applicable parts should be classified as type B applicable parts, parts applicable type BF or Type CF applied parts. The applicable parts can be classified as protected against defibrillator applicable parts.

## CONCLUSIONS

The objective of this standard is to provide rules for the design and construction for electrical medical equipment, in order to provide safety to the patient and the operators.

- For the "In-vivo Confocal Microscopy" and "Exvivo Confocal microscopy" with EC Certificate nr 7602 rev 1, because at the time of writing this document is not defined what new components will incorporate these sub-projects, we can not evaluate at this moment the application of this standard in them.

- The "3D Topography" sub-project includes with the information available at his moment the following components:
    - Ring window in contact with patient
    - Power supply – Must meet with EN 60601-1
    - 2 scientific cameras – Must meet with EN 60601-1
    - 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision – Must meet with EN 60601-1
    - 2 imaging lenses
    - A linear motion guide driven by a step motor– Must meet with EN 60601-1
    - CMOS Color camera – Must meet with EN 60601-1
    - Personal computer with USB supplying electric power – Must meet with EN 60601-1.

  For all the components mentioned above that must meet with EN 60601-1, the designer can ensure compliance with this standard purchasing these components certificate. Specifically for the "Personal computer with USB supplying electric power "with the certificate of Medical Grade. If the "Ring window" has metallic parts, the designer must assure that this metallic parts will never be in contact with any electrical part.

- The "Multispecral" sub-project includes with the information available at his moment the following components:
    - Ring window in contact with patient
    - Power supply – Must meet with EN 60601-1
    - Scientific camera – Must meet with EN 60601-1
    - Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670) – Must meet with EN 60601-1 for its associated electronics
    - 1 imaging lens and two polarizers
    - Personal computer with USB supplying electric power -Must meet with EN 60601-1

  For all the components mentioned above that must meet with EN 60601-1, the designer can ensure compliance with this standard purchasing these components with its certificate. Specifically for the "Personal computer with USB supplying electric power " with the certificate of Medical Grade. If the "Ring window" has metallic parts, the designer must assure that this metallic parts will never be in contact with any electrical part.

- The "OFI" sub-project, sub-project includes with the information available at his moment the following components:
    - Laser (pending class)
    - Power supply -Must meet with EN 60601-1
    - Personal computer with USB supplying electric power -Must meet with EN 60601-1

  For all the components mentioned above that must meet with EN 60601-1, the designer can ensure compliance with this standard purchasing these components with its certificate. Specifically for the "Personal computer with USB supplying electric power" with the certificate of Medical Grade.

# UNE-EN 60601-1-2:2008 Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic compatibility

## OBJECT

This collateral standard specifies general requirements and tests for electromagnetic compatibility of equipment and ME systems

## HIGHLIGHTED TERMS AND DEFINITIONS

Conformance Level:
Level less than or equal to the level of immunity to which the equipment or ME system meets the applicable requirements

Degradation:
Deviation unwanted operating characteristics of the equipment or ME system provided regarding the operation

Effective radiated power:
Required at the input of a reference antenna losses to produce power if, in a given direction at any specified distance, the same flow of radiated power density for a given device

Electromagnetic compatibility, EMC:
Ability of an equipment or system to function satisfactorily ME in its electromagnetic environment without introducing intolerable electromagnetic disturbances to anything that is in that environment in

Disturbance (electromagnetic):
Any electromagnetic phenomenon which may degrade the performance of a device, equipment or system

Emission (electromagnetic):
Phenomenon by which electromagnetic energy emanates from a source

Environment (electromagnetic):
Totality of electromagnetic phenomena existing at a given location

Electromagnetic noise:
Varying in time electromagnetic phenomenon that apparently carries information and can overlap or be combined with a desired signal

Electrostatic discharge ESD:
A transfer of electric charge between bodies with different electrostatic potential in proximity or through direct contact

Exclusion band:
Frequency band for an intended RF electromagnetic energy receiver extending from -5% to +5% of the frequency or frequency band, for receiving the same or higher than 80 MHz frequencies and from -10% to +10 % frequency or frequency band, reception desk for frequencies less than 80 MHz

Immunity (to a disturbance):
Equipment or system ME capacity to perform without degradation in the presence of an electromagnetic disturbance

Immunity Level:
Level of a given electromagnetic disturbance, incident on a particular device, equipment or system for which remains capable of operating at the required maximum operating level

Immunity Test level:
Level of a test signal used to used to simulate an electromagnetic disturbance when the immunity test is performed

ME equipment or life support system:
Equipment or ME system including at least one function that is expected to actively keep alive or revive patients

Low Voltage:
Voltage phase to phase or phase to neutral phenomenon or equal to 1000 V ac or 1500 V dc

Operating Frequency:
Fundamental frequency of a signal, electric or non-electric, which fits into an equipment or ME system intended to control a physiological parameter

ME equipment or system professional:
ME equipment or system or for use by health professionals and is not intended for sale to the general public

Frequency, RF:
Frequency in the range of the electromagnetic spectrum which is between the range of the radio frequency and infrared band; usual for radio frequency

Equipment or ME system coupled to the patient:
Equipment or ME system containing at least one applicable part that comes in contact with the patient, providing a point of reception or treatment necessary to the normal operation of equipment or ME system and provides a path for electromagnetic energy, if ganged conductively, capacitive or inductive, desired or undesired

Professional equipment or ME system type A:
Equipment or ME system that meets CISPR 11 group 2 Class B, except for the third harmonic of the fundamental frequency of the equipment or ME system, in which case the third harmonic comply with the limits of electromagnetic interference from Group 2 Class A

## GENERAL REQUIREMENTS

General requirements for electromagnetic compatibility of equipment and ME systems

- Electromagnetic compatibility
  ME equipment and systems shall not emit electromagnetic interference that could affect radio services, other essential equipment or operation of other equipment and ME systems. The equipment and ME system must have adequate immunity to offer its basic safety and normal operation in the presence of electromagnetic disturbances

- Electrical equipment other than ME
  Electrical equipment that are not ME and equipment to be supplied as part of the system of ME-exempt REQUIREMENTS are testing this rule provided that the following conditions are met:
  a) the equipment complies with the EMC standards
  b) both emissions immunity have been determined so as not to adversely affect the basic safety and essential performance of the system ME
  c) emissions are determined so as not cause the system ME emissions exceed the applicable limits

## CONCLUSIONS

The objective of this standard is to provide rules for the design and construction of electrical medical equipment, in order to provide immunity before electro-magnetic interference produced by other devices and do not degrade other devices, near to our medical device.

- For the "In-vivo Confocal Microscopy" and "Exvivo Confocal microscopy" with EC Certificate nr 7602 rev 1, because at the time of writing this document is not defined what new components will incorporate these sub-projects, we can not evaluate at this moment the application of this standard in them.
- The "3D Topography" sub-project includes with the information available at this moment the following components:
  - Ring window in contact with patient
  - Power supply – Must meet with EN 60601-1-2
  - 2 scientific cameras – Must meet with EN 60601-1-2
  - 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision – Must meet with EN 60601-1-2
  - 2 imaging lenses
  - A linear motion guide driven by a step motor– Must meet with EN 60601-1-2
  - CMOS Color camera – Must meet with EN 60601-1-2
  - Personal computer with USB supplying electric power – Must meet with EN 60601-1-2.

  For all the components mentioned above that must meet with EN 60601-1-2, the designer can ensure compliance with this standard purchasing these components certificate. Specifically for the "Personal computer with USB supplying electric power " with the certificate of Medical Grade.

- The "Multispecral" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply – Must meet with EN 60601-1-2

- Scientific camera – Must meet with EN 60601-1-2
- Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670) – Must meet with EN 60601-1-2 for its associated electronics
- 1 imaging lens and two polarizers
- Personal computer with USB supplying electric power -Must meet with EN 60601-1-2

  For all the components mentioned above that must meet with EN 60601-1-2, the designer can ensure compliance with this standard purchasing these components with its certificate. Specifically for the "Personal computer with USB supplying electric power " with the certificate of Medical Grade.

- The "OFI" sub-project, sub-project includes with the information available at his moment the following components:
  - Laser (pending class)
  - Power supply -Must meet with EN 60601-1-2
  - Personal computer with USB supplying electric power -Must meet with EN 60601-1-2

  For all the components mentioned above that must meet with EN 60601-1-2, the designer can ensure compliance with this standard purchasing these components with its certificate. Specifically for the "Personal computer with USB supplying electric power" with the certificate of Medical Grade.

# UNE-EN 62366:2009 - Medical devices- Application of usability engineering to medical devices

## PURPOSE AND SCOPE

This International Standard specifies a process for analyze, specify, design, and verify validity for usability, regarding a medical device safety. This process assesses and mitigates risks caused by problems associated with usability and correct errors for use. It can be used to identify but not to assess or mitigate risks associated with abnormal use.

## HIGLIGHTED TERMS AND DEFINITIONS

Abnormal use:
Action intentional or unintentional omission of an action by the company or a user medical device as the result of conduct that is beyond any reasonable means of control risk by the company

Effectiveness:
Measurement accuracy and degree of completeness so the users get the specified objectives.

Efficiency:
Effectiveness in relation to resources consumed.

Normal use:
Operation, including routine inspection and adjustments for any user, and rest under the instructions or in accordance with generally accepted practice for those medical devices supplied without instructions.

Main function of operation:
Function that involves user interaction that is frequently used or on the safety of the medical device

Responsible organization:
Entity responsible for the use and maintenance of a combination medical device medical device

Usability:
Feature of the user interface that provides the user efficiency, effectiveness in learning and user satisfaction

Usability Engineering:
Application of knowledge about human behaviour, abilities, limitations, and other characteristics for the design of tools, devices, systems, tasks, and work environments to achieve adequate usability

Usability engineering file:
Set of records and other documents produced by the process of usability engineering

Usage Scenario:
Specified sequence of events and tasks performed by a specified user in a specified environment.

User Interface (UI):
Means by which users interact with the medical device.

User profile:
Summary of mental, physical and demographic characteristics of anticipated user population characteristics as well as any special feature that can have an influence on design decisions, such as professional skills and job requirements.

Validation:
Confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been met.

**CONCLUSIONS**

- For the “In-vivo Confocal Microscopy” and “Exvivo Confocal microscopy” with EC Certificate nr 7602 rev 1, because at the time of writing this document is not defined what new components will incorporate these sub-projects, we can not evaluate at this moment the application of this standard in them.

- The "3D Topography" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - 2 scientific cameras
  - 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision
  - 2 imaging lenses
  - A linear motion guide driven by a step motor
  - CMOS Color camera
  - Personal computer with USB supplying electric power

  This standard is applicable to all the components mentioned above either through instructions, labelling or man-machine interface.

- The "Multispecral" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - Scientific camera
  - Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670)
  - 1 imaging lens and two polarizers
  - Personal computer with USB supplying electric power

  This standard is applicable to all the components mentioned above either through instructions, labelling or man-machine interface.

- The “OFI” sub-project, includes with the information available at his moment the following components:

- Laser (pending class)
- Power supply
- Personal computer with USB supplying electric power

This standard is applicable to all the components mentioned above either through instructions, labelling or man-machine interface.

# UNE-EN 62304:2007 - Medical device software - Software life cycle processes

## PURPOSE AND SCOPE

- Subject
  This standard defines the requirements lifecycle for the medical device software. Assembly processes, activities, and tasks described in this standard establishes a common framework for cycle processes life medical device software.

- Scope
  This standard applies to the development and maintenance of medical device software.
  This standard applies to the development and maintenance of medical device software when the software is itself a medical device or when the software is an integral or essential part of the final medical device.

- Compliance
  Compliance with this standard is defined as the full implementation of the processes, activities, and tasks identified in accordance with this standard class security software.
  Compliance is determined by inspection of all documents required by this standard, including risk management file, and evaluation of processes, activities and tasks required by the class software security.

## HIGHLIGHTED TERMS AND DEFINITIONS

For the purpose of this document, the following terms and definitions apply.

Activity:
Set of one or more interrelated or interacting tasks.

Anomaly:
Any condition that deviates from the expected based on requirements specifications, design documents, standards, etc., or perceptions or experiences of someone. The fault can be found in, but not limited to, reviewing, testing, analysis, compilation, or use of the software product or applicable documentation.

Architecture:
Organizational structure of a system or component

Configuration element:
Entity can be identified uniquely in a landmark since.

Deliverable:
Result or required output (including documentation) of an activity or task.

Evaluation:

A systematic determination of the extent to which an entity meets its specified criteria

Medical device software:
System software that has been developed to be incorporated in the medical device is being developed or planned for use as a medical device in its own right.

Report problem:
A record of the actual or potential behaviour of a software product a user or another person provided deemed to be unsafe, improper or contrary to the intended use of the specification.

Regression testing:
Tests required to determine that a change to a component of a system has not been adversely affected functionally, reliability or performance and which have not been introduced additional defects.

Serious injury:
Injury or disease directly or indirectly:

1. life-threatening;
2. results in a permanent injury of human body function or permanent damage to a structure of human body, or
3. requires medical or surgical intervention to prevent permanent injury of a function of the human body or permanent structure of the human body injury.

Model development life cycle of software:
Conceptual structure that spans the life of the software from the definition of its requirements to its dissemination to the manufacture which

- Identifies the process activities and tasks involved in the development of a software product;
- Describes the sequence and independence between the activities and tasks, and
- Identifies milestones in the completion of specified deliverables are verified.

Item software:
Any identifiable part of a computer program.

Software product:
Set of computer programs, procedures, and possibly associated documentation and data.

System software:
European integrated software items organized to perform a specific function or set of functions.

Unit software:
Item software that is not subdivided into other elements.

SOUP (software of unknown origin):
Element software that has already been developed and generally available and has not been developed for the purpose of being incorporated in the medical device (also known as software ready to use) or software previously developed for which adequate records of the development process are not available

System:

Integrated combination consisting of one or more of the processes, hardware, software, features, and people who provides a fitness function to satisfy a stated need or objective.

Task:
A unique piece of work that needs to be done

Traceability:
Grade for which a relationship can be established between two or more products of the development process.

Verification:
Confirmation provisions on objective evidence that specified requirements are met.

**CONCLUSIONS**

- For the "In-vivo Confocal Microscopy" and "Exvivo Confocal microscopy" with EC Certificate nr 7602 rev 1, because at the time of writing this document is not defined what new components will incorporate these sub-projects, we can not evaluate at this moment the application of this standard in them.

- The "3D Topography" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - 2 scientific cameras
  - 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision
  - 2 imaging lenses
  - A linear motion guide driven by a step motor
  - CMOS Color camera
  - Personal computer with USB supplying electric power

  For all the components mentioned above, must meet with this standard the software running in the "Personal computer with USB supplying electric power". The designer must identify if in any other component there are software, and also apply the standard for this software.

- The "Multispecral" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - Scientific camera
  - Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670)
  - 1 imaging lens and two polarizers
  - Personal computer with USB supplying electric power

  For all the components mentioned above, must meet with this standard the software running in the "Personal computer with USB supplying electric power". The designer

must identify if in any other component there are software, and also apply the standard for this software.

- The "OFI" sub-project, sub-project includes with the information available at his moment the following components:
  - Laser (pending class)
  - Power supply
  - Personal computer with USB supplying electric power

  For all the components mentioned above, must meet with this standard the software running in the "Personal computer with USB supplying electric power". The designer must identify if in any other component there are software, and also apply the standard for this software.

# UNE-EN 60825-1:2008 - Safety of laser products - Part 1: Equipment classification and requirements

## PURPOSE AND SCOPE

The IEC 60825-1 Standard is applicable to safety of laser products emitting laser radiation in the range of wavelength between 180 nm and 1 mm.

A laser product may consist of a single laser with or without separate power supply or may incorporate one or more lasers in a complex optical , electrical or mechanical . Typically, laser products are used to shows physical and optical phenomena , materials processing, and storing data read , transmission and presentation of information, etc. Such systems have found use in industry, business, entertainment, research, education , medicine and consumer products .

Laser products that are sold to other companies to be used as components of any system for subsequent sale are not subject to IEC 60825-1, since the final product will be subjected to this standard. However, if the laser system laser product can work when separated from the team, the unit separable must meet the requirements of this standard.

## HIGHLIGHTED TERMS AND DEFINITIONS

Accessible emission:
Radiation level determined at a position and with a diaphragm (when the LEA is given in units of Watts or Joules) or limiting apertures.

Accessible emission limit LEA:
The maximum accessible emission permitted within a particular class.

Acceptance angle:
Angle of a plane in which a detector will respond to optical radiation, is typically measured in radians.

Opening:
Any opening in the protective cover, or other enclosure of a laser product through which light is emitted, thereby allowing human access to said radiation.

Diaphragm:
Opening which serves to define the area over which the radiation is measured.

Apparent source:
For a smaller retinal assessment given danger, real or virtual object that forms the image position possible on the retina (considering the range of accommodation of the human eye).

Beam:
Laser radiation can be characterized by the direction, divergence, diameter or specifications sweep. Scattered radiation from a non-specular reflection is not considered to be a beam.

Beam attenuator:
A device which reduces the laser beam to the specified level or below it.

Beam diameter, beam width:
Beam diameter at a point in space is the diameter of the smallest circle containing the power (or energy) laser total. For the purpose of this standard is used d63.

Beam divergence:
Plane angle in the far field of the cone defined by the beam diameter.

Beam expander:
Combination of optical elements that will increase the diameter of a laser beam.

Component of the beam path:
Optical component is in a defined path of the beam (for example, a beam steering mirror or a lens focus).

Shutter.
Device that interrupts beam propagation path.

Class 1 laser product:
Any laser product during operation does not permit human access to laser radiation accessible than exceed the accessible emission limits of Class 1 in wavelengths and durations applicable emission.

Class 1M laser product:
Any product in the laser wavelength region of from 302.5 nm to 4000 nm that during operation does not permit human access to laser radiation in excess of the accessible emission limits accessible Class 1 in wavelengths and durations applicable emission

Class 2 laser product:
Any product in the laser wavelength region between 400 nm and 700 nm that during operation not allows human access to laser radiation in excess of the accessible emission limits of Class 2 accessible in wavelengths and durations applicable emission

Class 2M laser product:
Any product in the laser wavelength region between 400 nm and 700 nm that during operation not allows human access to laser radiation in excess of accessible emission limits of Class 2M accessible to wavelengths and durations applicable emission.

3R laser product and 3B classes:
Any laser product during operation permits human access to the laser radiation which exceeds accessible limits of Class 1 and Class 2 emission, as the case, but does not allow human access to laser radiation in excess of the accessible emission limits of 3R and 3B classes (respectively) for any wavelength and emission duration

Class 4 laser product:
Any laser product that permits human access to laser radiation in excess of the accessible emission limits of 3B. class.

Collateral radiation:
Any electromagnetic radiation in the range of wavelength between 180 nm and 1 mm, a except for the laser radiation, which is emitted by a laser product as a result of its operation, or it physically necessary.

Collimated beam:
Radiation beam with small divergence or convergence angle.

Continues Wave CW:
A laser operating with a continuous emission with a duration greater than or equal 0.25 s is considered as a CW laser.

Defined beam path:
Projected path of a laser beam inside the laser product.

Emission duration:
The temporal duration of a pulse, a train or a series of pulses, or the continuous operation, during which could result in human access to laser radiation as a result of the operation, maintenance or repair of a laser product. For a single pulse, that is the length between the half-power point of the peak of the rising ramp and the corresponding point on the descending ramp. For a train of pulses (or subsections of a pulse train), it is the duration between the first half-power point of the peak of the first pulse and the last point of power half that of the peak of the last pulse.

Self-protection system:
Design designed so that failure of one component does not increase the risk.
If a fault occurs, the system stops functioning or is not dangerous.

Lockdown self:
A blockage in case of system failure leaves inoperative security protection, such as a lock acts by disconnecting the system provided as soon as a hinge cover begins to open, or try remove a removable cover, which keeps tripping until the hinge cover is closed or cover removable secured in the closed position.

Human access:
a) Possibility of a human body part in contact with the radiation emitted by a laser product laser, ie, radiation which can be intercepted outside of the protective cover, or b) possibility of a cylindrical tube with a diameter of 100 mm and length up to 100 mm intercept radiation levels and lower class 3B, or
c) possibility of a hand or arm of a person to intercept radiation levels above the LEA class 3B, or
d) Also, to levels of radiation within the protective cover that are equivalent to 3B or 4 classes, possibility that any part of the body comes into contact with hazardous laser radiation can be directly reflected from the interior of the product through any opening in the protective cover,
any plain surfaces is introduced into the product.

Integrated radiance:
Integral of the radiance over a period of exposure expressed as radiant energy per unit area of the radiant and per unit solid angle of emission surface.

Irradiance:
Ratio of the radiant flux $d\Phi$ incident on a surface element and area $dA$ of that element.

Laser:
Any device that it could produce or amplify electromagnetic radiation in the range of wavelengths between 180 nm and 1 mm primarily by the process of controlled stimulated emission .

Light Emitting Diode (LED):
Any pn junction semiconductor device that can be done to produce electromagnetic radiation by recombination in the semiconductor in the range of wavelengths between 180 nm and 1 mm.

Opening limit:
Circular surface over which irradiance and radiant exposure is averaged.

Maximum emission:
The maximum radiant power and, when applicable, the maximum radiant energy per pulse, of the total laser radiation accessible emitted in all directions by a laser product throughout the range of operability in any time after manufacture.

Maximum permissible exposure. EMP:
The level of laser radiation to which people may be exposed, in normal circumstances, without suffering adverse effects.

Blocking modes:
A mechanism or regular occurrence, inside the laser resonator, which produces a train of very short pulses (by example sub-nanosecond).
While there may be a deliberate feature, it can occur spontaneously as a "self-locking modes ". The resulting peak powers can be significantly larger than the average power.

More restrictive position:
Position in the beam in which the ratio of accessible emission is maximum and the LEA.

Nominal ocular hazard zone (ZNRO):
The area in which the irradiance or radiant exposure beam exceeds the allowable maximum exposure level (EMP) appropriate to the cornea, including the possibility of a change of direction of the laser beam by accident.

Nominal ocular hazard distance (DNRO):
The distance from the exit aperture at which the irradiance or radiant exposure equals beam exposure maximum allowable (EMP) appropriate for the cornea.

Photochemical limit risk:
An EMP level or LEA obtained for protecting people against adverse photochemical effects.
In the range of ultraviolet wavelengths, the risk limit photochemical protect against adverse effects on The cornea and lens, while the limit of retinal photochemical hazard, as defined in the range of wavelengths between 400 nm and 600 nm, protects against photochemical retinal damage caused by radiation exposure.

Protective enclosure:
A physical means to prevent human exposure to laser radiation, unless such disclosure is necessary for functions for which it was conceived installation.

Protective cover:
Those parts of a laser product (including a product with laser incorporated) that are designed to prevent human access to laser radiation in excess of the prescribed value LEA (the protective cover installed usually a company).

Pulse duration:
The time interval measured between half-power points than the peak in the ascending and descending ramps a boost.

Laser pulse:
A laser that emits energy in the form of a single pulse or pulse train.
In this standard, the pulse duration is less than 0.25 s.

Reflectance:
The ratio of the reflected radiant power and radiant power incident on the given conditions.

Security Lock:
An automatic device associated with each part of the protective cover of a laser product to prevent human access to laser radiation of Class 3R, Class 3B or Class 4 when removed, opens or moves that part of the deck.

Scanning Laser Radiation:
Laser radiation having an address, a source or propagation pattern that varies over time with respect to a stationary reference system.

Single fault condition:
Any single failure that may occur in a product and the direct consequences of that failure.

Specular reflection:
Reflection on one surface which can be considered as a beam, including reflections from surfaces mirror.

Thermal limit risk:
Both EMP and LEA level to be obtained to protect individuals against adverse thermal effects, opposed to photochemical damage.

Transmittance:
Ratio of the radiant flux transmitted and incident flux in the given conditions.

Density (optical) transmittance:
Decimal logarithm of the inverse of transmittance τ.

## CONCLUSIONS

For the "In-vivo Confocal Microscopy" and "Exvivo Confocal microscopy" with EC Certificate nr 7602 rev 1, because at the time of writing this document is not defined what new components will incorporate these sub-projects, we can not evaluate at this moment the application of this standard in them.

- The "3D Topography" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - 2 scientific cameras
  - 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision -Applicable
  - 2 imaging lenses
  - A linear motion guide driven by a step motor
  - CMOS Color camera
  - Personal computer with USB supplying electric power

  In " light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision" component is applicable EN 60285-1 because include a class 2 Laser for alignement.

- The "Multispecral" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - Scientific camera
  - Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670)
  - 1 imaging lens and two polarizers
  - Personal computer with USB supplying electric power

  In any component of this sub-project is applicable EN 60285-1.

- The "OFI" sub-project, sub-project includes with the information available at his moment the following components:
  - Laser (pending class) – Applicable see Note 1
  - Power supply
  - Personal computer with USB supplying electric power

  Note 1: If Laser finally will be class 1 EN 60285-1 will be applicable, but if the Laser class will be 3B or 4 EN 60601-2-22 will be applicable.

# UNE-EN 62471:2009 – Photo-biological safety of lamps and lamp systems

## PURPOSE AND SCOPE

This International Standard provides guidance for evaluating the photo-biological safety of lamps and appliances luminary including lamps. Specifically, exposure limits specified, the measurement technique reference and classification scheme for the evaluation and control of photo-biological hazards from all sources broadband incoherent optical radiation, electrically powered. LED's including but excluding Lasers in the wavelength range from 200 nm to 3000 nm.

## HIGHLIHTED DEFINITIONS, SYMBOLS AND ABBREVIATIONS

Actinic dose:
Quantity spectrally weighting the doses obtained with the value of the actinic action spectrum wavelength corresponding.

Aperture diaphragm:
Aperture defining the area over which the average optical emission is measured. In the measurements of the spectral irradiance entrance aperture is usually a small area located opposite the entrance slit of the radiometer / spectro-radiometer.

Blue light hazard (BLH, Blue Light Hazard):
Photo-chemically induced retinal potential damage resulting from exposure to radiation of wavelengths between 400 nm and essentially 500 nm. This damage mechanism dominates over thermal damage mechanisms for times exceeding 10 s.

Lamp continuous wave (CW, Continuous Wave):
Lamp operating with a continuous output for a time greater than 0.25 s, ie, a lamp which emits impulses.

Erythema:
Skin redness, as used in this rule, the redness of the skin resulting from the effects inflammatory solar radiation or artificial optical radiation.

Exposure Limit (EL):
Level of exposure of the eye or the skin is not expected to produce adverse biological effects.

General-lighting service lamps (GLS):
Term lamp designed to illuminate spaces that are occupied or are typically viewed by people.
Examples include lamps to illuminate offices, schools, homes, factories, roads or cars. Not includes lamps for applications such as film projection, reprographic processes, "tanning" process industrial, medical, and spotlights.

Luminance (at a point of a surface) (Ev):

Quotient of the luminous flux dΦv incident on an element of the surface containing the point and area dA of that element.

Irradiance (at a point of a surface):
Ratio of the radiant flux dΦ incident on an element of a surface containing the point and area dA of that element.

Lamp:
Font made to produce, usually visible optical radiation.

Largest source:
Size of the source image on the retina is so great that the radial heat flow in the radial direction from the image center to the surrounding biological tissue is negligibly small compared with the flow heat in the axial direction.

Light-emitting diode (LED):
Solid state device embodying a pn junction emitting optical radiation without gain when excited with an electric current.

Lumen:
SI unit of luminous flux luminous flux emitted into a unit solid angle (steroadian) by a point source having a uniform luminous intensity of one candela, or equivalently, the luminous flux of a beam of monochromatic radiation whose frequency is 540.1012 Hz and whose radiant flux is 1/683 watts.

Luminary:
Apparatus which distributes, filters or transforms light emitted from one or more lamps and which includes, but the lamps themselves, all necessary to secure and protect the lamps and, when necessary parts, circuits auxiliaries together with the means to connect to the power supply.

Lux:
SI unit of luminance. luminance produced on a surface of one square meter area by a luminous flux of one lumen uniformly distributed over the surface.

Ocular hazard distance:
Distance from a source that the radiance or irradiance for a given exposure duration exceeds the limit applicable exposure.

Optical Radiation:
Electromagnetic radiation of wavelengths between the transition region to the X-rays (wavelength 1 nm approximately) and the transition region to the radio waves (wavelength about 106 nm).

Pulse lamp:
Lamp energy supplied by a single pulse or a pulse train in which it is assumed that each pulse has a duration less than 0.25 s. A lamp of a continuous or burst of radiant energy modulated in which peak power is radiated at least ten times the average radiated power.

Radiant energy:
The integral of the radiant power, Φ in a given time period, Δ t .

Radiant exposure (at a point of a surface, for a given time period):
The ratio of the radiant energy, dQ, incident on an element of the surface containing the point, for a given period of time, and the area dA of that element.

Radiant power (Φ):
Power emitted, transferred or received as radiation. The radiant power flow is often called radiant.

Spectral distribution:
The magnitude ratio between radiant light or photonic dX (λ) contained in a basic environment wavelength dλ at the wavelength λ, and this basic environment.

Spectral irradiance:
Ratio of the radiant power dΦ (λ) in a range of wave length dλ incident on an element of surface, and the area element dA and interval dλ wave length.

Spectral radiance (for an interval of dλ wave length in a given direction at a given point) (Lλ):
Ratio of the radiant power dΦ (λ) that passes through that point and propagates in the solid angle dΩ in given direction, and the product of the interval of dλ wave length, the solid angle dΩ and the area of a section of the beam in a plane perpendicular to this direction (cos θ dA) containing the given point.

Steradian:
Unit solid angle of the SI system. Solid angle which, having its vertex at the center of a sphere, cut area of the surface of the sphere equal to that of a square with sides of length equal to the radius of the sphere.

**CONCLUSIONS**

For the "In-vivo Confocal Microscopy" and "Exvivo Confocal microscopy" with EC Certificate nr 7602 rev 1, because at the time of writing this document is not defined what new components will incorporate these sub-projects, we can not evaluate at this moment the application of this standard in them.

- The "3D Topography" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - 2 scientific cameras
  - 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision – Applicable 62471,see Note 1
  - 2 imaging lenses
  - A linear motion guide driven by a step motor
  - CMOS Color camera
  - Personal computer with USB supplying electric power

  Note 1. Applicable but classification pending .

- The "Multispecral" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient

- Power supply
- Scientific camera
- Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670) - Applicable 62471,see Note 2
- 1 imaging lens and two polarizers
- Personal computer with USB supplying electric power

Note 2. Applicable but classification pending .

- The “OFI” sub-project, sub-project includes with the information available at his moment the following components:
  - Laser (pending class) – Applicable see Note 1
  - Power supply
  - Personal computer with USB supplying electric power

  In any component of this sub-project is applicable EN 62471.

# UNE-EN ISO 14155:2012 - Clinical investigation of medical devices for human subjects - Good clinical practice

## PURPOSE AND SCOPE

This international standard provides good clinical practice for designing, conducting, recording and reporting clinical investigations involving human subjects to assess the safety or performance of medical devices regulatory purposes.
The principles set out in this International Standard are also applicable to all other clinical investigations and should be followed as far as possible, considering the nature of clinical research and the requirements of national regulations.
This International Standard specifies general requirements for:

- Protect the rights, safety and welfare of human subjects;
- Ensure the scientific conduct of the clinical investigation and the credibility of the results thereof;
- Define the responsibilities of the sponsor and principal investigator, and
- Assist developers, researchers, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of medical devices .

## HIGHLIGHTED TERMS AND DEFINITIONS

ADE, adverse device effect:
Adverse event related to the use of a medical device research.

AE, adverse event:
Any medical episode unwanted, unforeseen illness or injury, or unwanted (including abnormal laboratory findings) in patients, users or other persons, whether or not related to the investigational product clinical signs.

Blinded / masked:
A procedure in which one or more parts of clinical research not knowledgeable of the (s) remain allocation (s) of treatment.

CRF, case report forms:
All printed, optical or electronic documents for each subject in which the information to notify the sponsor, as required by the CIP register.

Clinical Research:
Systematic research in one or more human subjects, undertaken to assess the safety or performance of a medical device.

CIP, clinical investigation plan:
A document that states the rationale, objectives, design and proposed analysis, methodology, monitoring, execution and registration of clinical research data.

Report of clinical research:
Document describing the design, execution, statistical analysis and results of a clinical investigation.

Control:
Medical device therapy (i.e., active control), placebo or no treatment, used in the reference group in clinical research.

CRO, contract research organization:
Person or organization contracted by the sponsor to perform one or more of the functions and duties of the developer in relation to clinical research.

Research Coordinator:
Researcher who is appointed by the developer to coordinate work in a multi-center clinical research.

DMC, data monitoring committee:
Independent Committee that the developer can set to determine, given intervals, the progress of clinical research, data security or criteria critical appraisal of benefits and to recommend to the sponsor whether to continue, suspend, modify, or stop clinical research.

Objectives or criteria(s) of assessment:
(Primary(s)): indicator(s) Principal used to evaluate the primary hypothesis of a clinical investigation.
(Secondary(s)) indicator used to evaluate the secondary hypothesis of clinical research.

EC, ethics committee:
Independent body whose responsibility is to review the clinical research to protect the rights, safety and welfare of subjects participating in clinical research.

The process of informed consent:
The process by which information is provided to an individual and is asked to voluntarily participate in a clinic research.

IB, investigator's brochure:
Reports of clinical and non-clinical update on the product(s) health(s) in research relevant to clinical research.

Legally authorized representative:
Natural or legal person or other officer authorized by that consent laws apply on behalf of a prospective subject to the subject's participation in clinical research organization.

Monitoring:
Action to monitor the progress of a clinical research and to ensure it is performed, recorded and reported in accordance with the CIP, written procedures, with the international standards and applicable regulatory requirements.

Multi-center Research:
Clinical research running with a single CIP and is done in two or more research centers.

Objective:
Main purpose for clinical research.

Timing of inclusion:
At which point, after enrolment, an individual sign and date the informed consent form.

Main Investigator:
Qualified Person responsible for conducting clinical research in a research center.

Randomization:
Process of assigning subjects to groups of medical device research or control using a recognized statistical methodology to determine the allocation established in order to reduce bias.

Recruitment:
Active efforts to identify subjects that may be suitable for inclusion in clinical research.

SADE, serious adverse device effect:
Adverse effect of the product that has produced any property following a serious adverse event.

SAE , serious adverse event:
Adverse event

a) resulted in death;
b ) led to a serious deterioration in the health of the subject;
c) resulted in fetal distress, fetal death or a congenital anomaly or birth defect.

Data source:
All information in original records, certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the clinical research.

Source document:
Printed, optical or electronic document containing source data.

Promoter:
Individual or organization that takes responsibility and obligation to the initiation or implementation of research clinic.

Subject:
Individual who participates in a clinical investigation.

USADE, un-anticipated serious adverse device effect:
Serious adverse product which by their nature, incidence, severity or outcome has not been identified in the updated risk analysis report.

Error of use:
Act or omission of an act that results in a response to a different medical device intended by the company or expected by the user.

Vulnerable-Subject:
Individual whose agreement to participate in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation or retaliation by senior members of a hierarchy in case of his resignation to participate.

**CONCLUSIONS**

The purpose of this standard to provide a common framework to verify with patients in a hospital, that a medical device works as intended and does not cause spindle side effects.
The standard mentions various terms and definitions useful for understanding this standard.
The standard discusses the role of the various parties involved and the procedures to be followed to achieve the desired goal.

## UNE-EN 980:2008 - Symbols for use in the labelling of medical devices

This is the European standard for symbols used by medical device company. It provides guidance on meeting European Directive labelling requirements. All medical device companies must use symbols to avoid mistranslation of essential information into multiple languages. This standard aims to simplify labelling and ensure the consistent use of symbols across all medical devices. It also ensures that medical device companies communicate clearly with customers and meet their product expectations.

**CONCLUSIONS**

- For the "In-vivo Confocal Microscopy" and "Exvivo Confocal microscopy" with EC Certificate nr 7602 rev 1, because at the time of writing this document is not defined what new components will incorporate these sub-projects, we can not evaluate at this moment the application of this standard in them.

- The "3D Topography" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - 2 scientific cameras
  - 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision
  - 2 imaging lenses
  - A linear motion guide driven by a step motor
  - CMOS Color camera
  - Personal computer with USB supplying electric power

  Applicable for all the above components. In labelling and instructions for use.

- The "Multispecral" sub-project includes with the information available at his moment the following components:
  - Ring window in contact with patient
  - Power supply
  - Scientific camera
  - Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670)
  - 1 imaging lens and two polarizers
  - Personal computer with USB supplying electric power

  Applicable for all the above components. In labelling and instructions for use.

- The "OFI" sub-project, sub-project includes with the information available at his moment the following components:
  - Laser (pending class)
  - Power supply
  - Personal computer with USB supplying electric power

  Applicable for all the above components. In labelling and instructions for use.

# OTHER STANDARDS PENDING TO REVIEW

The standards mentioned so far are to be applied to "Diagnoptics" project.

There are other standards that could be implemented in case some components are used so they are taken into account as following:

### EN 12052:2011 - Health informatics. Digital imaging and communication in medicine (DICOM) including workflow and data management

Within the field of health informatics this standard addresses the exchange of digital images, and information related to the production and management of those images, between both medical imaging equipment and systems concerned with the management and communication of that information. This standard is intended to facilitate interoperability of medical imaging equipment and information systems by specifying a set of protocols to be followed by systems claiming conformance to this International Standard.

### EN 28077:2006 – Photo-carcinogenesis action spectrum (non-melanoma skin cancers)

Solar ultraviolet radiation is recognized as a major cause of non-melanoma skin cancer in man. Skin cancer occurs most frequently in the most heavily exposed areas and correlates with degree of outdoor exposure. Describing the relationship of exposure (dose) to risk (skin cancer) requires the availability of a biological hazard function or action spectrum for photo-carcinogenesis. This standard proposes the adoption of an action spectrum (weighting function) derived from experimental laboratory data and modified to estimate the non-melanoma tumor response in human skin. The experimental data are sufficient for estimating effectiveness down to about 250 nm, but experimental data are not sufficient for specifying effectiveness above 400 nm.

### EN 17166:1999 - Erythema reference action spectrum and standard erythema dose

The CIE undertook a major review of its official recommendations on photobiological effects, their dose relationships and measurement. Based on these investigations the present standard describes present day knowledge of the erythemal effect.
The problem of dosimetry in skin photobiology lies in the fact that the ability of ultraviolet (UV) radiation to elicit erythema in human skin depends strongly on wavelength, encompassing a range of four orders of magnitude between 250 nm and 400 nm. Thus a statement that a subject received an exposure dose of 1 J. cm -2 (10 4J. m -2) of UV radiation conveys nothing about the consequences of that exposure in terms of erythema. If the radiation source was a UVA fluorescent lamp, no erythemal response would be seen apart from in people exhibiting severe, abnormal pathological photosensitivity. The same dose delivered from an unfiltered mercury arc lamp or fluorescent sun-lamp would result in marked violaceous erythema in most white skinned individuals. Consequently, photobiologists have long recognised the need to express the exposure as an erythemally-weighted quantity.
Recently the term minimal erythema dose (MED) has been used widely as a 'measure' of erythemal radiation. This is unreasonable because the MED is not a standard measure of anything but, on the

contrary, encompasses the variable nature of individual sensitivity to ultraviolet radiation. Variables which affect the MED include optical and radiometric characteristics of the source; determinants of the exposure such as dose increment and field size; nature of the skin such as pigmentation, previous light exposure, and anatomical site; and observational factors such as definition of the end point, time of reading after exposure, and ambient illumination.
To avoid further confusing misuse of the term MED, we propose that this term be reserved solely for observational studies in humans and other animals, and that a new term, the standard erythema dose (SED) be used as a standardized measure of erythemogenic UV radiation.
This Standard specifies the erythema reference action spectrum s er (lambda), and the Standard Erythema Dose.

### EN 62563-1:2010 - Medical image display systems. Evaluation methods

The standard describes the evaluation methods for testing medical image display systems. It is directed to practical tests that can be visually evaluated or measured using basic test equipment. More advanced or more quantitative measurements can be performed on these devices, but these are beyond the scope of this document. It applies to medical image display systems, which can display monochrome image information in the form of greyscale values on colour and greyscale image display systems (e.g. cathode ray tube (CRT) monitors, flat panel displays, projection system). This standard applies to medical image display systems used for diagnostic (interpretation of medical images toward rendering clinical diagnosis) or viewing (viewing medical images for medical purposes other than for providing a medical interpretation) purposes and therefore having specific requirements in terms of image quality. Head mounted image display systems and image display systems used for confirming positioning and for operation of the system are not covered by this standard.

### BS 8440-1:2005 - Health informatics. Medical digital imaging. Profiles format General principles

This standard defines the concept of a medical digital imaging profile and the way in which a medical digital imaging (MDI) profile can be documented in an MDI profile standard. It provides principles and outlines a taxonomy for MDI profiles submitted for ratification as MDI profile standard. It merely provides a capability to identify uniquely such a profile and to enable evaluation of MDI profile standards.

### EN 60601-2-22:2013 - Medical electrical equipment - Part 2-22: Particular requirements for basic safety and essential performance of surgical, cosmetic, therapeutic and diagnostic laser equipment

Applies to the safety and essential performance of laser equipment for either surgical, therapeutic, medical diagnostic, cosmetic, or veterinary applications, intended for its use on humans or animals, classified as a class 3B or class 4 laser product as defined in IEC 60825-1, hereafter referred to as laser equipment. This standard can also be applied to surgical, cosmetic, therapeutic and diagnostic laser equipment used for compensation or alleviation of disease, injury or disability.

| Technology | Design responsible | Status of system & its components | CE Mark MDD 93/42 | ISO 13485 | EN 14971 | EN 60601-1 | EN 60601-1-2 | EN 62366 | EN 62304 | EN 60285-1 |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Medical Device Directive | Quality medical devices | Risk analysis | Electrical safety | EMC compliance | Usability | Software | Laser till 3R |
| InVivo Confocal Microscopy | MAVIG | Commercial product | Certificate nr 7602 rev 1 | | | | | | | |
| Contact Person: Giuseppe Solomita | | Vivascope 3000 | | | | | | | | |
| | | R&D under Diagnoptics: software development | | PD | PD | PD | PD | PD | PD | PD |
| Multispectral | CD6 | Prototype | not available | | | | | | | |
| Contact Person: Meritxell Vilaseca | | Ring window in contact with patient | | Y | Y | N | N | Y | Y | N |
| | | Power supply | | Y | Y | Y | Y | Y | N | N |
| | | Scientific camera | | Y | Y | Y | Y | Y | Y | N |
| | | Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670) | | Y | Y | Y | Y | Y | Y | N |
| | | 1 imaging lens and two polarizers | | Y | Y | N | N | Y | N | N |
| | | Personal computer with USB supplying electric power | | Y | Y | Y | Y | Y | Y | N |
| 3D Topography | CD6 | Prototype | not available | | | | | | | |
| Contact Person: Miguel Ares | | Ring window in contact with patient | | Y | Y | N | N | Y | Y | N |
| | | Power supply | | Y | Y | Y | Y | Y | N | N |
| | | 2 scientific cameras | | Y | Y | Y | Y | Y | Y | N |
| | | 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision | | Y | Y | Y | Y | Y | Y | Y |
| | | 2 imaging lenses | | Y | Y | N | N | Y | N | N |
| | | A linear motion guide driven by a step motor | | Y | Y | Y | Y | Y | Y | N |
| | | CMOS Color camera | | Y | Y | Y | Y | Y | Y | N |
| | | Personal computer with USB supplying electric power | | Y | Y | Y | Y | Y | Y | N |
| OFI blood flow | LPNT | Prototype | not available | | | | | | | |
| Contact Person: Thierry Tomas | | Laser (pending class) | | Y | Y | Y | Y | Y | N | N |
| | | Power supply | | Y | Y | Y | Y | Y | N | N |
| | | Personal computer with USB supplying electric power | | Y | Y | Y | Y | Y | Y | N |
| ExVivo Confocal Microscopy | MAVIG | Commercial product | Certificate nr 7602 rev 1 | | | | | | | |
| Contact Person: Giuseppe Solomita | | Vivascope 2500 | | | | | | | | |
| | | R&D under Diagnoptics: software development | | PD | PD | PD | PD | PD | PD | PD |

| Requires implementation ? | |
|---|---|
| Yes | Y |
| Pending of specs | PD |
| No | N |

| Technology | Design responsible | Status of system & its components | EN 62471 | EN 14155 | EN 10993-1 | EN 980 | EN 12052 | ISO 28077 | ISO 17166 | EN 62563-1 | BS 8440-1 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Lamps | Clinical tests | Biocompatibility | Symbols labelling | DICOM | Photo-Carcinogen. | Erythema | Imaging devices. | Medical Imaging protocol. |
| **InVivo Confocal Microscopy** | **MAVIG** | **Commercial product** | | | | | | | | | |
| Contact Person: Giuseppe Solomita | | Vivascope 3000 | | | | | | | | | |
| | | R&D under Diagnoptics: software development | PD | PD | PD | PD | PD | PD | PD | PD | PD |
| **Multispectral** | **CD6** | **Prototype** | | | | | | | | | |
| Contact Person: Meritxell Vilaseca | | Ring window in contact with patient | N | Y | Y | Y | N | N | N | N | N |
| | | Power supply | N | Y | N | Y | N | N | N | N | N |
| | | Scientific camera | N | Y | N | Y | PD | N | N | PD | PD |
| | | Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670) | Y | Y | N | Y | N | Y | Y | N | PD |
| | | 1 imaging lens and two polarizers | N | Y | N | Y | N | N | N | N | N |
| | | Personal computer with USB supplying electric power | N | Y | N | Y | PD | PD | PD | PD | PD |
| **3D Topography** | **CD6** | **Prototype** | | | | | | | | | |
| Contact Person: Miguel Ares | | Ring window in contact with patient | N | Y | Y | Y | N | N | N | N | N |
| | | Power supply | N | Y | N | Y | N | N | N | N | N |
| | | 2 scientific cameras | N | Y | N | Y | PD | N | N | PD | PD |
| | | 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision | Y | Y | N | Y | PD | Y | Y | N | N |
| | | 2 imaging lenses | N | Y | N | Y | N | N | N | N | N |
| | | A linear motion guide driven by a step motor | N | Y | N | Y | N | N | N | N | N |
| | | CMOS Color camera | N | Y | N | Y | PD | N | N | PD | PD |
| | | Personal computer with USB supplying electric power | N | Y | N | Y | PD | PD | PD | PD | PD |
| **OFI blood flow** | **LPNT** | **Prototype** | | | | | | | | | |
| Contact Person: Thierry Tomas | | Laser (pending class) | N | Y | Y | Y | N | N | N | N | N |
| | | Power supply | N | Y | Y | Y | N | N | N | N | N |
| | | Personal computer with USB supplying electric power | N | Y | Y | Y | PD | PD | PD | PD | PD |
| **ExVivo Confocal Microscopy** | **MAVIG** | **Commercial product** | | | | | | | | | |
| Contact Person: Giuseppe Solomita | | Vivascope 2500 | | | | | | | | | |
| | | R&D under Diagnoptics: software development | PD | PD | PD | PD | PD | PD | PD | PD | PD |

| Requires implementation ? | |
|---|---|
| Yes | Y |
| Pending of specs | PD |
| No | N |

| Technology | Design responsible | Status of system & its components | EN 60601-2-22 |
|---|---|---|---|
| | | | Laser 3B and 4 |
| **InVivo Confocal Microscopy** | **MAVIG** | **Commercial product** | |
| Contact Person: Giuseppe Solomita | | Vivascope 3000 | |
| | | R&D under Diagnoptics: software development | PD |
| **Multispectral** | **CD6** | **Prototype** | |
| Contact Person: Meritxell Vilaseca | | Ring window in contact with patient | N |
| | | Power supply | N |
| | | Scientific camera | N |
| | | Ring of LED's (RLCU-440-410, RLCU-440-720, RLCU-440-880, RLCU-440-1020, Luxeon 440-460, 490-520, 520-550, 584.5-597, 610-620, 650-670) | N |
| | | 1 imaging lens and two polarizers | N |
| | | Personal computer with USB supplying electric power | N |
| **3D Topography** | **CD6** | **Prototype** | |
| Contact Person: Miguel Ares | | Ring window in contact with patient | N |
| | | Power supply | N |
| | | 2 scientific cameras | N |
| | | 1 light projector with a laser for alignement PicoP® Display Engine Evaluation Kit Microvision | N |
| | | 2 imaging lenses | N |
| | | A linear motion guide driven by a step motor | N |
| | | CMOS Color camera | N |
| | | Personal computer with USB supplying electric power | N |
| **OFI blood flow** | **LPNT** | **Prototype** | |
| Contact Person: Thierry Tomas | | Laser (pending class) | PD |
| | | Power supply | N |
| | | Personal computer with USB supplying electric power | N |
| **ExVivo Confocal Microscopy** | **MAVIG** | **Commercial product** | |
| Contact Person: Giuseppe Solomita | | Vivascope 2500 | |
| | | R&D under Diagnoptics: software development | PD |

| Requires implementation ? | |
|---|---|
| Yes | Y |
| Pending of specs | PD |
| No | N |

| Project Number |
|---|
| |

**DESIGN CONTROL FORM**

**Project Name:…….**

Project purpose:…….

# 1. INPUTS:

| **Inputs / Design Requeriments** | *** Valication Protocol** *( Document PRT-xxx)* | **Validation satisfactory ?** |
|---|---|---|
| **1.** | | |
| **2.** | | |
| **3.** | | |
| **4.** | | |
| **5.** | | |
| **6.** | | |
| **7.** | | |
| **8.** | | |
| **9.** | | |
| **10.** | | |
| **11.** | | |

| Project Number |
|---|
| |

## 2. Results:

| **Outputs / Final conclusions:** | | Date: |
|---|---|---|
| - Protocols: | | |
| - Manufacturing procedures: | - Drawings: | |
| - BOM: | - Control Plans related: | |
| - Test Procedures | | |
| _____ Signature | _____ Signature | _____ Date |

# DESIGN REVIEW FORM

| Project name:<br>Project number: | Design stage: | Date: |
|---|---|---|

**Attendants**

| Name | Function | Signature |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |

**Inputs Review/Design Output**

References for design entry and exit to check at this stage are:

| | Y | N | N/A | Comment |
|---|---|---|---|---|
| The design input requirements are complete, unambiguous and are not in conflict. | | | | |
| The design output conforms to the entry requirements. | | | | |
| The design output includes acceptance criteria. | | | | |
| The output identifies design features necessary for safety and effective functionality. | | | | |
| The previously assigned action items are followed and properly aimed. | | | | |
| Design projects are sufficient at this stage to proceed. | | | | |
| Design projects require further action before proceeding. | | | | |
| Revision of MDD essential requirements | | | | |

**Action Items (attach additional pages if necessary)**

| Assigned actions | Assigned to | Date |
|---|---|---|
| | | |
| | | |
| | | |
| | | |

Comments:

**PROTOCOL**

**PRT#_____**

**OBJECTIVE:**

**REFERENCE(S) ON WHICH MAKES THE PROTOCOL:**

**METERS USED:**

**TESTS DONE:**

**CONCLUSIONS:**

Signature: Date:

# I. GENERAL REQUIREMENTS, 93/42/MDD

| Paragrph MDD 93/42/EEC | Requirement | Conclusion | Location in the Technical File |
|---|---|---|---|
| Paragraph 1 | The devices must be designed and manufactured in such a way that, when used under the conditions and for the purposes intended, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their intended use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.<br>This shall include:<br>reducing, as far as possible, the risk of use error due to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety), and consideration of the technical knowledge, experience, education and training and where applicable the medical and physical conditions of intended users (design for lay, professional, disabled or other users). | | |
| Paragraph 2 | The solutions adopted by the manufacturer for the design and construction of the devices must conform to safety principles, taking account of the generally acknowledged state of the art.<br>In selecting the most appropriate solutions, the manufacturer must apply the following principles in the following order:<br>— eliminate or reduce risks as far as possible (inherently safe design and construction),<br>— where appropriate take adequate protection measures including alarms if necessary, in relation to | | |

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| | risks that cannot be eliminated,<br>— inform users of the residual risks due to any shortcomings of the protection measures adopted. | | |
| **Paragraph 3** | The devices must achieve the performances intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions referred to in Article 1 (2) (a), as specified by the manufacturer. | | |
| **Paragraph 4** | The characteristics and performances referred to in Sections 1, 2 and 3 must not be adversely affected to such a degree that the clinical conditions and safety of the patients and, where applicable, of other persons are compromised during the lifetime of the device as indicated<br>by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use. | | |
| **Paragraph 5** | The devices must be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected during transport and storage taking account of the instructions and information provided by the manufacturer. | | |
| **Paragraph 6** | Any undesirable side-effect must constitute an acceptable risk when weighed against the performances intended. | | |
| **Paragraph 6.A** | Demonstration of conformity with the essential requirements must include a clinical evaluation in accordance with Annex X. | | |

# II. REQUIREMENTS REGARDING DESIGN AND CONSTRUCTION 93/42/MDD

| Paragraph MDD 93/42/EEC | Requirement | Conclusion | Aplicable Yes-Not | Location in the Technical File |
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| **Paragraph 7.1** | The devices must be designed and manufactured in such a way as to guarantee the characteristics and performances referred to in Section I on the 'General requirements'. Particular attention must be paid to:<br>— the choice of materials used, particularly as regards toxicity and, where appropriate, flammability,<br>— the compatibility between the materials used and biological tissues, cells and body fluids, taking account of the intended purpose of the device,<br>— where appropriate, the results of biophysical or modelling research whose validity has been demonstrated beforehand. | | | |
| **Paragraph 7.2** | The devices must be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to the patients, taking account of the intended purpose of the product.<br>Particular attention must be paid to the tissues exposed and to the duration and frequency of exposure. | | | |
| **Paragraph 7.3** | The devices must be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they must be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their performance is maintained in accordance with the intended use. | | | |

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| **Paragraph 7.4** | Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product as defined in Article 1 of Directive 2001/83/EC and which is liable to act upon the body with action ancillary to that of the device, the quality, safety and usefulness of the substance must be verified by analogy with the methods specified in Annex I to Directive 2001/83/ EC.<br><br>For the substances referred to in the first paragraph, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking account of the intended purpose of the device, seek a scientific opinion from one of the competent authorities designated by the Member States or the European Medicines Agency (EMEA) acting particularly through its committee in accordance with Regulation (EC) No 726/2004 (1) on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the substance into the device.<br><br>When issuing its opinion, the competent authority or the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the substance into the device as determined by the notified body.<br><br>Where a device incorporates, as an integral part, a human blood derivative, the notified body shall, having verified the usefulness of the substance as part of the medical device and taking into account the intended purpose of the device, seek a scientific opinion from the EMEA, acting particularly through its committee, on the quality and safety of the substance including the clinical benefit/risk profile of the incorporation of the human blood derivative into the device. When issuing its opinion, the EMEA shall take into account the manufacturing process and the data related to the usefulness of incorporation of the | | | |

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| | substance into the device as determined by the notified body.<br><br>Where changes are made to an ancillary substance incorporated in a device, in particular related to its manufacturing process, the notified body shall be informed of the changes and shall consult the relevant medicines competent authority (i.e. the one involved in the initial consultation), in order to confirm that the quality and safety of the ancillary substance are maintained. The competent authority shall take into account the data related to the usefulness of incorporation of the substance into the device as determined by the notified body, in order to ensure that the changes have no negative impact on the established benefit/risk profile of the addition of the substance in the medical device.<br><br>When the relevant medicines competent authority (i.e. the one involved in the initial consultation) has obtained information on the ancillary substance, which could have an impact on the established benefit/risk profile of the addition of the substance in the medical device, it shall provide the notified body with advice, whether this information has an impact on the established benefit/risk profile of the addition of the substance in the medical device or not.<br><br>The notified body shall take the updated scientific opinion into account in reconsidering its assessment of the conformity assessment procedure. | | | |

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| **Paragraph 7.5** | The devices must be designed and manufactured in such a way as to reduce to a minimum the risks posed by substances leaking from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction, in accordance with Annex I to Council Directive 67/548/EEC of 27 June 1967 on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.<br>If parts of a device (or a device itself) intended to administer and/or remove medicines, body liquids or other substances to or from the body, or devices intended for transport and storage of such body fluids or substances, contain phthalates which are classified as carcinogenic, mutagenic or toxic to reproduction, of category 1 or 2, in accordance with Annex I to Directive 67/548/EEC, these devices must be labelled on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging as a device containing phthalates.<br><br>If the intended use of such devices includes treatment of children or treatment of pregnant or nursing women, the manufacturer must provide a specific justification for the use of these substances with regard to compliance with the essential requirements, in particular of this paragraph, within the technical documentation and, within the instructions for use, information on residual risks for these patient groups and, if applicable, on appropriate precautionary measures. | | | |
| **Paragraph 7.6** | Devices must be designed and manufactured in such a way as to reduce, as much as possible, risks posed by the unintentional ingress of substances into the device taking into account the device and the nature of the environment in which it is intended to be used. | | | |
| **Paragraph 8.1** | The devices and manufacturing processes must be designed in such a way as to eliminate or reduce as far as possible the risk of infection to the patient, user and | | | |

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| | third parties. The design must allow easy handling and, where necessary, minimize contamination of the device by the patient or vice versa during use. | | | |
| **Paragraph 8.2** | Tissues of animal origin must originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues. Notified bodies shall retain information on the geographical origin of the animals.<br>Processing, preservation, testing and handling of tissues, cells and substances of animal origin must be carried out so as to provide optimal security. In particular safety with regard to viruses and other agents must be addressed by implementation of validated methods of elimination or viral inactivation in the course of the manufacturing process. | | | |
| **Paragraph 8.3** | Devices delivered in a sterile state must be designed, manufactured and packed in a non-reusable pack and/or according to appropriate procedures to ensure that they are sterile when placed on the market and remain sterile, under the storage and transport conditions laid down, until the protective packaging is damaged or opened. | | | |
| **Paragraph 8.4** | Devices delivered in a sterile state must have been manufactured and sterilized by an appropriate, validated method. | | | |
| **Paragraph 8.5** | Devices intended to be sterilized must be manufactured in appropriately controlled (e. g. environmental) conditions. | | | |
| **Paragraph 8.6** | Packaging systems for non-sterile devices must keep the product without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system must be suitable taking account of the method of sterilization indicated by the manufacturer. | | | |

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| **Paragraph 8.7** | The packaging and/or label of the device must distinguish between identical or similar products sold in both sterile and non-sterile condition. | | | |
| **Paragraph 9.1** | If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system must be safe and must not impair the specified performances of the devices. Any restrictions on use must be indicated on the label or in the instructions for use. | | | |
| **Paragraph 9.2** | Devices must be designed and manufactured in such a way as to remove or minimize as far as is possible:<br>— the risk of injury, in connection with their physical features, including the volume/pressure ratio, dimensional and where appropriate ergonomic features, | | | |
| | — risks connected with reasonably foreseeable environmental<br>conditions, such as magnetic fields, external electrical influences, electrostatic discharge, pressure, temperature or variations in pressure and acceleration, | | | |
| | — the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given, | | | |
| | — risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism. | | | |

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| **Paragraph 9.3** | Devices must be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention must be paid to devices whose intended use includes exposure to flammable substances or to substances which could cause combustion. | | | |
| **Paragraph 10.1** | Devices with a measuring function must be designed and manufactured in such a way as to provide sufficient accuracy and stability within appropriate limits of accuracy and taking account of the intended purpose of the device. The limits of accuracy must be indicated by the manufacturer. | | | |
| **Paragraph 10.2** | The measurement, monitoring and display scale must be designed in line with ergonomic principles, taking account of the intended purpose of the device. | | | |
| **Paragraph 10.3** | The measurements made by devices with a measuring function must be expressed in legal units conforming to the provisions of Council Directive 80/181/EEC. | | | |
| **Paragraph 11.1.1** | Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to radiation shall be reduced as far as possible compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes. | | | |
| **Paragraph 11.2.1** | Where devices are designed to emit hazardous levels of radiation necessary for a specific medical purpose the benefit of which is considered to outweigh the risks inherent in the emission, it must be possible for the user to control the emissions. Such devices shall be designed and manufactured to ensure reproducibility and tolerance of relevant variable parameters. | | | |
| **Paragraph 11.2.2** | Where devices are intended to emit potentially hazardous, visible and/ or invisible radiation, they must be fitted, where practicable, with visual displays and/or audible warnings of such emissions. | | | |

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| **Paragraph 11.3.1** | Devices shall be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as possible. | | | |
| **Paragraph 11.4.1** | The operating instructions for devices emitting radiation must give detailed information as to the nature of the emitted radiation, means of protecting the patient and the user and on ways of avoiding misuse and of eliminating the risks inherent in installation. | | | |
| **Paragraph 11.5.1** | Devices intended to emit ionizing radiation must be designed and manufactured in such a way as to ensure that, where practicable, the quantity, geometry and quality of radiation emitted can be varied and controlled taking into account the intended use. | | | |
| **Paragraph 11.5.2** | Devices emitting ionizing radiation intended for diagnostic radiology shall be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose whilst minimizing radiation exposure of the patient and user. | | | |
| **Paragraph 11.5.3** | Devices emitting ionizing radiation, intended for therapeutic radiology shall be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy and where appropriate the quality of radiation. | | | |
| **Paragraph 12.1** | Devices incorporating electronic programmable systems must be designed to ensure the repeatability, reliability and performance of these systems according to the intended use. In the event of a single fault condition (in the system) appropriate means should be adopted to eliminate or reduce as far as possible consequent risks. | | | |
| **Paragraph 12.1 A** | For devices which incorporate software or which are medical software in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification. | | | |

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| **Paragraph 12.2** | Devices where the safety of the patients depends on an internal power supply must be equipped with a means of determining the state of the power supply. | | | |
| **Paragraph 12.3** | Devices where the safety of the patients depends on an external power supply must include an alarm system to signal any power failure. | | | |
| **Paragraph 12.4** | Devices intended to monitor one or more clinical parameters of a patient must be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health. | | | |
| **Paragraph 12.5** | Devices must be designed and manufactured in such a way as to minimize the risks of creating electromagnetic fields which could impair the operation of other devices or equipment in the usual environment. | | | |
| **Paragraph 12.6** | Devices must be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks during normal use and in single fault condition, provided the devices are installed correctly. | | | |
| **Paragraph 12.7.1** | Devices must be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with, for example, resistance, stability and moving parts. | | | |
| **Paragraph 12.7.2** | Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performances. | | | |
| **Paragraph 12.7.3** | Devices must be designed and manufactured in such a way as to reduce to the lowest possible level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance. | | | |

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| **Paragraph 12.7.4** | Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle must be designed and constructed in such a way as to minimize all possible risks. | | | |
| **Paragraph 12.7.5** | Accessible parts of the devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings must not attain potentially dangerous temperatures under normal use. | | | |
| **Paragraph 12.8.1** | Devices for supplying the patient with energy or substances must be designed and constructed in such a way that the flow-rate can be set and maintained accurately enough to guarantee the safety of the patient<br>and of the user. | | | |
| **Paragraph 12.8.2** | Devices must be fitted with the means of preventing and/or indicating any inadequacies in the flow-rate which could pose a danger.<br>Devices must incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy from an energy and/or substance source. | | | |
| **Paragraph 12.9** | Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information must be understandable to the user and, as appropriate, the patient. | | | |
| **Paragraph 13.1** | Each device must be accompanied by the information needed to use it safely and properly, taking account of the training and knowledge of the potential users, and to identify the manufacturer.<br>This information comprises the details on the label and the data in the instructions for use.<br>As far as practicable and appropriate, the information needed to use the device safely must be set out on the device itself and/or on the packaging for each unit or, where appropriate, on the sales packaging. If individual packaging of each unit is not practicable, the information must be set out in the leaflet supplied with one or more devices.<br>Instructions for use must be included in the | | | |

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| | packaging for every device.<br>By way of exception, no such instructions for use are needed for devices in Class I or IIa if they can be used safely without any such instructions. | | | |
| **Paragraph 13.2** | Where appropriate, this information should take the form of symbols.<br>Any symbol or identification colour used must conform to the<br>harmonized standards. In areas for which no standards exist, the symbols and colours must be described in the documentation supplied with the device. | | | |
| **Paragraph 13.3** | The label must bear the following particulars:<br>(a) the name or trade name and address of the manufacturer. For devices imported into the Community, in view of their distribution in the Community, the label, or the outer packaging, or instructions for use, shall contain in addition the name and address of the authorised representative where the manufacturer does not have a registered place of business in the Community;<br>(b) the details strictly necessary to identify the device and the contents of the packaging especially for the users;<br>(c) where appropriate, the word 'STERILE';<br>(d) where appropriate, the batch code, preceded by the word 'LOT', or the serial number;<br>(e) where appropriate, an indication of the date by which the device<br>should be used, in safety, expressed as the year and month;<br>(f) where appropriate, an indication that the device is for single use. A manufacturer's indication of single use must be consistent across the Community;<br>(g) if the device is custom-made, the words 'custom-made device';<br>(h) if the device is intended for clinical investigations, the words 'exclusively for clinical investigations';<br>(i) any special storage and/or handling conditions;<br>(j) any special operating instructions; | | | |

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| | (k) any warnings and/or precautions to take;<br>(l) year of manufacture for active devices other than those covered by<br>(e). This indication may be included in the batch or serial number;<br>(m) where applicable, method of sterilization;<br>(n) in the case of a device within the meaning of Article 1(4a), an indication that the device contains a human blood derivative. | | | |
| **Paragraph 13.4** | If the intended purpose of the device is not obvious to the user, the manufacturer must clearly state it on the label and in the instructions for use. | | | |
| **Paragraph 13.5** | Wherever reasonable and practicable, the devices and detachable components must be identified, where appropriate in terms of batches, to allow all appropriate action to detect any potential risk posed by the devices and detachable components. | | | |
| **Paragraph 13.6** | Where appropriate, the instructions for use must contain the following particulars:<br>(a) the details referred to in Section 13.3, with the exception of (d) and (e); | | | |
| | (b) the performances referred to in Section 3 and any undesirable side effects; | | | |
| | c) if the device must be installed with or connected to other medical devices or equipment in order to operate as required for its intended purpose, sufficient details of its characteristics to identify the correct devices or equipment to use in order to obtain a safe combination; | | | |
| | d) all the information needed to verify whether the device is properly installed and can operate correctly and safely, plus details of the nature and frequency of the maintenance and calibration needed to ensure that the devices operate properly and safely at all times; | | | |

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| | e) where appropriate, information to avoid certain risks in connection with implantation of the device; | | | |
| | f) information regarding the risks of reciprocal interference posed by the presence of the device during specific investigations or treatment; | | | |
| | g) the necessary instructions in the event of damage to the sterile packaging and, where appropriate, details of appropriate methods of re-sterilization; | | | |
| | h) if the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging and, where appropriate, the method of sterilization of the device to be re-sterilized, and any restriction on the number of reuses.<br>Where devices are supplied with the intention that they be sterilized<br>before use, the instructions for cleaning and sterilization must be such that, if correctly followed, the device will still comply with the requirements in Section I.<br>If the device bears an indication that the device is for single use, information on known characteristics and technical factors known to the manufacturer that could pose a risk if the device were to be re-used. If in accordance with Section 13.1 no instructions for use are needed, the information must be made available to the user upon request; | | | |
| | i) details of any further treatment or handling needed before the device can be used (for example, sterilization, final assembly, etc.); | | | |
| | j) in the case of devices emitting radiation for medical purposes, details of the nature, type, intensity and distribution of this radiation.<br>The instructions for use must also include details allowing the medical staff to brief the patient on any contra-indications and any precautions to be taken. These details should cover in particular: : | | | |

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| | k) precautions to be taken in the event of changes in the performance of the device; | | | |
| | l) precautions to be taken as regards exposure, in reasonably foreseeable environmental conditions, to magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, acceleration, thermal ignition sources, etc; | | | |
| | m) adequate information regarding the medicinal product or products which the device in question is designed to administer, including any limitations in the choice of substances to be delivered; | | | |
| | n) precautions to be taken against any special, unusual risks related to the disposal of the device; | | | |
| | o) medicinal substances, or human blood derivatives incorporated into the device as an integral part in accordance with Section 7.4; | | | |
| | p) degree of accuracy claimed for devices with a measuring function; | | | |
| | q) date of issue or the latest revision of the instructions for use. | | | |
| **Paragraph 14** | If the conformity with the Essentials Requirements must be done according the clinical data, as in point 6 from part I, such data must be refered to Annex X. | | | |

## CLINICAL EVALUATION FOR MEDICAL DEVICES

## ANNEX X

| **Paragraph** MDD 93/42/EEC modified by 2007/47/EEC | **Title** | **Applicable Yes-Not** | **Location in the Technical File** |
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| **1** | **General provisions**<br><br>As a general rule, confirmation of conformity with the requirements concerning the characteristics and performances referred to in Sections 1 and 3 of Annex I, under the normal conditions of use of the device, and the evaluation of the side-effects and of the acceptability of the benefit/risk ratio referred to in Section 6 of Annex I, must be based on clinical data. The evaluation of this data, hereinafter referred to as 'clinical evaluation', where appropriate taking account of any relevant harmonised standards, must follow a defined and methodologically sound procedure based on:<br><br>1.1.1. Either a critical evaluation of the relevant scientific literature currently available relating to the safety, performance, design characteristics and intended purpose of the device, where there is demonstration of equivalence of the device to the device to which the data relates, and the data adequately demonstrate compliance with the relevant essential requirements.<br><br>1.1.2. Or a critical evaluation of the results of all clinical investigations made.<br><br>1.1.3. Or a critical evaluation of the combined clinical data provided in 1.1.1 and 1.1.2. | | |
| **2** | **Clinical Investigations**<br>The objectives of clinical investigation are:<br><br>— to verify that, under normal conditions of use, the performance of the devices conform to those referred to in Section 3 of Annex I, and<br><br>— to determine any undesirable side-effects, under normal conditions of use, and assess whether they constitute risks when weighed against the intended performance of the device.<br><br>Clinical investigations must be performed on the basis of an appropriate plan of | | |

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| | investigation reflecting the latest scientific and technical knowledge and defined in such a way as to confirm or refute the manufacturer's claims for the device; these investigations must include an adequate number of observations to guarantee the scientific validity of the conclusions.<br><br>The procedures used to perform the investigations must be appropriate to the device under examination.<br><br>Clinical investigations must be performed in circumstances similar to the normal conditions of use of the device.<br><br>All the appropriate features, including those involving the safety and performances of the device, and its effect on patients must be examined.<br><br>All serious adverse events must be fully recorded and immediately notified to all competent authorities of the Member States in which the clinical investigation is being performed.<br><br>The investigations must be performed under the responsibility of a medical practitioner or another authorized qualified person in an appropriate environment.<br><br>The medical practitioner or other authorized person must have access to the technical and clinical data regarding the device.<br><br>The written report, signed by the medical practitioner or other authorized person responsible, must contain a critical evaluation of all the data collected during the clinical investigation. | | |

HISTORICAL REVISION

| Revision | Description | ECN Reference |
|---|---|---|
| A | Initial release | DI-14-0001 |
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| | RISK | Initial level | RISK MITIGATION ACTION | New risks? | P final | S final | RPN |
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# BIOLOGICAL RISK MANAGEMENT

## 1. RISK ANALYSIS PRODUCT:

### 1.1 Intended use of product characteristics.

### 1.2 Identification of the biohazard.

### 1.3 Determination of exposure

### 1.4 Risk Estimation

### 1.5 Risk Assessment

### 1.6 Risk Control

### 1.7 Risk assessment / global residual benefit.

### 1.8 Report of the biological assessment.

### 1.9 Information on post-production.

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Signature Date

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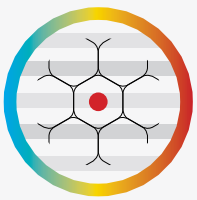
# Deliverable 4.1.

## Reduced Version*

Regulations and legal issues at European Union to be fulfilled to the purposed pilot service



diagnoptics