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05 February 2015 – part 5

Conformity Assessment Europe

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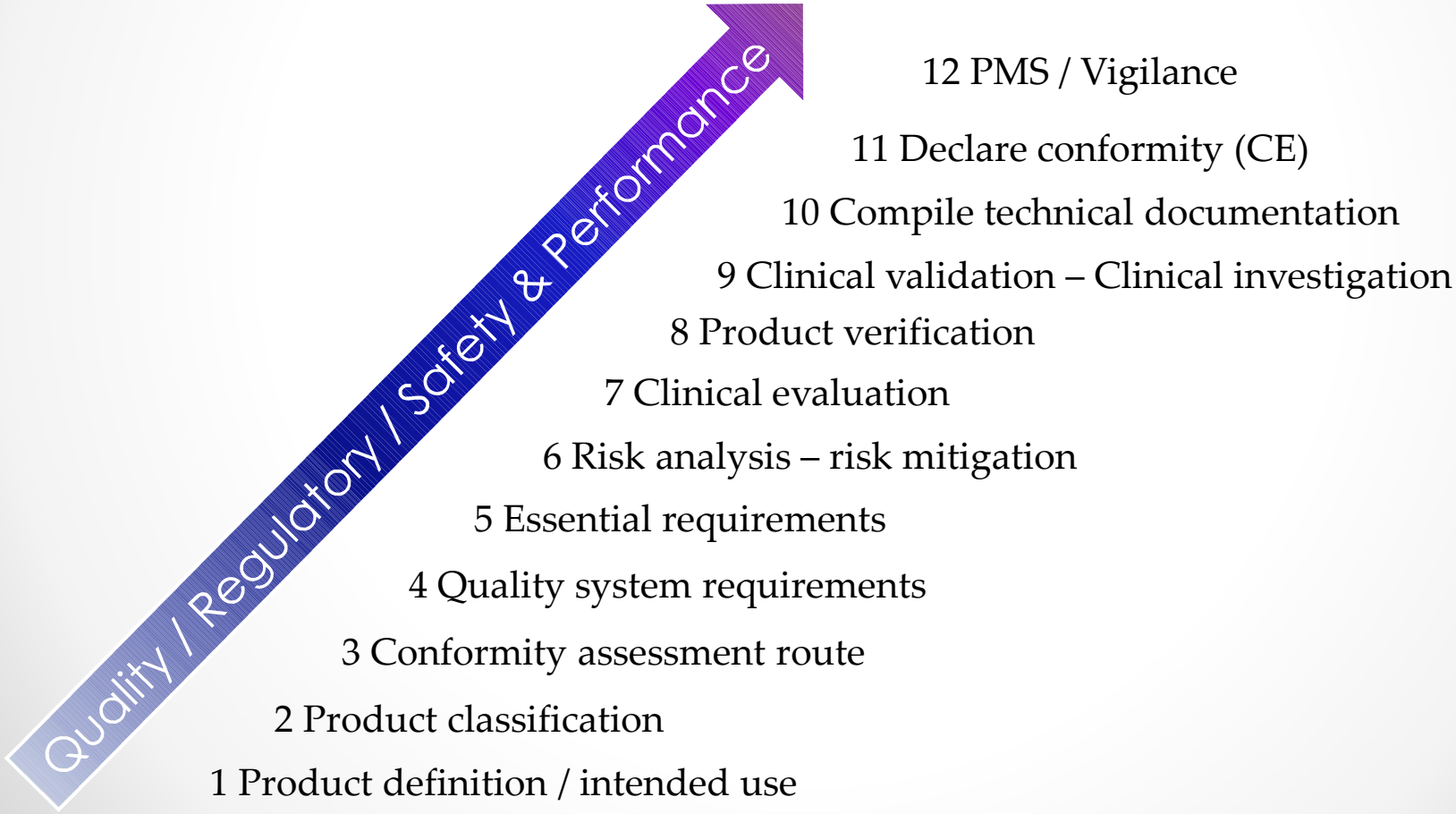
EU Regulatory system

Conformity assessment

Steps to market - overview

Conformity assessment (CE-marking) Medical Devices



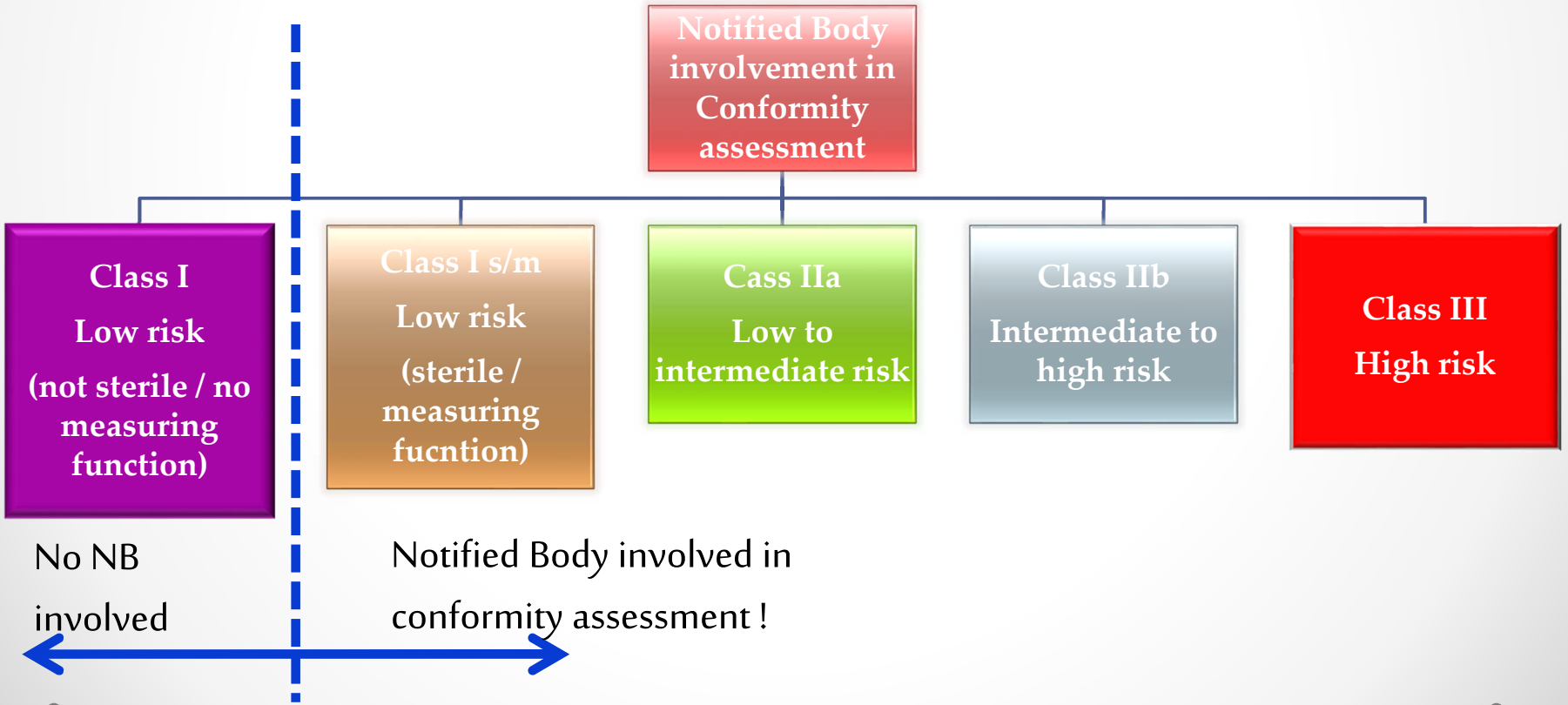
Conformity Assessment

Principles and routes to CE mark, NB assessment

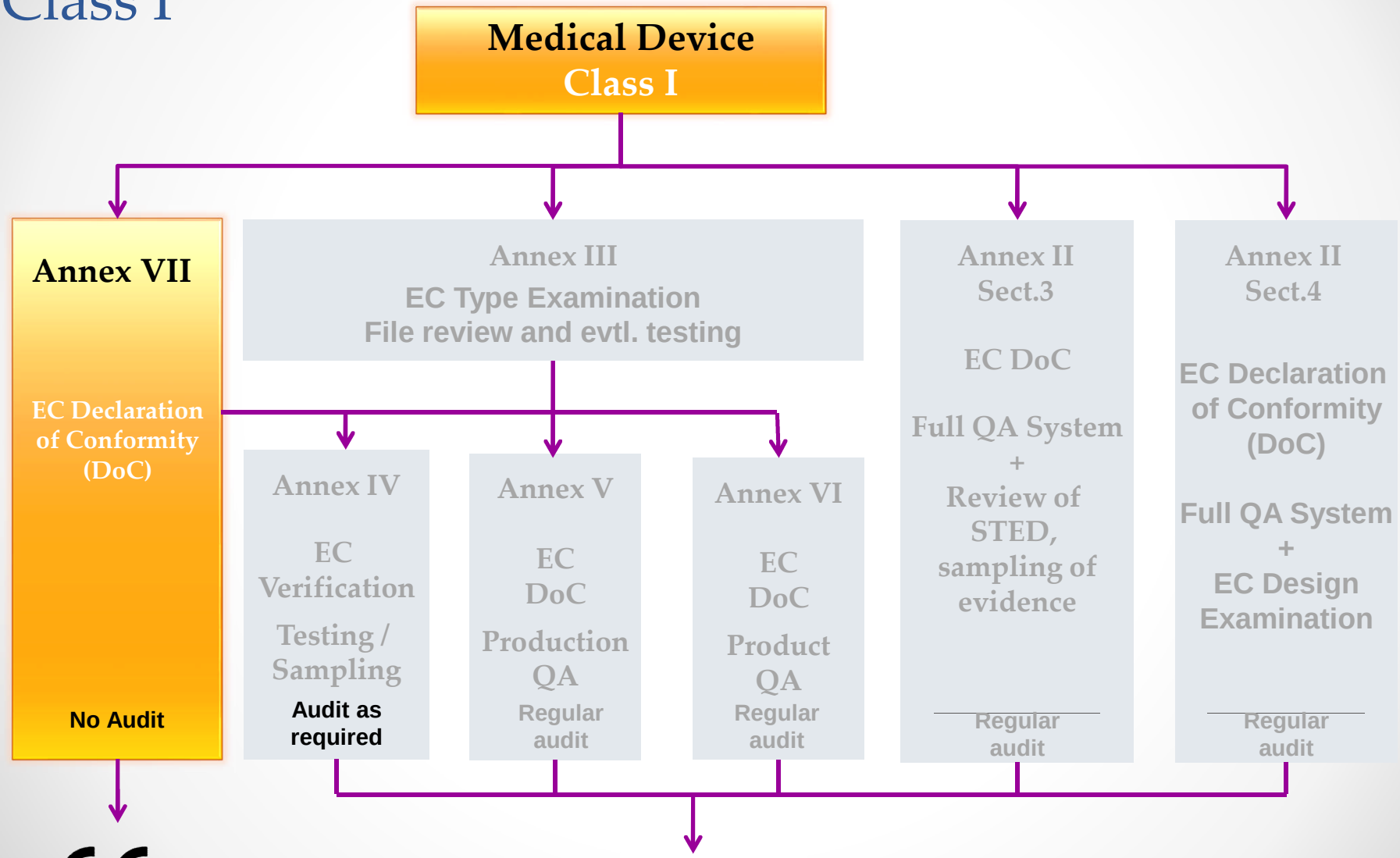
Conformity assessment routes

Conformity assessment routes are defined in Article 11 MDD,

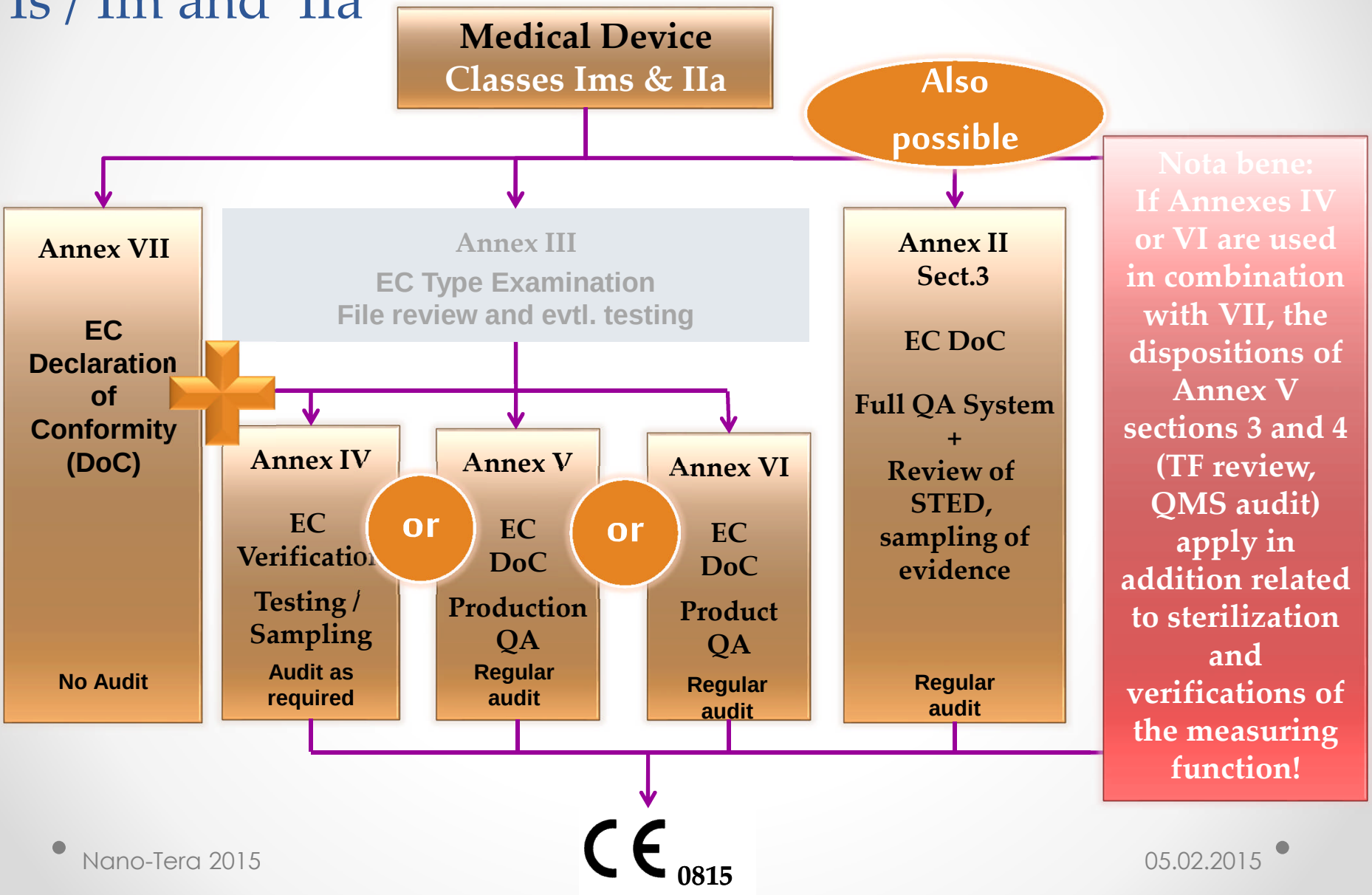
- **Pathway depends on device classification**
- **Classification depends on intended use and risk profile**



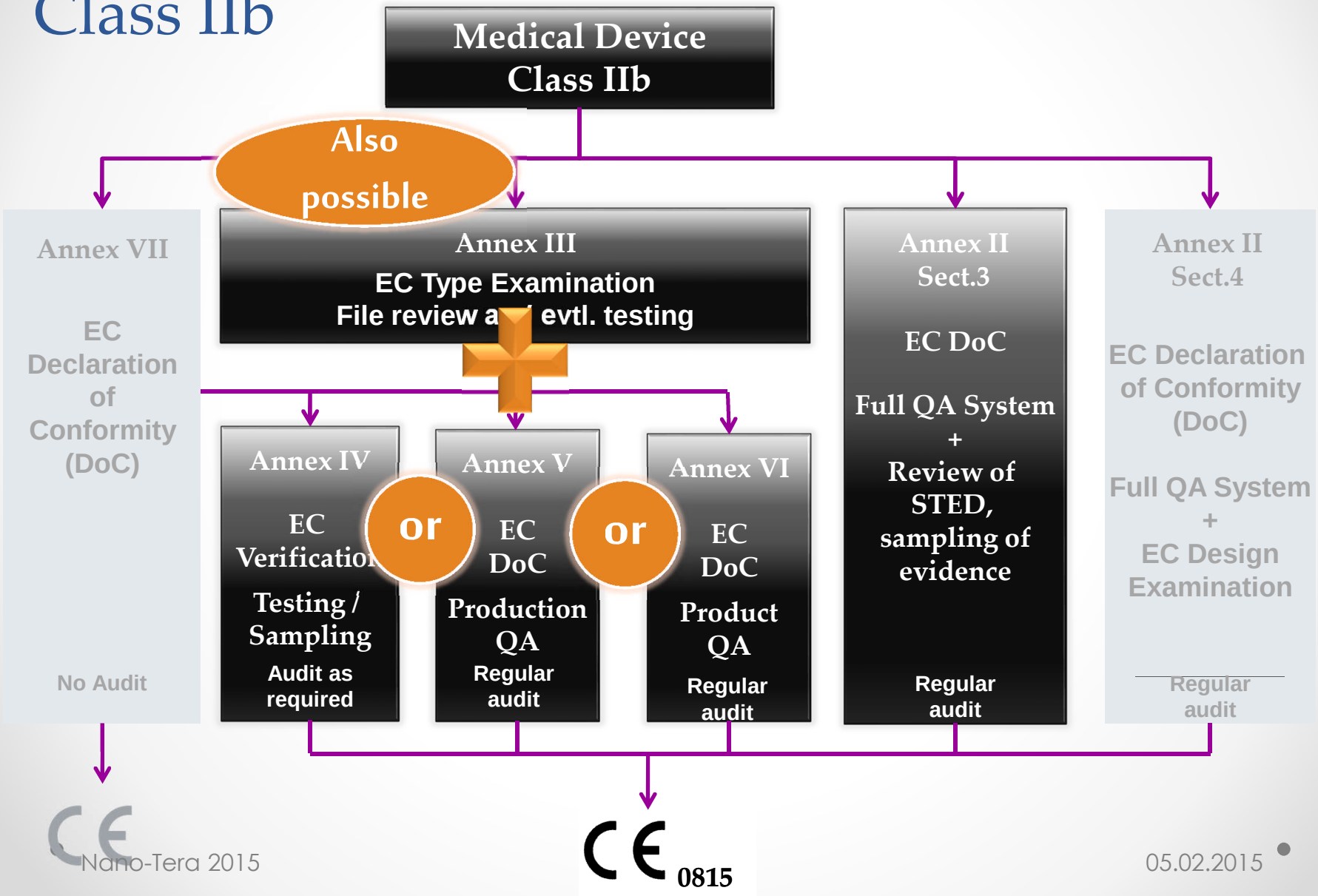
CE Mark conformity assessment pathway Class I



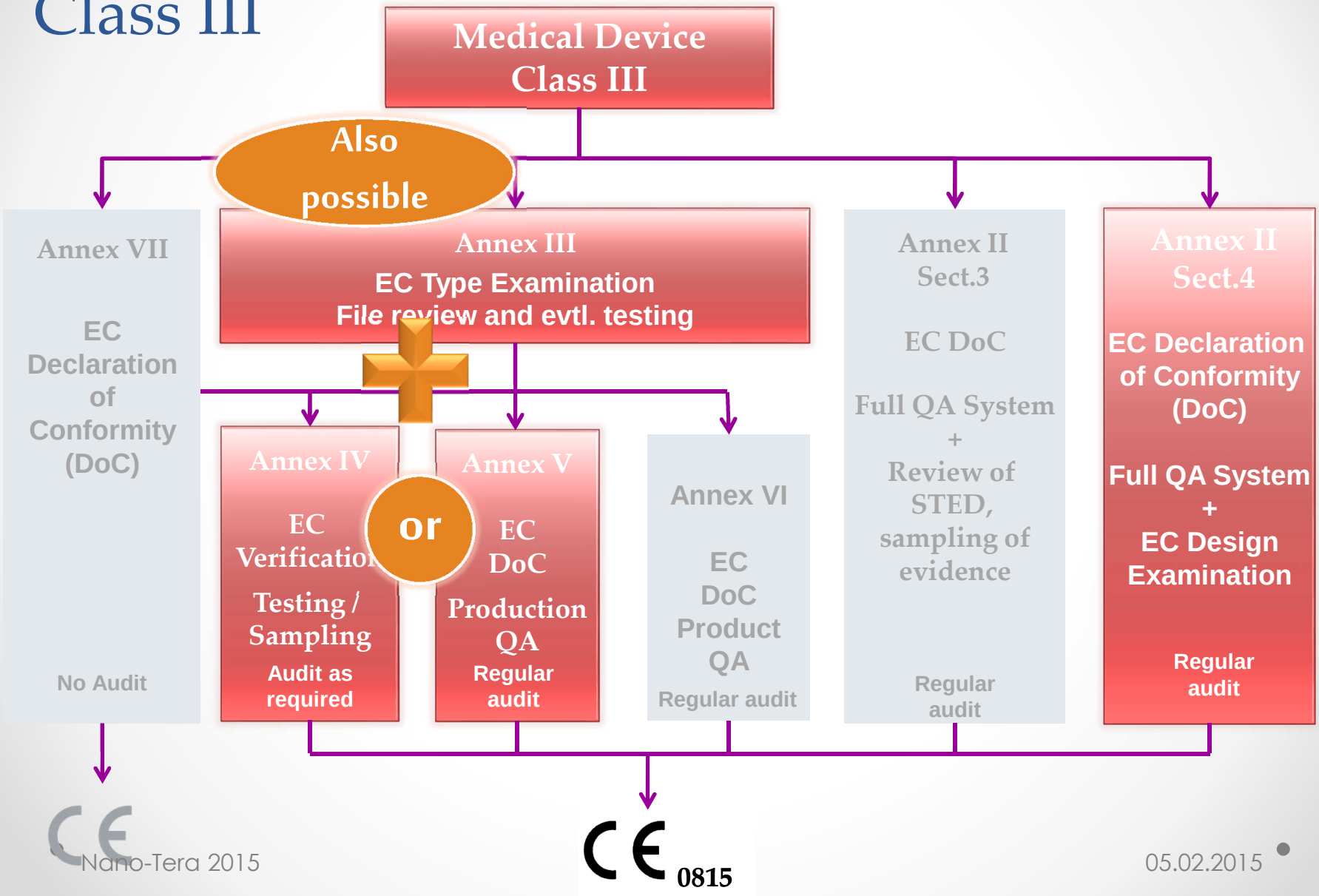
CE Mark conformity assessment pathway Classes Is / Im and IIa



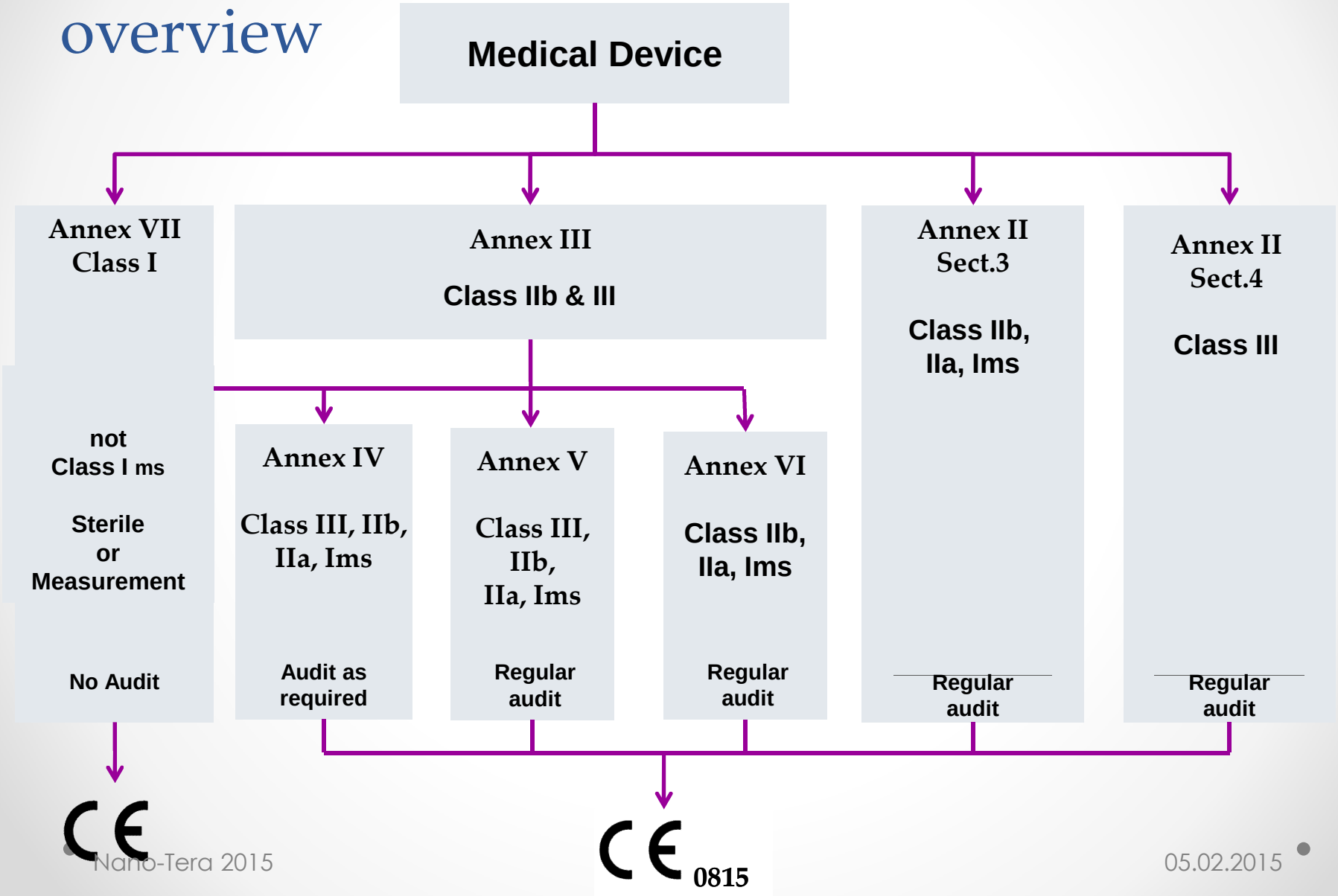
CE Mark conformity assessment pathway Class IIb



CE Mark conformity assessment pathway Class III



CE Mark conformity assessment summary overview



Conformity Assessment

- Market access requires for devices from of a risk class > I to mandate a Notified Body
- The manufacturer fulfils the requirements of the directive / national transpositions
- A Notified Body verifies due state of the Art of the evidence for fulfilling the requirements
- Conformity assessment pathways may be chosen by the manufacturer in relation to the class of risk of medical devices
- The manufacturer gets a confirmation from the Notified Body that the requirements have been fulfilled – CE certificate e.g. CE0123
- The manufacturer declares conformity with the applicable directives: DoC – declaration of conformity

Medical Device Classification

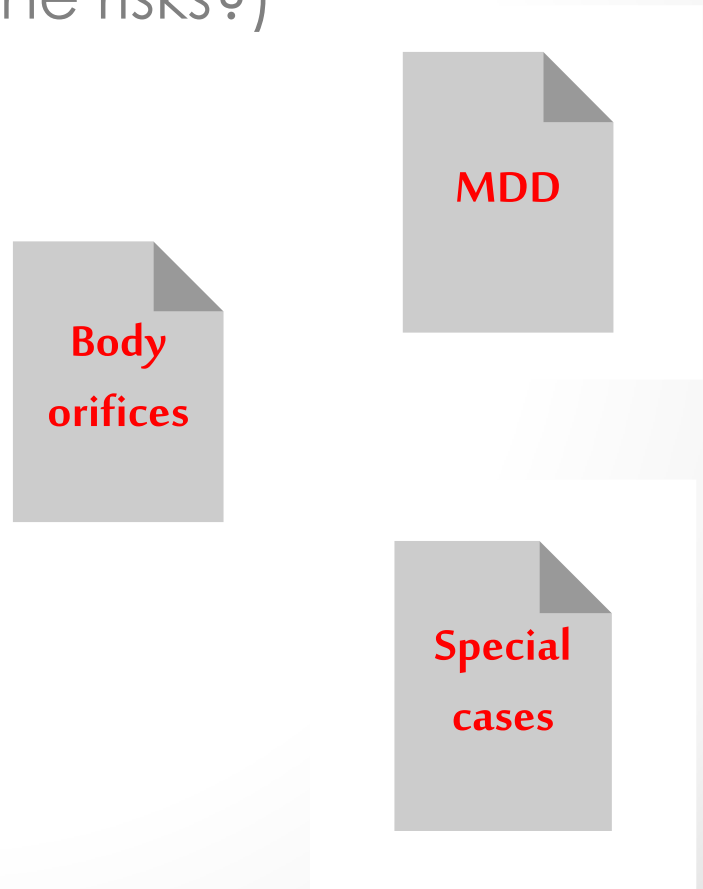
Europe – 93/42 EEC

Classification, risk based approach

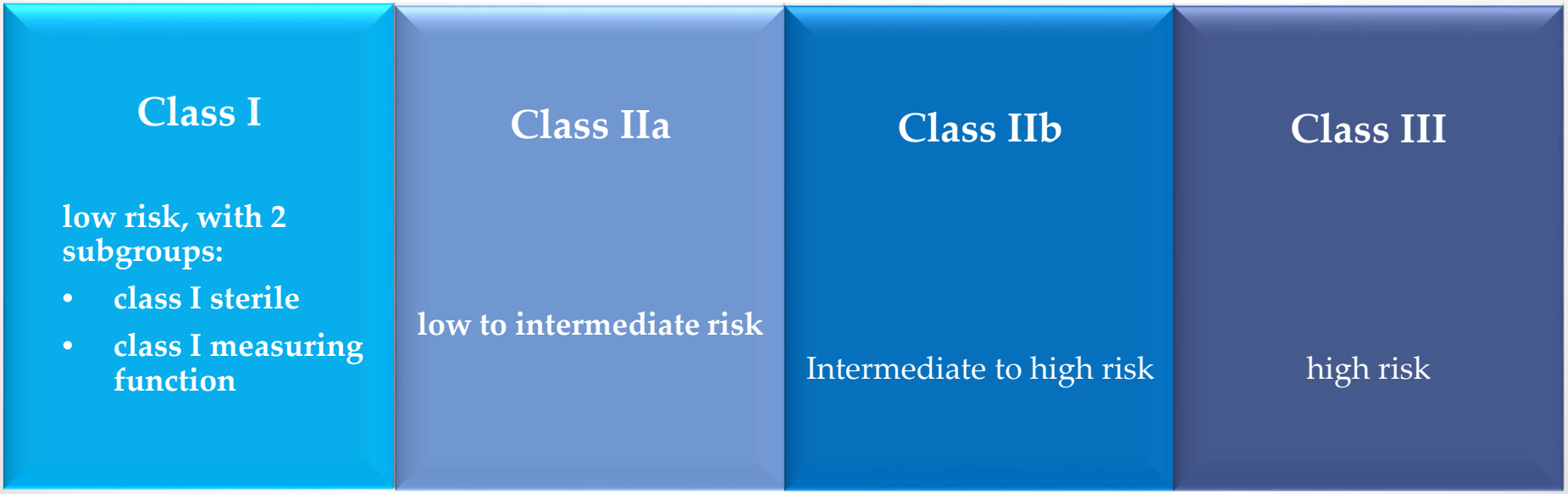
- **Class based on risk, duration of use and invasiveness**
- **Described in MDD Article 9 and Annex IX**
- **Intended use determines class**
- **Highest individual classification applies to systems**
- **The higher the classification the more scrutiny for conformity assessment**
- **Guidance : MEDDEV 2.4/1**

Classification

- 1- Is it a medical device (within scope of directive?)
- 2- Intended use (what are the risks?)
  - Duration
    - Transient < 60 min
    - Short term > 60 min < 30 days
    - Long term > 30 days
  - Invasiveness
    - Non Invasive devices
    - Invasive devices
      - Body orifice
      - Surgically invasive
  - Special cases
    - Reusable surgical instruments
    - Active medical devices
    - Special rules



Classification, examples



Classification, criteria related to use

Duration of Contact	**Transient** – < 60 minutes **Short Term** – < 30 days **Long Term** – over 30 days
Invasiveness	**Body Orifice** – Natural opening or stoma **Surgically invasive** – penetrating body surface **Implantable** – in the body, remains after intervention
Active	Any source of power other than that generated directly by the human body or gravity

Classification, criteria related to anatomy

Central Circulatory System

VESSELS

- Arteriae Pulmonales
- Aorta Ascendens
- Arcus Aorta
- Aorta Descendens to the Bifurcatio Aortae
- Arteriae Coronariae
- Arteria Carotis Communis
- Arteria Carotis Externa
- Arteria Carotis Interna
- Arteriae Cerebrales
- ….

Central Nervous System

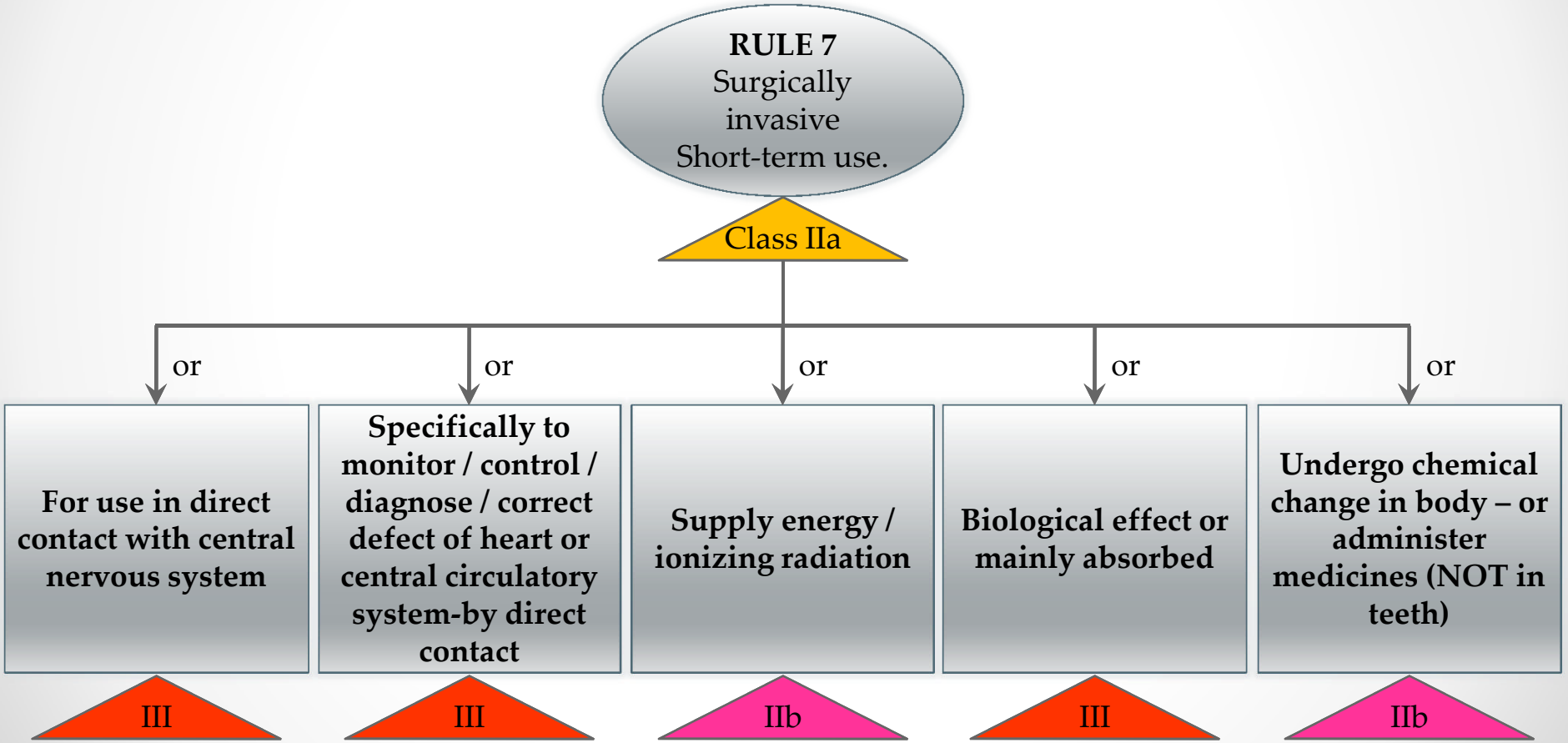
Central nervous system : brain, meninges, spinal cord.

Classification, rules and device type

Rule applied to…	
Non invasive devices	Rule 1 to 4
Invasive devices	Rules 5 to 8
Active devices	Rules 9 to 12
Special rules	Rules 13 to 18

Careful: all applicable rules must be taken into account !

Classification, example flowchart from Meddev 2.4.1



Classification, example explanation from Meddev 2.4.1

Rule 7 – Surgically invasive devices intended for short-term use (>60 minutes, < 30 days)

General explanation of the rule

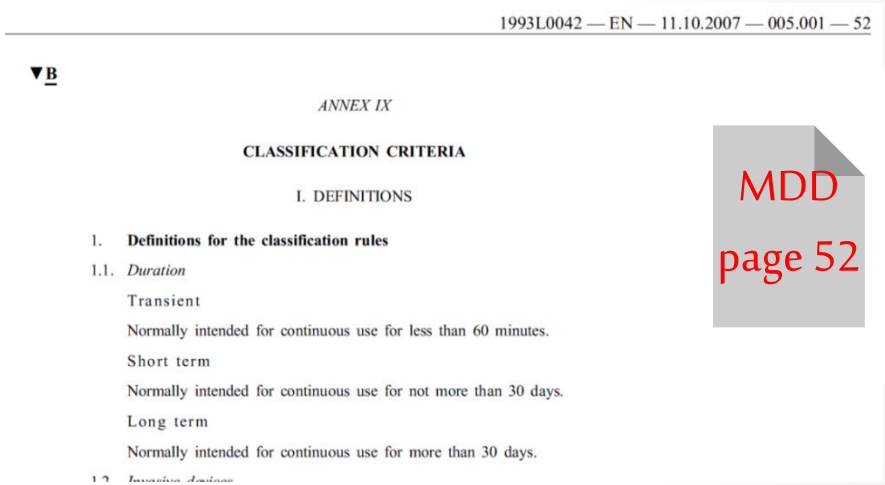
These are mostly devices used in the context of surgery or post-operative care (e.g. clamps, drains), infusion devices (cannulae, needles) and catheters of various types.

RULE 7	EXAMPLES
All surgically invasive devices intended for short term use are in Class IIa unless they are intended:	- Clamps - Infusion cannulae - Skin closure devices - Temporary filling materials - Tissue stabilisers[2] used in cardiac surgery
- either specifically to control, diagnose, monitor or correct a defect[2] of the heart or of the central circulatory system through direct contact with these parts of the body, in which case they are in Class III,	- Cardiovascular catheters - Cardiac output probes - Temporary pacemaker leads - Thoracic catheters intended to drain the heart, including the pericardium - Carotid artery shunts - Ablation catheter
- or specifically for use in direct contact with the central nervous system, in which case they are in Class III,	- Neurological catheters - Cortical electrodes
- or to supply energy in the form of ionising radiation in which case they are in Class IIb,	- Brachytherapy devices
- intended to have a biological effect or to be wholly or mainly absorbed in which case they are in Class III,	- Absorbable sutures - Biological adhesives
- or to undergo chemical change in the body, except if the devices are placed in the teeth, or to administer medicines1, in which case they are Class IIb.	- Adhesives

Practical issues of classification

Classification summary

- 2 main source documents to consider:
- Annex IX MDD
- Meddev 2.4.1



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ANNEX IX

CLASSIFICATION CRITERIA

I. DEFINITIONS

1. **Definitions for the classification rules**

1.1. *Duration*

Transient

Normally intended for continuous use for less than 60 minutes.

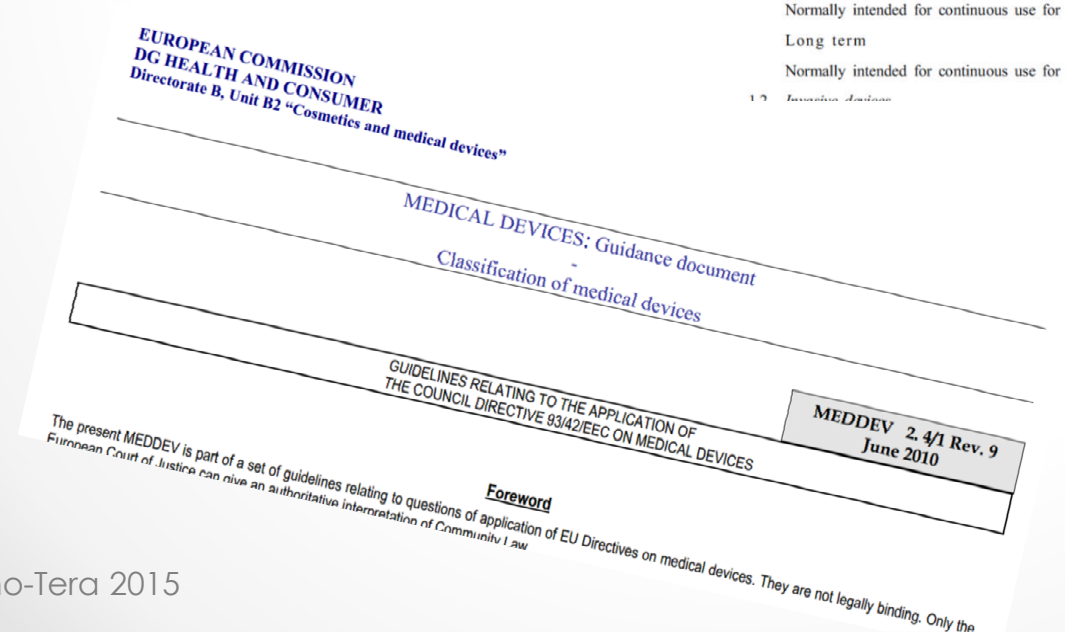
Short term

Normally intended for continuous use for not more than 30 days.

Long term

Normally intended for continuous use for more than 30 days.

MDD page 52



EUROPEAN COMMISSION
DG HEALTH AND CONSUMER
Directorate B, Unit B2 "Cosmetics and medical devices"

MEDICAL DEVICES: Guidance document
-
Classification of medical devices

GUIDELINES RELATING TO THE APPLICATION OF
THE COUNCIL DIRECTIVE 93/42/EEC ON MEDICAL DEVICES

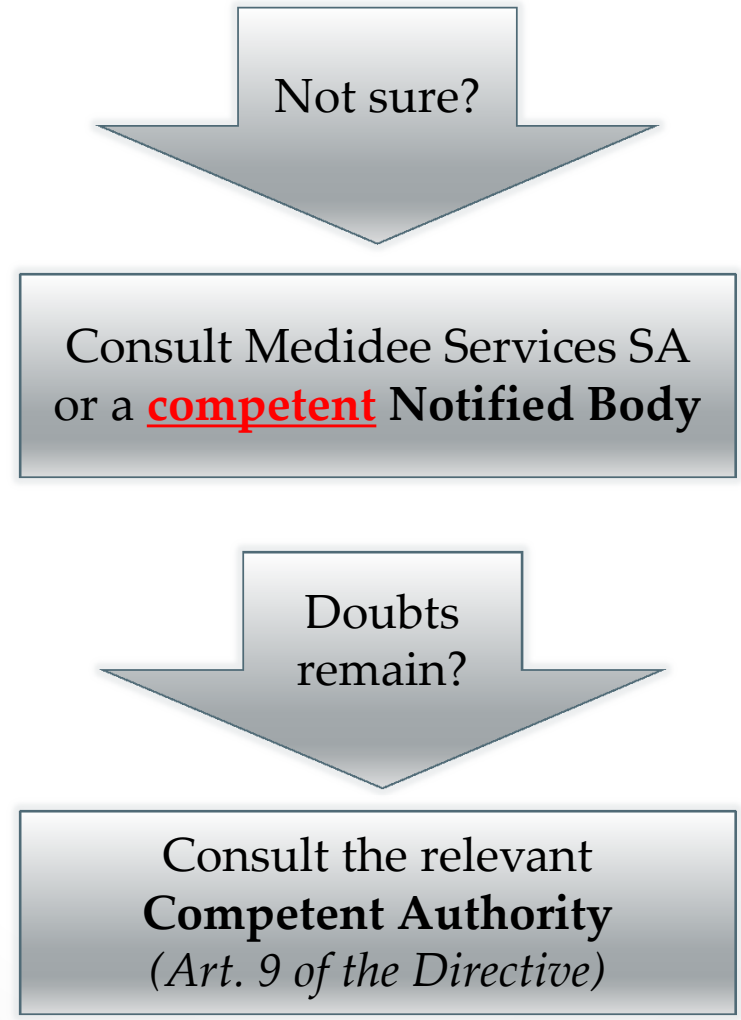
MEDDEV 2. 4/1 Rev. 9
June 2010

Foreword

The present MEDDEV is part of a set of guidelines relating to questions of application of EU Directives on medical devices. They are not legally binding. Only the European Court of Justice can give an authoritative interpretation of Community Law

Meddev 2.4.1

Classification: conclusions



Summary:
Device classification -
What does this mean for Medtec Companies

- **Device classification must be clear latest with FRS**
- **Claims for intended use are directly impacting the classification**
- **Classification impacts on scope to be covered by the product documentation (technical file / design dossier)**
- **Classification impacts scrutiny of NB / CA review**
- **Classification impacts the choice of conformity assessment pathways eligible and the possible choice of Notified Bodies competent for the product**
- **Classification together with the degree of “novelty” of the device impacts on clinical data to be generated -> impact on time to market**
- **Change of “intended use” (URS) and FRS must be covered by change control**

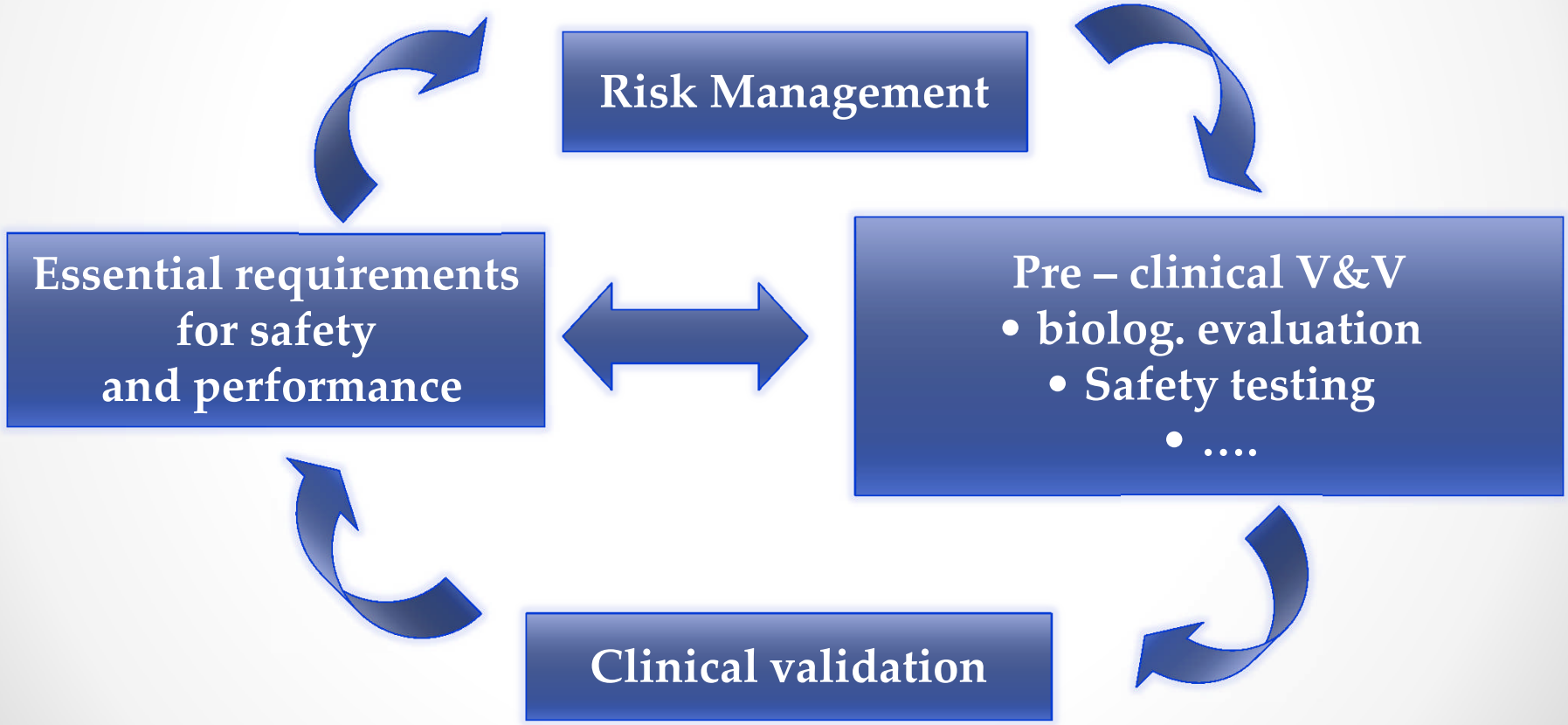
Summary: Device classification - What does this mean for Medtec Corps

- **The conformity assessment pathway chosen influences qualitative and quantitative aspects of technical documentation :**
- **MDD Class III: (also applicable to AIMDD)**
  - **Design Dossier (incl. design history for Annex II – Full QA incl. DE) or**
  - **Technical file (no design history – Production QA + TE or EC verification + TE) + samples and test documentation / support for TE**
- **MDD all other classes:**
  - **Technical file (+ samples and test documentation / support if TE chosen)**
- **Timeframes for DE vary between 2 months and X – depending on question rounds**
- **Timeframes for TE depend on the availability of test facilities working with the NB or (in case review based TE) on availability of internal experts (between 2 months and x – depending on question rounds)**

Essential Requirements and use of standards

Conformity assessment MDD

Essential Requirements, MDD Annex I: 4 pillars for maintaining devices safe and performing



Essential Requirements, MDD Annex I: 4 pillars for maintaining devices safe and performing

Essential requirements	
I. GENERAL REQUIREMENTS	Applicable to all medical devices: (1-6) - Safety and performance as intended, risk benefit balance, clinical validation
II. REQUIREMENTS REGARDING DESIGN AND CONSTRUCTION	As applicable: (7) - Chemical, physical and biological properties. (8) - Infection and microbial contamination. (9) - Construction and environmental properties (10) - Devices with a measuring function (11) - Protection against radiation (12) - Requirements for medical devices connected to or equipped with an energy source (13) - Information supplied by the manufacturer

How to demonstrate that Essential Requirements are fulfilled?

"State of Art" concept means…

the use of standards and other documents representing the state of the art to show compliance with Essential Requirements.

State of the Art concept

- **State of the art requirements can be located in standards and guidance documents.**
- **Regulators worldwide recognize standards and guidance documents as a mirror of state of the art of science and technology.**

  - EU-MDD Annex I: 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.
  - US-FDA QSR Introduction: …Rather, the regulation provides the framework that all manufacturers must follow by requiring that manufacturers develop and follow procedures and fill in the details that are appropriate to a given device according to the current state-of-the-art manufacturing for that specific device.
  - US-FDA Guidance for Industry and FDA Staff - Recognition and Use of Consensus Standards
  - Germany ZLG - Normen und technische Vorschriften 3.5 A 1
  - Health Canada - Recognition and Use of Standards under the Medical Devices Regulations
  - GHTF: Role of Standards in the Assessment of Medical Devices Study Group 1 Final Document GHTF/SG1/N044:2008

State of the Art concept – use of standards

- When setting up design inputs, check:
  - Harmonized standards / consensus standards (EU / US) and other standards for applicability
    - http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/search.cfm
    - http://ec.europa.eu/enterprise/policies/european-standards/documents/harmonised-standards-legislation/list-references/index_en.htm
  - Further sources for standards :
    - http://www.astm.org/Standard/index.shtml
    - http://www.nssn.org/search/IntelSearch.aspx
    - http://www.beuth.de/
    - http://shop.bsigroup.com/en/Browse-by-Sector/Healthcare/?t=r
    - http://www.iso.org/iso/iso_catalogue.htm

State of the Art concept – use of guidance

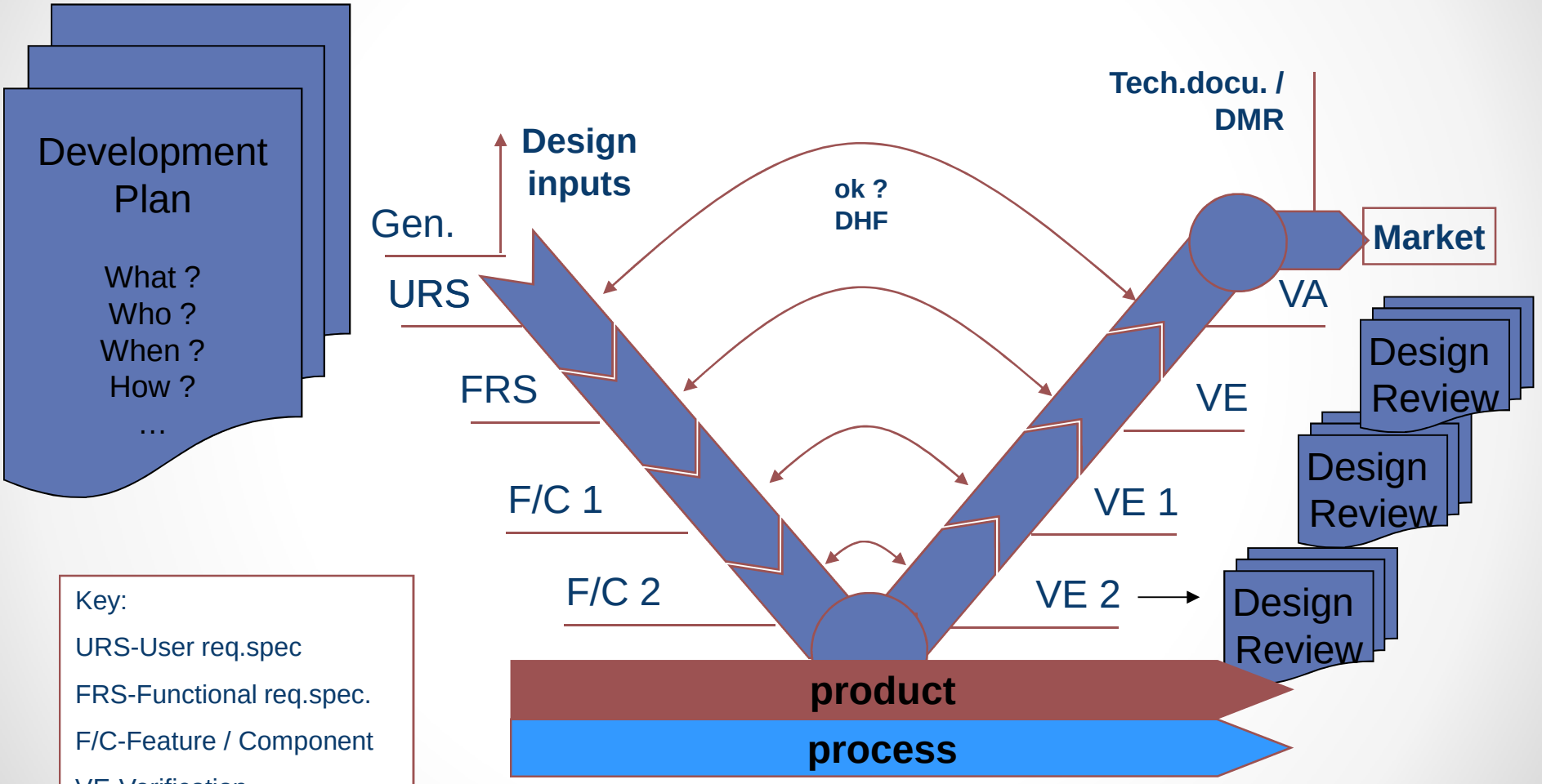
- When setting up design inputs, check:
  - International / national guidance for applicability
    - http://ec.europa.eu/consumers/sectors/medical-devices/documents/index_en.htm
    - http://ec.europa.eu/consumers/sectors/medical-devices/documents/guidelines/index_en.htm
    - http://www.imdrf.org/documents/documents.asp - go then to GHTF final documents
    - http://www.hc-sc.gc.ca/dhp-mps/md-im/index-eng.php
    - http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm
    - https://www.zlg.de/medizinprodukte/dokumente/antworten-und-beschluesse-ek-med.html

State of the art concept

- Following Standards and Guidance is not mandatory, however, the use of a recognized / harmonized standard gives presumption of conformity with relevant Essential Principles of Safety and Performance….(Essential Requirements)

- If you plan a different approach you need sound scientific arguments and evidence that the way you want to do it is at least equivalent to the state of the art represented by standards and guidance.

Design process overview – V&V



Essential Principles of Safety and Performance I

The STED / ToC shall contain an EP checklist that identifies:

- the Essential Principles;
- whether each Essential Principle applies to the device and if not, why not;
- the method(s) used to demonstrate conformity with each Essential Principle that applies;
  - a reference for the method(s) employed (e.g., standard), and
- the precise identity of the controlled document(s) that offers evidence of conformity with each method used.

Essential Principles of Safety and Performance II

Methods used to demonstrate conformity may include one or more of the following:

- conformity with recognised or other standards;
- conformity with a commonly accepted industry test method;
- conformity with an in-house test method;
- the evaluation of pre-clinical and clinical evidence.
- comparison to a similar device already available on the market.

The EP checklist should incorporate a cross-reference to the location of such evidence both within the full technical documentation held by the manufacturer and within the STED / ToC.

Clinical evaluation

Rough summary of required steps

Clinical Evaluation - Steps

1. Determine what you need to know and formulate questions based upon required clinical safety and performance (based on Claims, Essential Requirements and Risk Analysis)
2. Determine what information you need to answer questions
3. Formulate methodology - ISO 14155 / Meddev 2.7.1
4. Collect information / data (literature, clinical investigation, experience, other)
5. Analyze information with regard to validity, relevance, quality and clinical significance
6. Analyze information for conclusions on performance and safety
   - Consider claims, labeling, IFU
   - Patient information
7. Formulate conclusions
8. Is available information adequate to address original questions?
   - If no, return to Step 2.
9. Create Clinical Evaluation Report
10. Create Post Market Plan
11. Close the loop with your PMCFU / PMS procedures

Clinical Investigation - Steps

1. Determine what you need to know and formulate questions based upon required clinical safety and performance (based on Claims, Essential Requirements and Risk Analysis)
2. Determine what information you need to answer questions
3. Create clinical protocol / CIP
4. Create supporting documentation (QMS) for clinical investigation
5. Obtain ethics committee opinion and notify CA
6. Execute clinical investigation
7. Create clinical investigation report -> Input to Step 4 of Clinical Evaluation Process

Post Market Surveillance Process

- Must have process to update clinical evaluation
- Establish, document and maintain a Post Market Surveillance System to collect information in production and post-production phases (ISO 14971)
  - System must include inputs, evaluation, actions and output

Inputs: **Feedback e.g. sales; Complaints / CAPA, Risk-management, Vigilance; active data mining incl. PMCFU**

Result: **Up to Date Clinical Evaluation, Risk management file, Continuously fulfil ER**

Technical Documentation

IMDRF ToC

Summary: ToC - What does this mean for Medtec Corps

- Start structuring technical documentation along Toc chapters
- Link URS to FRS to EP to ToC chapters
- Create a summary for each evidence data set*
- Maintain full document & change control from the very beginning**

- *E.g. a 2 pager document explaining what has been done for packaging validation referencing evidence documentation contained in the related technical file section. The 2 pager will later be – copy/paste - part of the ToC summary part
- **The use of a paper folder as master copy has proven to be effective – easily auditable, easily retrievable, easily sortable etc.

Summary: ToC - What does this mean for Medtec Corps

- Checklist for establishing technical documentation:

- Content:
- MDD Annex I, Annex II, Annex VII
- Applicable harmonized / consensus standards and other standards representing state of the art

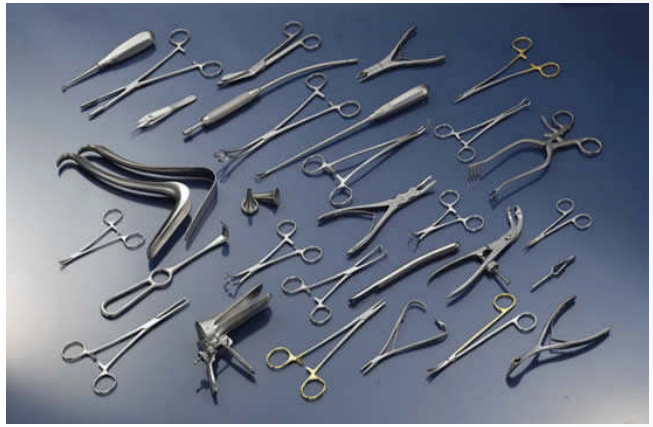
- Structure and content:
- IMDRF ToC
- http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140630-rps-nivd-toc.pdf

End of part
5. Conformity Assessment Europe

Followed by Workshop clinical experience (Prof. Weber)

Special cases

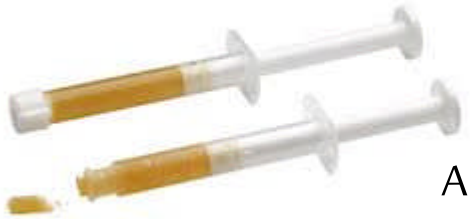
Reusable Surgical Instruments



Active devices

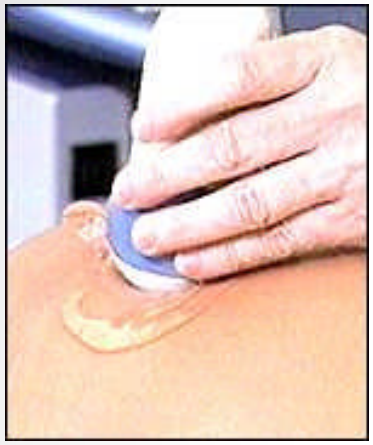
Special rules...

Blood bags



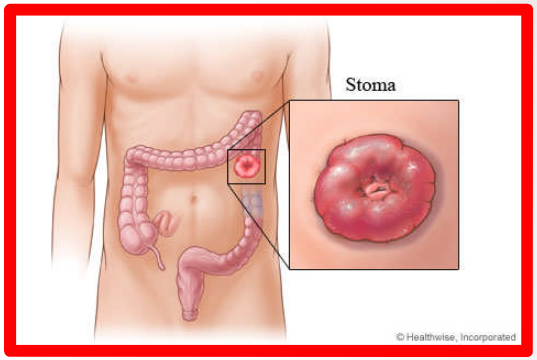
Animal tissue

Class I examples

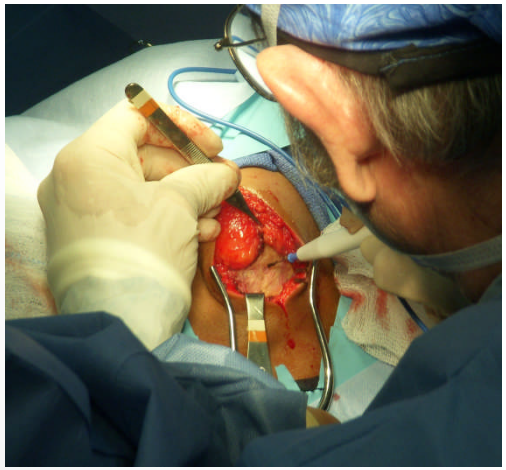


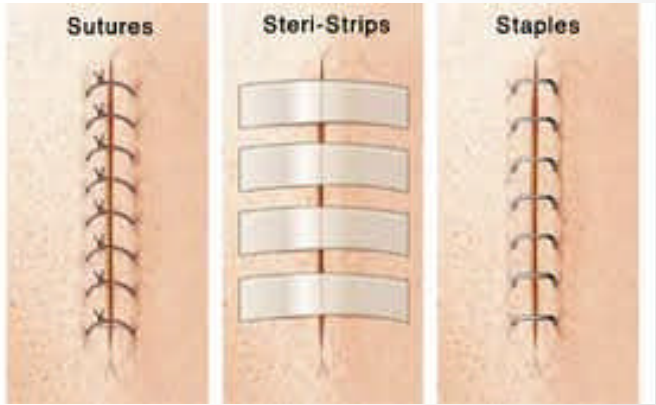
Body orifices

Invasive devices

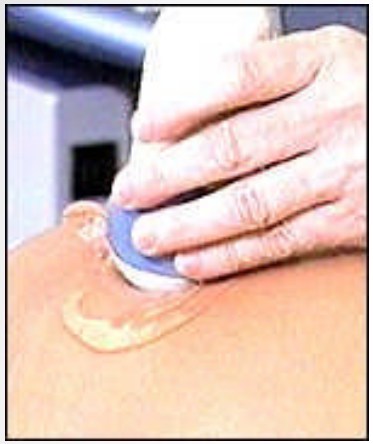


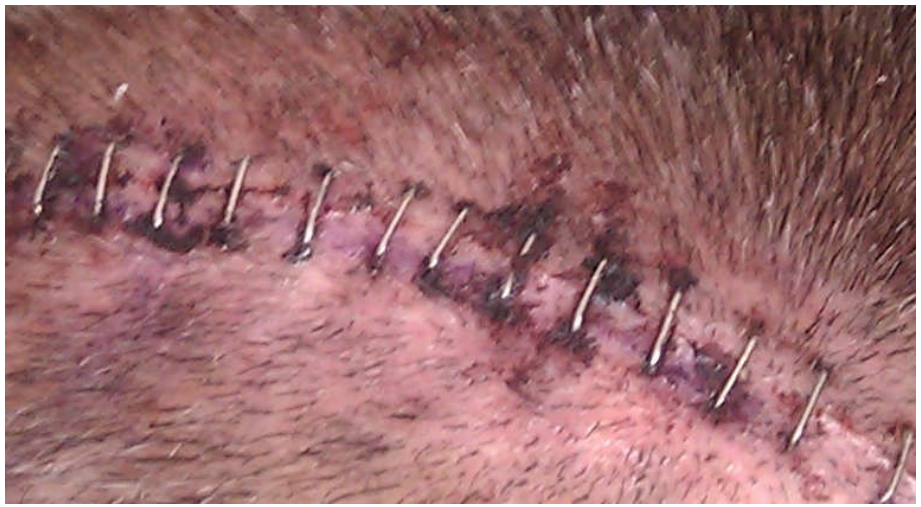
Surgical Invasive devices



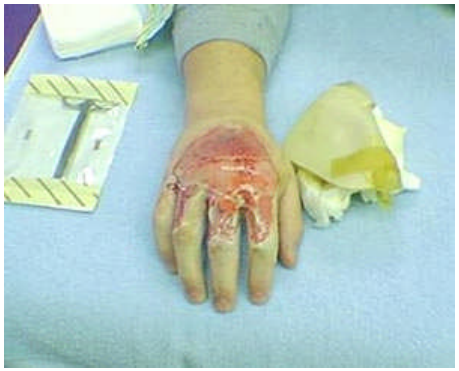


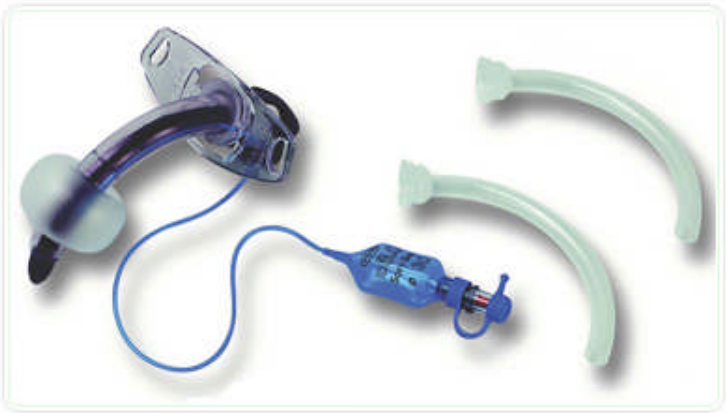
Class IIa examples

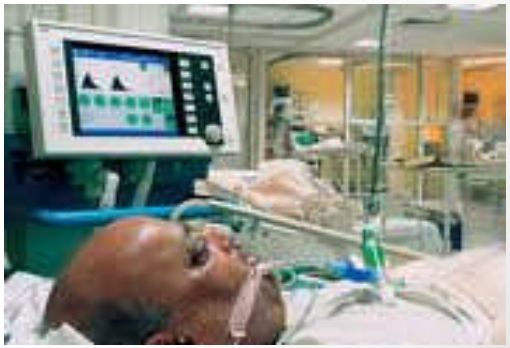




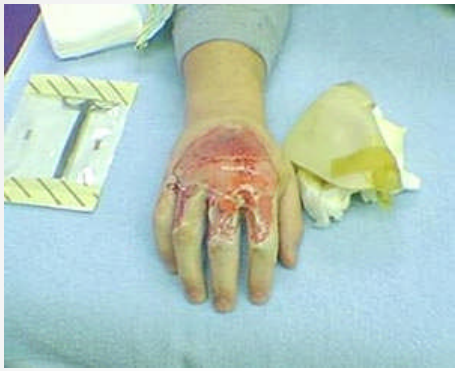
Class IIb examples

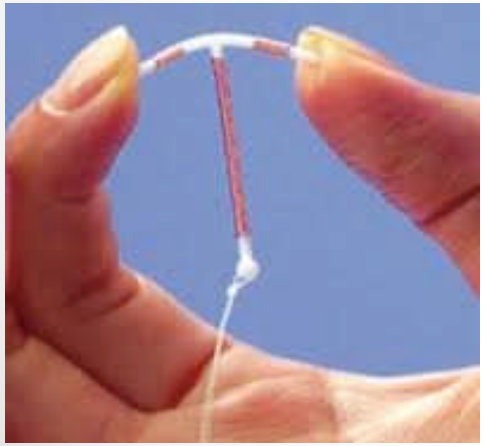


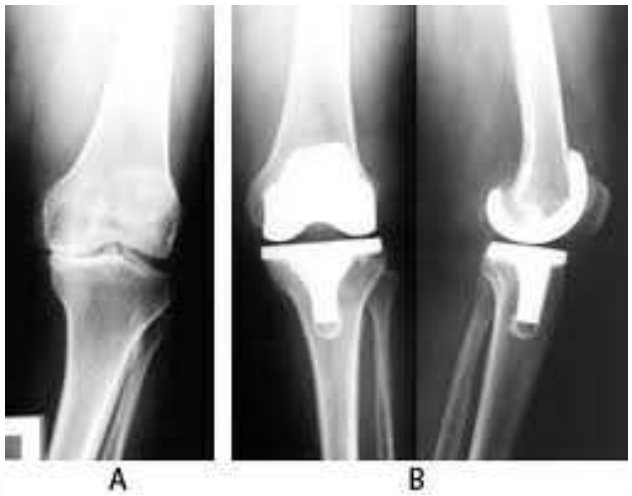


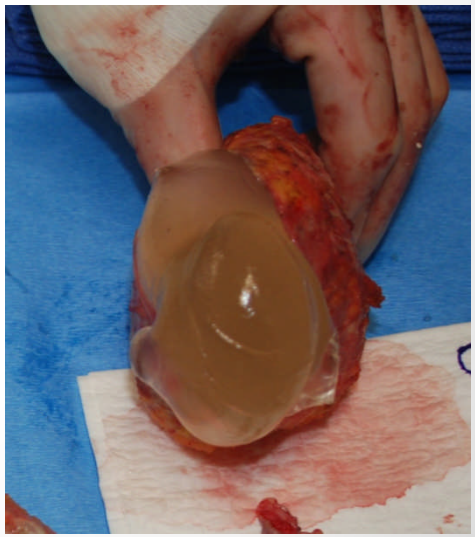


Class III examples









MDD – Article 1
Definition & Scope

1. This Directive shall apply to medical devices and their accessories.
For the purposes of this Directive, accessories shall be treated as medical devices in their own right. Both medical devices and accessories shall hereinafter be termed devices.

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