
unitron
Creating life-science devices

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Development and manufacturing of medical electrical products

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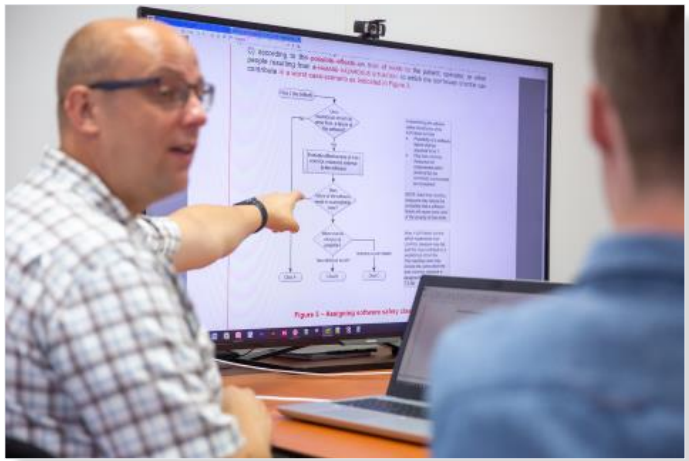
Regulatory

Advice and support with certification and regulatory compliance



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The EU legislative system

In the European Union, most products carry the *CE mark*

https://single-market-economy.ec.europa.eu/single-market/ce-marking/manufacturers_en

‘CE’ can mean something different for various products, for example:

- Construction products
- Hot water boilers
- Lifts
- Toys
- Batteries
- *Medical devices*

With the CE mark, a manufacturer *declares* conformity to *all relevant* regulatory requirements

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The EU legislative system

Steps in the general CE marking process:

1. *ensure conformity* with all relevant EU-wide requirements
2. determine whether you can assess your product *by yourself* or if you have to *involve a Notified Body*
3. put together a *technical dossier*, documenting the conformity
4. draft and sign an *EU declaration of conformity*
5. affix the *CE mark* to your product

https://europa.eu/youreurope/business/product-requirements/labels-markings/ce-marking/

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The EU Medical Device Regulation (MDR)

The MDR is mainly concerned with:

- *safety* of product *use* (to be guaranteed as far as possible)
- honest, complete and accurate *user information*

↳ this is the foundation of your strategy

One product could be either medical or non-medical, depending on its *intended purpose* as defined by its manufacturer

(12) 'intended purpose' means the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation;

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The EU Medical Device Regulation (MDR)

First question: is my product a *medical device*?

↳ your product's purpose should fit the *definition* for medical device

Or, can my product be:

- an *accessory* to a medical device?
- a *custom made* device?
- without a *medical purpose*? (MDR Annex XVI)
- a *combination product*?
- *outside the scope* of the MDR?

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Article 2 Definitions

For the purposes of this Regulation, the following definitions apply:

(1) 'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,

and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.

The following products shall also be deemed to be medical devices:

- devices for the control or support of conception;
- products specifically intended for the cleaning, disinfection or sterilisation of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point.

The EU Medical Device Regulation (MDR)

Second question: what *conformity assessment route* do I need to take?

↳ determined by the *risk class* of the device

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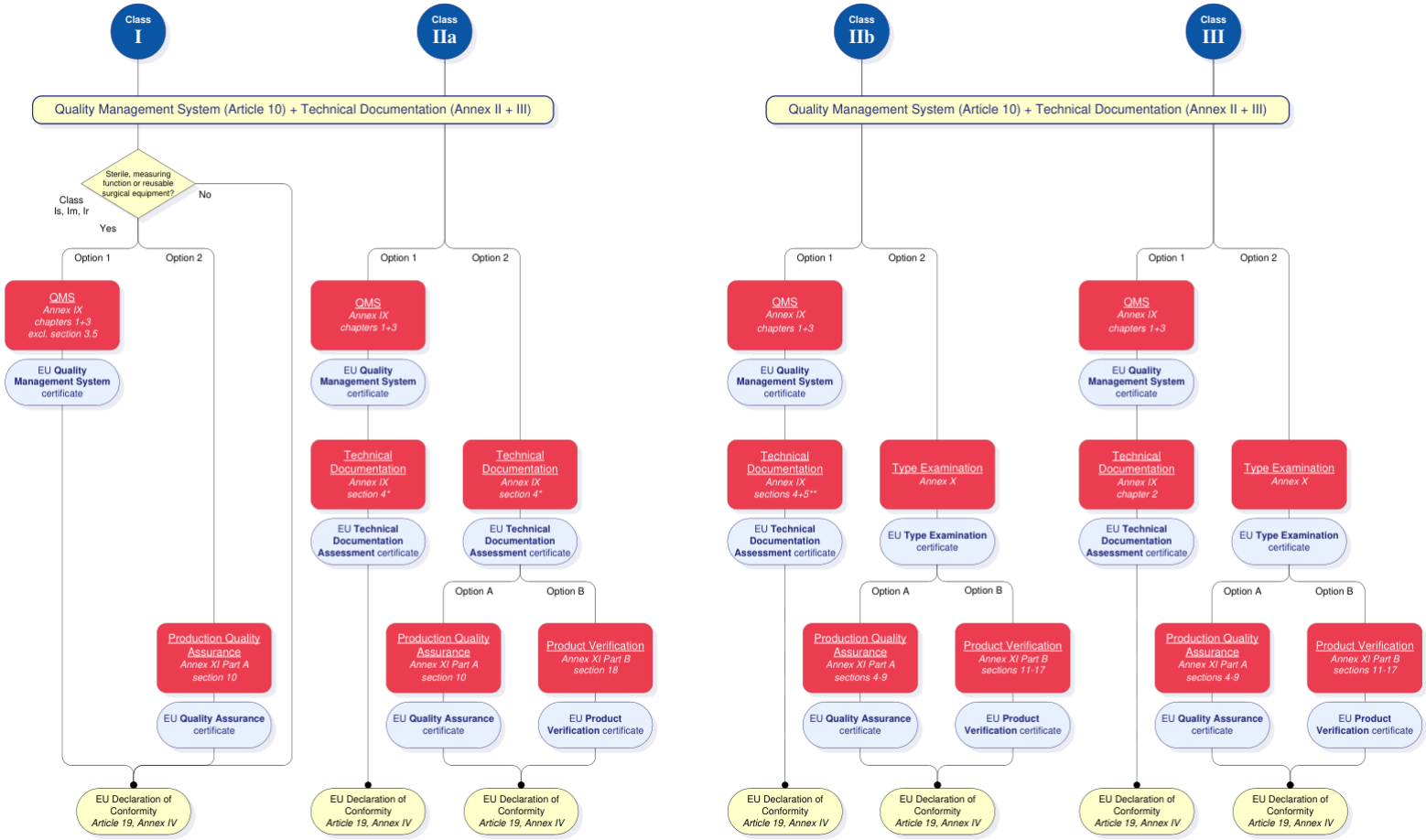

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Diagram taken from Unitron Regulatory's MDR book, freely downloadable from www.unitronregulatory.nl

Device classification

In the EU

- Class I, IIa, IIb, III
- Class Is, Im, Ir

Based on the *intended use* and potential risks associated with the *technical design and manufacture*

Found by following a list of *rules* in the MDR (Annex VIII)

In the US

- Class I, II and II

Based on *intended use* and *indications for use*, and *risk to the patient*

Found by searching your product code in the *classification database*

https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745

https://www.fda.gov/medical-devices/overview-device-regulation/classify-your-medical-device

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Conformity assessment

In the EU

Always: *design + production*

Level of independence based on device class:

- *manufacturer* controlled (class I)
- *Notified Body* evaluation / testing
  ↳ required for class IIa, IIb and III

In the US

- for class I and II (class I mostly exempt):
  premarket notification = *510(k)* = equivalence to predicate device
- for class III (and not exempt):
  premarket approval (PMA)
- for unknown devices:
  premarket approval, unless: class I or II controls would be sufficient => *De Novo* request

https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/de-novo-classification-request

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Quality management

In the EU

- MDR article 10: general *QMS obligations for manufacturers*
- Notified Body assessment of the QMS depends on device class and conformity assessment route. When applicable:
  - Stage 1: procedures & policies
  - Stage 2: on-site inspection & records
- Design and development procedures only assessed in *full quality assurance* route
- ISO 13485 is mostly used

In the US

- 21 CFR part 820: *quality system regulations* (current good manufacturing practices)
- Applies to *finished device manufacturers* who intend to commercially distribute medical devices
- FDA *inspections* at manufacturing sites

https://www.fda.gov/medical-devices/postmarket-requirements-devices/quality-system-qs-regulationmedical-device-good-manufacturing-practices

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Financial planning

In the EU

- Technical safety testing (electrical safety, EMC, biocompatibility)
- Initial and recurring product certification fees
- Initial and yearly QMS certification fees
- ‘CE+ countries’ can have their own (yearly) registration fees

In the US

- Technical safety testing (electrical safety, EMC, biocompatibility)
- Initial certification fee
- Yearly registration fees
- Yearly US agent fees

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How to approach the Notified Body challenge?

Of the 114 *MDD* Notified Bodies:

- 50 still active
- 2 suspended
- 62 expired / withdrawn

Only 39 *MDR* Notified Bodies active, of which:

- 10 in both Germany and Italy
- 3 in the Netherlands
- 2 in both Finland and Poland

Categories of designation:

- Active implantable devices
- Active non-implantable devices for imaging, monitoring and/or diagnosis
- Active non-implantable therapeutic devices and general active non-implantable devices
- Non-active implants and long term surgically invasive devices
- Non-active non-implantable devices

The Notified Body process

1. Pre-application (suitability review, obtain quotation)
   - company information
   - any relevant certificates
   - brochures, IFUs, photographs, animations, etc.

2. Application (certification agreement)
   - medical application submission & review by project manager
   - certification agreement
   - scheduling of TD review and on-site audit

± 6-9 months

3. MDR TD review & on-site initial audit
   - TD submission according to Notified Body checklist
   - off-site review, first report with questions and findings
   - on-site audit + report with non-conformities, corrective action plan, correction (at both manufacturer and critical suppliers, if deemed necessary)

4. Certification
   - Verification & issuance of MDR certificates

± 9-12 months

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How to approach the Notified Body challenge?

- *Hire a competent consultant* (#1 tip from Notified Bodies)
- Prepare your *technical documentation* according to the Team-NB best practice guidance
  (poor preparation and lengthy discussions delay the review process)
- Take the *costs* for Notified Body review into account: at least €50.000 - €150.000
- *Submit* your complete MDR application as soon as possible
- Build a good *relationship* with your Notified Body

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Some resources

- Be sure to check the *Blue Guide on the implementation of EU product rules 2022*

  https://ec.europa.eu/growth/news/blue-guide-implementation-product-rules-2022-published-2022-06-29_en

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Summary: medical device regulatory approach

Layer		Regulatory / risk management approach
4	Intended market	Conformity to legislation, certifications, market surveillance
3	Clinical / use safety	Process standards, clinical evaluation, hazard analysis, benefit-risk
2	Technical safety	Technical safety standards, basic safety, biocompatibility
1	Product (design / manufacturing)	Quality management, dFMEA / pFMEA

Regulatory strategy

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Medical Precision b.v.

Medical Precision's start in Medical Devices

The Comfort Marker 2.0 System

Market & Partners

Regulatory Journey

- The Comfort Marker 2.0 is an easy to use system designed and intended for placing reference marks to enable radiotherapy in clinical setting. The product consists of a system and single patient consumables in sets of 50pcs.
- Comfort Marker 2.0 by Medical Precision b.v. – YouTube

Medical

Precision b.v.

World Wide Distributor

*With the exception of

Dutch Market and University

Hospital Zagreb, Croatia who are reserved territories for Medical Precision.

CQ MEDICAL

Formerly CIVCO RT™ and Qfix®

Regulatory support and consultancy

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Regulatory Journey

CE Class IIa

FDA Class II DeNovo cleared + additional device claims approved through 510K submission.

ISO

CE

FDA

ISO 13485 Certified – Currently with BSI, soon recertifying with CE Notified Body ECM.