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EAMBES Fellows Meeting, 12th March 2018, London

EU Medical Device Regulations Challenges to Research and Startups

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Pirkanmaa Hospital District

‘EU funded research
is shaping your future’

BASIC RESEARCH

APPLIED RESEARCH

Science push

What do I know of the future?

CONCEPT

PROOF OF CONCEPT

CLINICAL EVIDENCE

DISCOVERY

PROTOTYPE

FIELD EVALUATION

INCUBATION & ITERATION

SCALE UP & COMMERCIALIZATION

technology design

field tests & user input

business & economic model

SPIN OUT

ENGAGEMENT OF USERS

Market pull

CO-CREATION

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The future seems to be more

Volatile - The nature and dynamics of change, and the nature and speed of change forces and change catalysts.

Uncertain - The lack of predictability, the prospects for surprise, and the sense of awareness and understanding of issues and events.

Complex - The multiplex of forces, the confounding of issues, no cause-and-effect chain and confusion that surrounds organization.

Ambiguous - The haziness of reality, the potential for misreads, and the mixed meanings of conditions; cause-and-effect confusion

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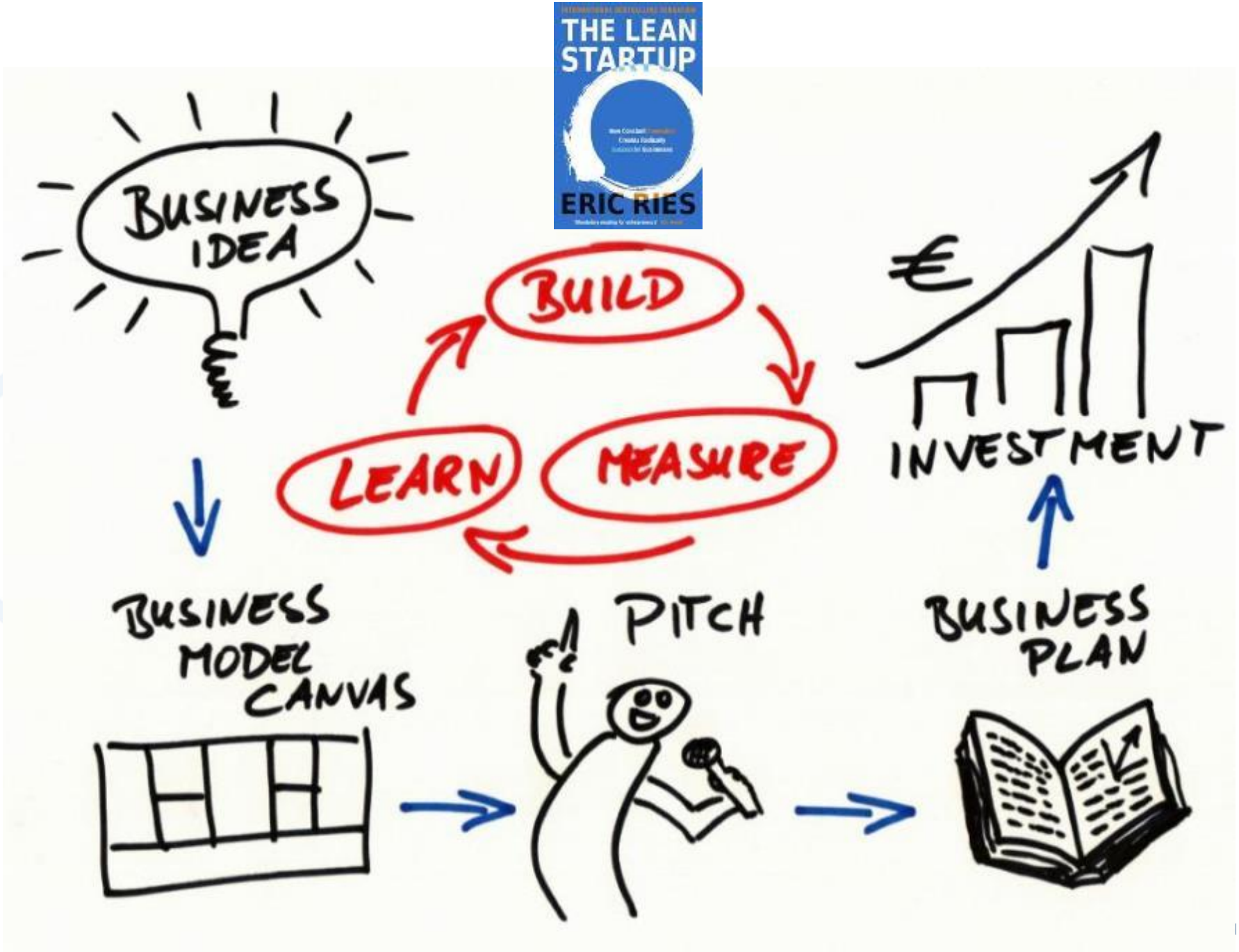
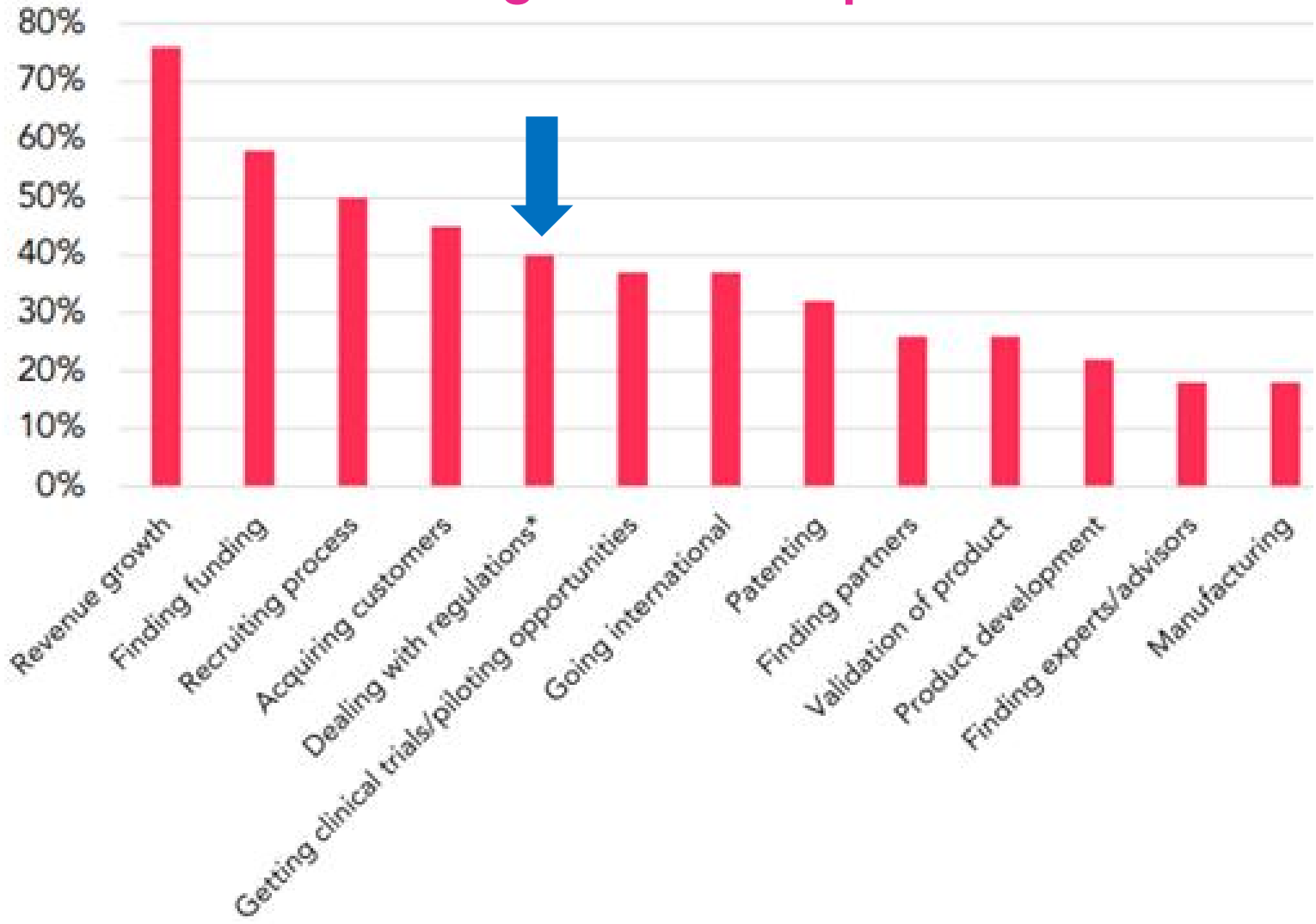

THE LEAN STARTUP
ERIC RIES
BUSINESS IDEA
BUILD
LEARN
MEASURE
INVESTMENT
BUSINESS MODEL CANVAS
PITCH
BUSINESS PLAN

Challenges Startups Face



The Finnish Health Startup Industry Report 2017

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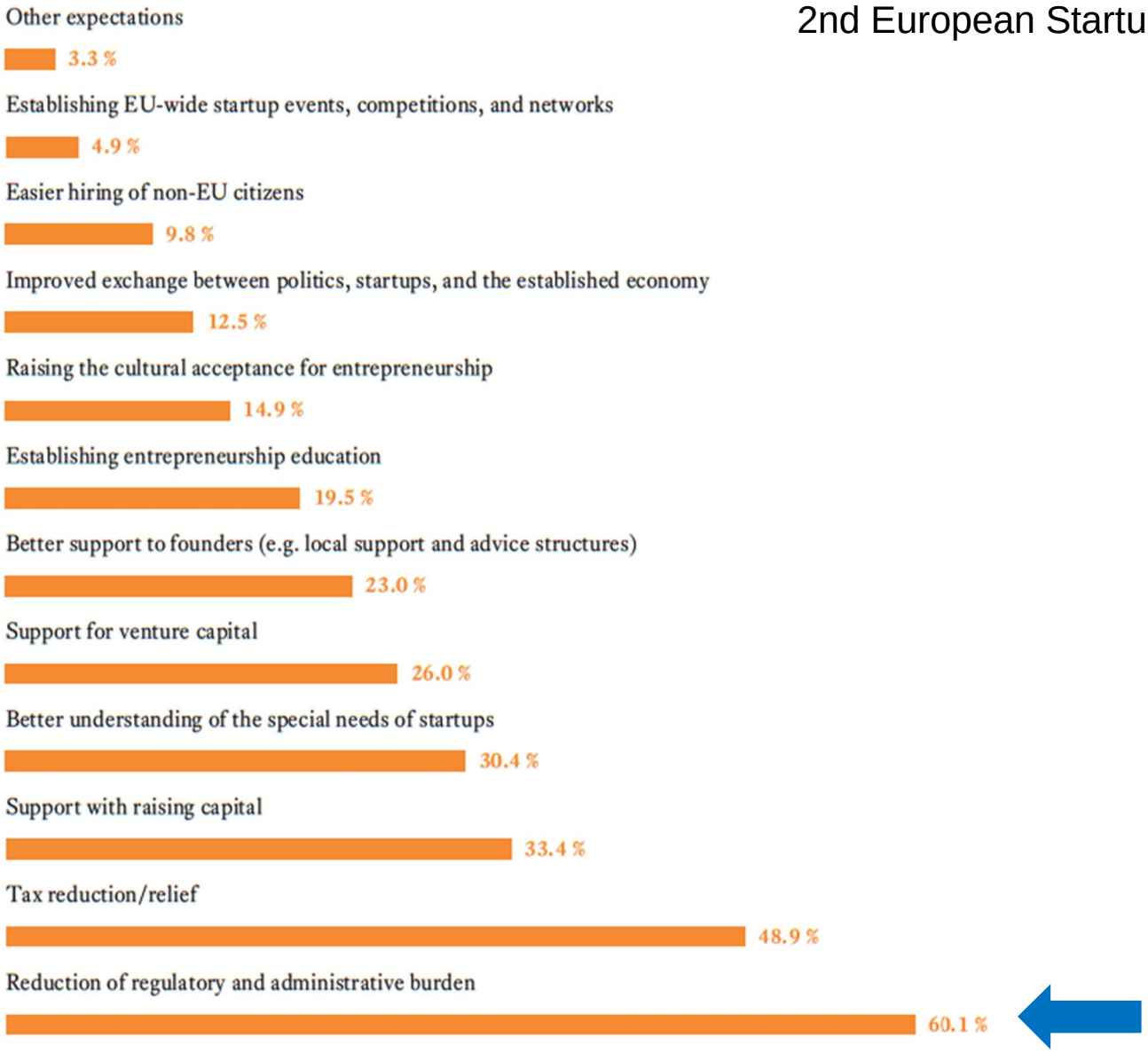
Startup expectations about politics in EU

2nd European Startup Monitor 2016



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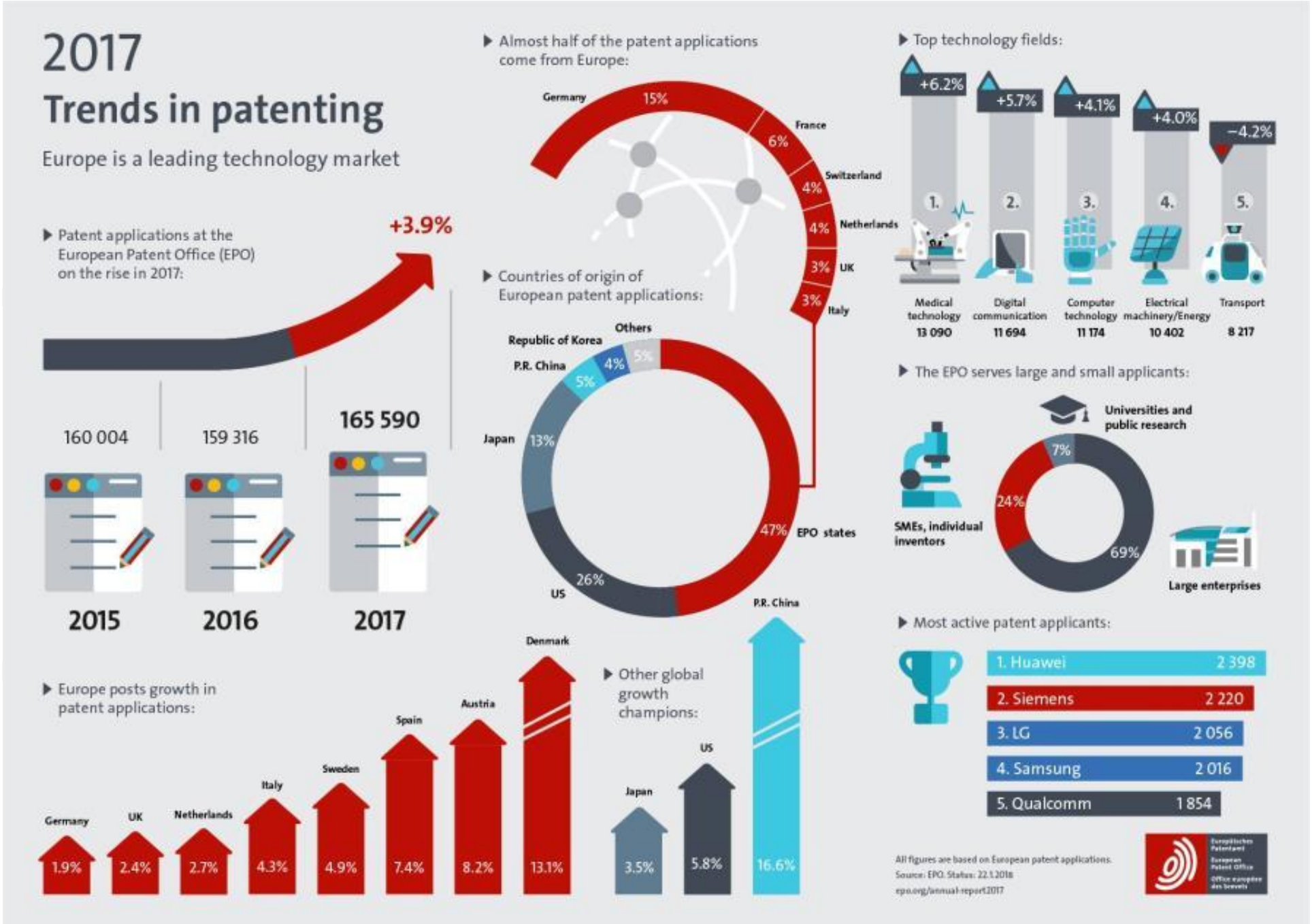
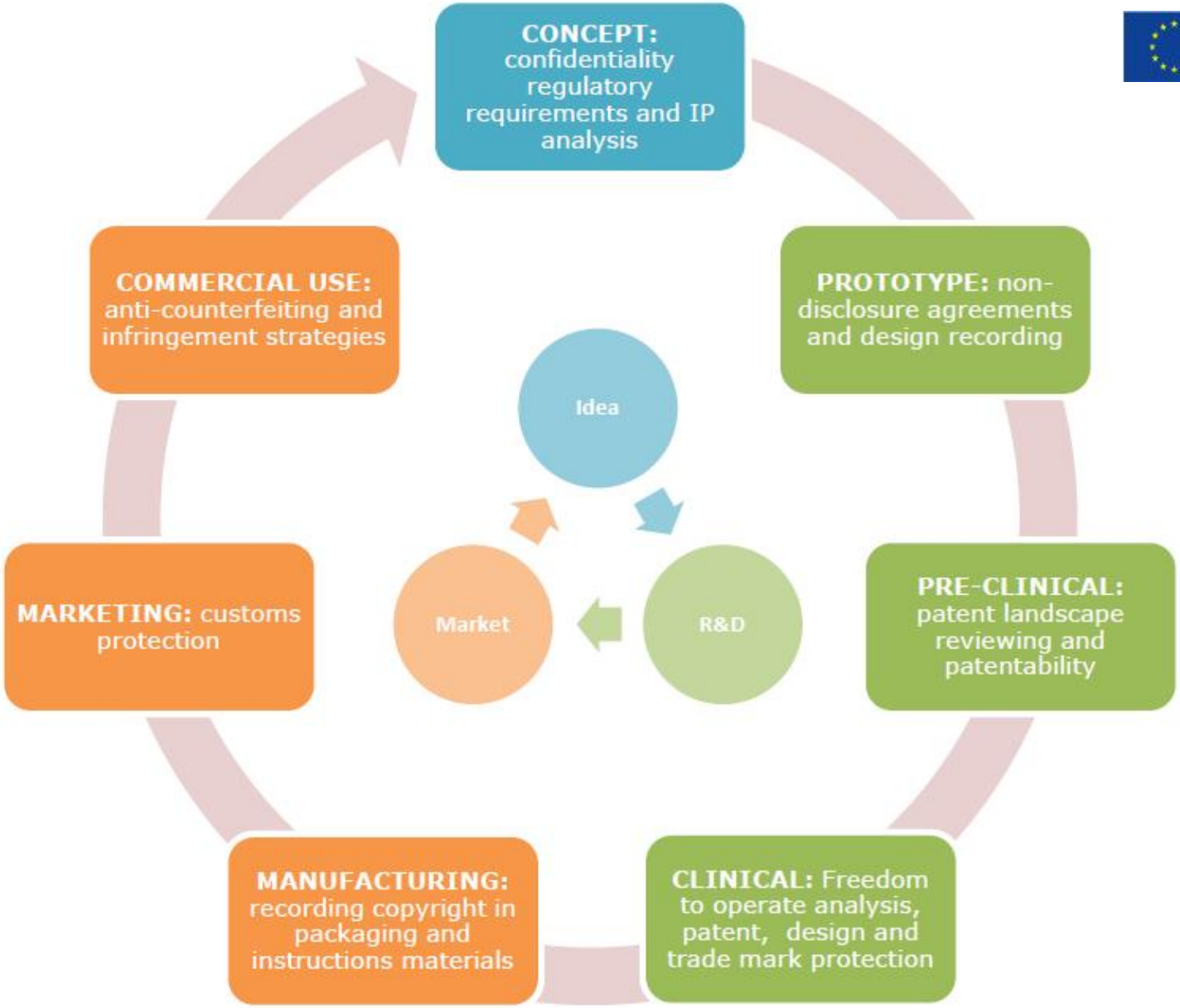

2017
Trends in patenting
Europe is a leading technology market
Patent applications at the European Patent Office (EPO) on the rise in 2017:
+3.9%
160 004
159 316
165 590
2015
2016
2017
Almost half of the patent applications come from Europe:
Germany 15%
France 6%
Switzerland 4%
Netherlands 4%
UK 3%
Italy 3%
Countries of origin of European patent applications:
Others 5%
Republic of Korea 4%
P.R. China 5%
Japan 13%
US 26%
47% EPO states
Top technology fields:
+6.2%
+5.7%
+4.1%
+4.0%
−4.2%
1. Medical technology 13 090
2. Digital communication 11 694
3. Computer technology 11 174
4. Electrical machinery/Energy 10 402
5. Transport 8 217
The EPO serves large and small applicants:
SMEs, individual inventors
Universities and public research 7%
24%
69%
Large enterprises
Most active patent applicants:
1. Huawei 2 398
2. Siemens 2 220
3. LG 2 056
4. Samsung 2 016
5. Qualcomm 1 854
Europe posts growth in patent applications:
Germany 1.9%
UK 2.4%
Netherlands 2.7%
Italy 4.3%
Sweden 4.9%
Spain 7.4%
Austria 8.2%
Denmark 13.1%
Other global growth champions:
Japan 3.5%
US 5.8%
P.R. China 16.6%
All figures are based on European patent applications.
Source: EPO. Status: 22.1.2018
epo.org/annual-report2017

European IPR Helpdesk

2014



Intellectual property considerations for medical devices

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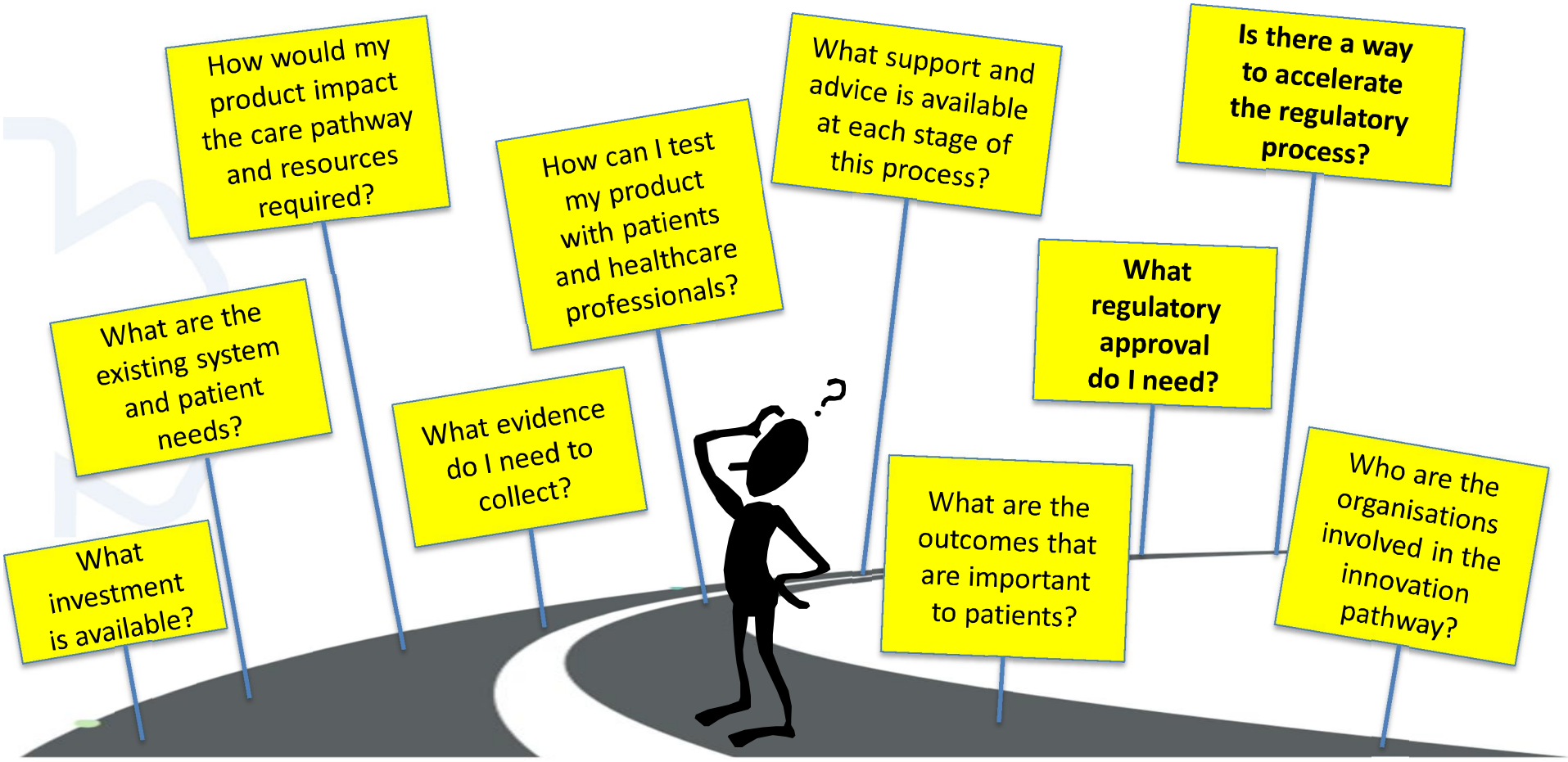
Navigating the innovation pathway



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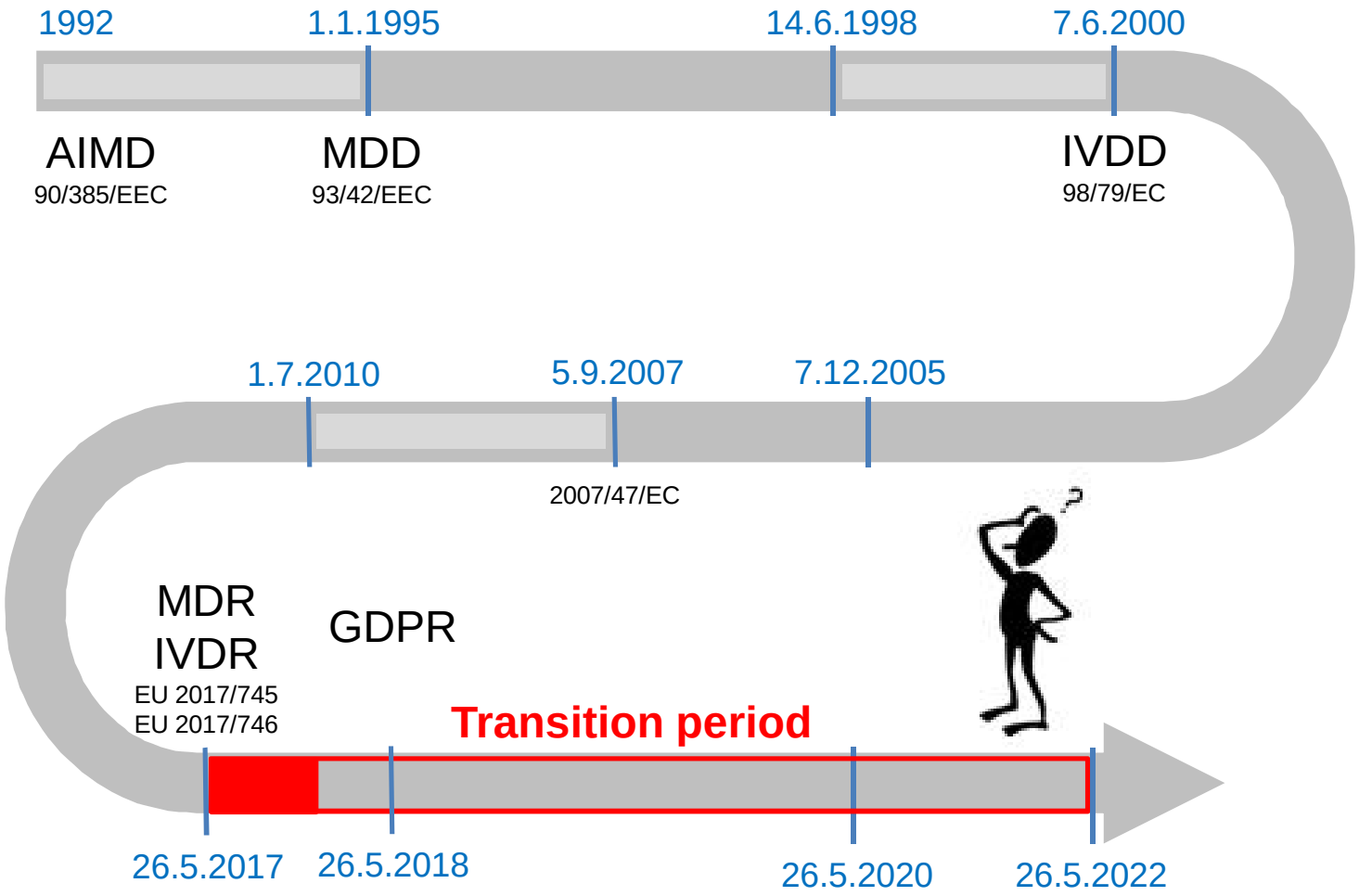

AIMD = Active Implantable Medical Device Directive
MDD = Medical Device Directive
IVDD = In vitro Diagnostic Medical Device Directive
MDR = Medical Device Regulation
IVDR = In vitro Diagnostic Medical Device Regulation

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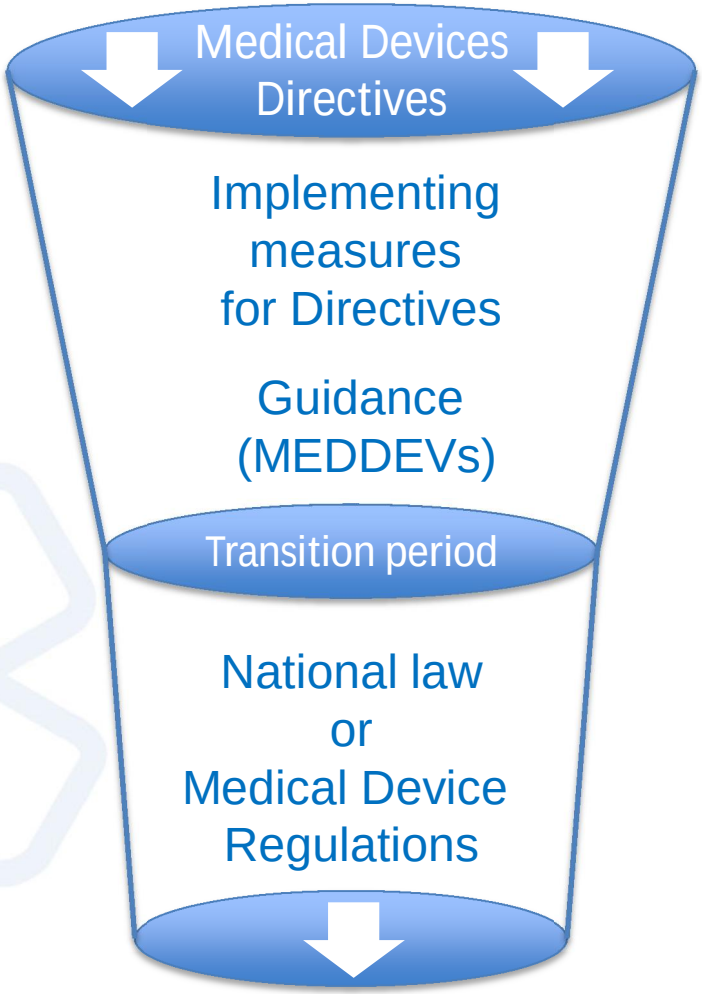

Medical Device Regulations Implementing acts

CAMD
Competent Authorities for Medical Devices

Published: Medical Devices Regulation/In-vitro Diagnostics Regulation (MDR/IVDR) Roadmap
07/11/2017

Available now: MDR and IVDR transitional FAQs
17/01/2018

https://ec.europa.eu/growth/sectors/medical-devices/dialogues-parties_en#taskforces

http://www.camd-europe.eu/news

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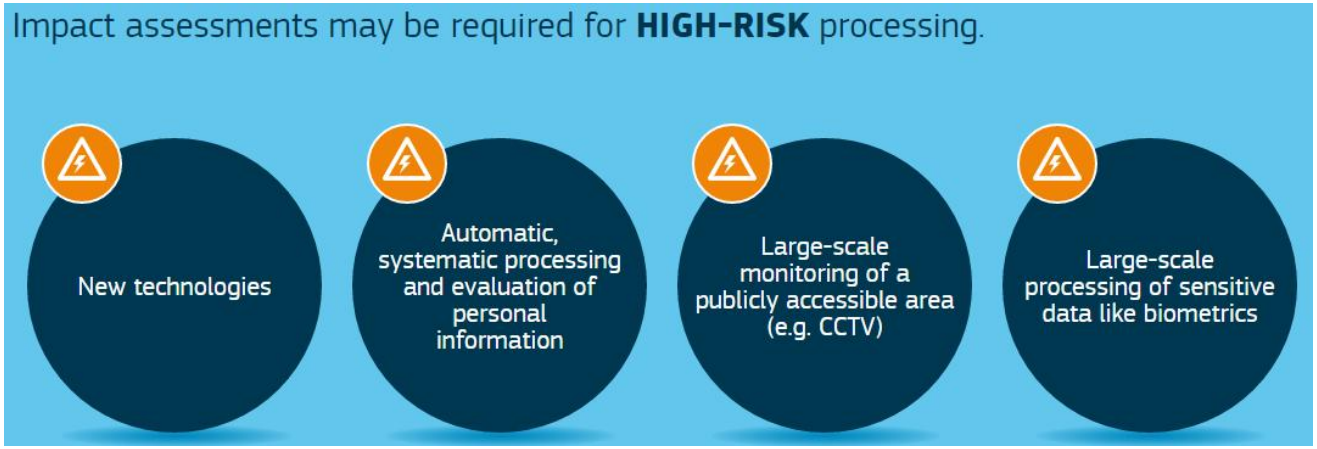

http://ec.europa.eu/justice/smedataprotect/index_en.htm

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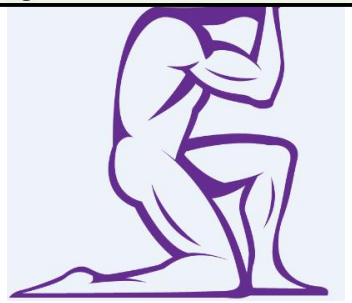
Do you understand MDR / IVDR?

	Recitals	Articles	Annexes
MDR	1–101	1–123	I–XVII
	13 pages	79 pages	83 pages

	Recitals	Articles	Annexes
IVDR	1–101	1–113	I–XV
	11 pages	71 pages	73 pages



"This Regulation shall be binding in its entirety and directly applicable in all Member States."

European Commission > Growth > Sectors > Medical devices > Regulatory framework

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54 a §

Language requirements according to MD and IVD Regulations

For the information and the documents specified in Article 10 (11) of the MD Regulation and Article 10 (10) of the IVD Regulation, the provisions on the languages of Section 12, subsection 2 of this Act applies.

The information in accordance with the first subparagraph of Article 18 (1) of the MD Regulation shall be drawn up in Finnish, Swedish and English.

The documents referred to in Articles 19 (1), 41 (1) and 56 (1) of the MD Regulation and Article 17 (1), the first paragraph of Article 37 and Article 51 of the IVD Regulation shall be drawn up in Finnish, Swedish or English. The documents referred to in Article 52 (12) of the MD Regulation and Article 48 (12) of the IVD Regulation shall be required available in Finnish, Swedish or English.

The National Supervisory Authority for Welfare and Health may, if required, require that the manufacturer and the authorized representative must provide the Supervisory Authority with free of charge the information and documents referred to in, or parts thereof, Article 10 (14) and Article 11 (3), second subparagraph, (d) of the MD Regulation and Articles 10 (13) and 11 (3), second subparagraph, (d) of the IVD Regulation in Finnish or Swedish.

The National Supervisory Authority for Welfare and Health may order the manufacturer to make a free of charge the notifications specified in Article 89 (8) of the MD Regulation and Article 84 (8) of the IVD Regulation in the languages necessary for safety.

The National Supervisory Authority for Welfare and Health may issue more specific provisions of the language requirements of the information and documents specified in this section and of the procedures to comply these provisions.

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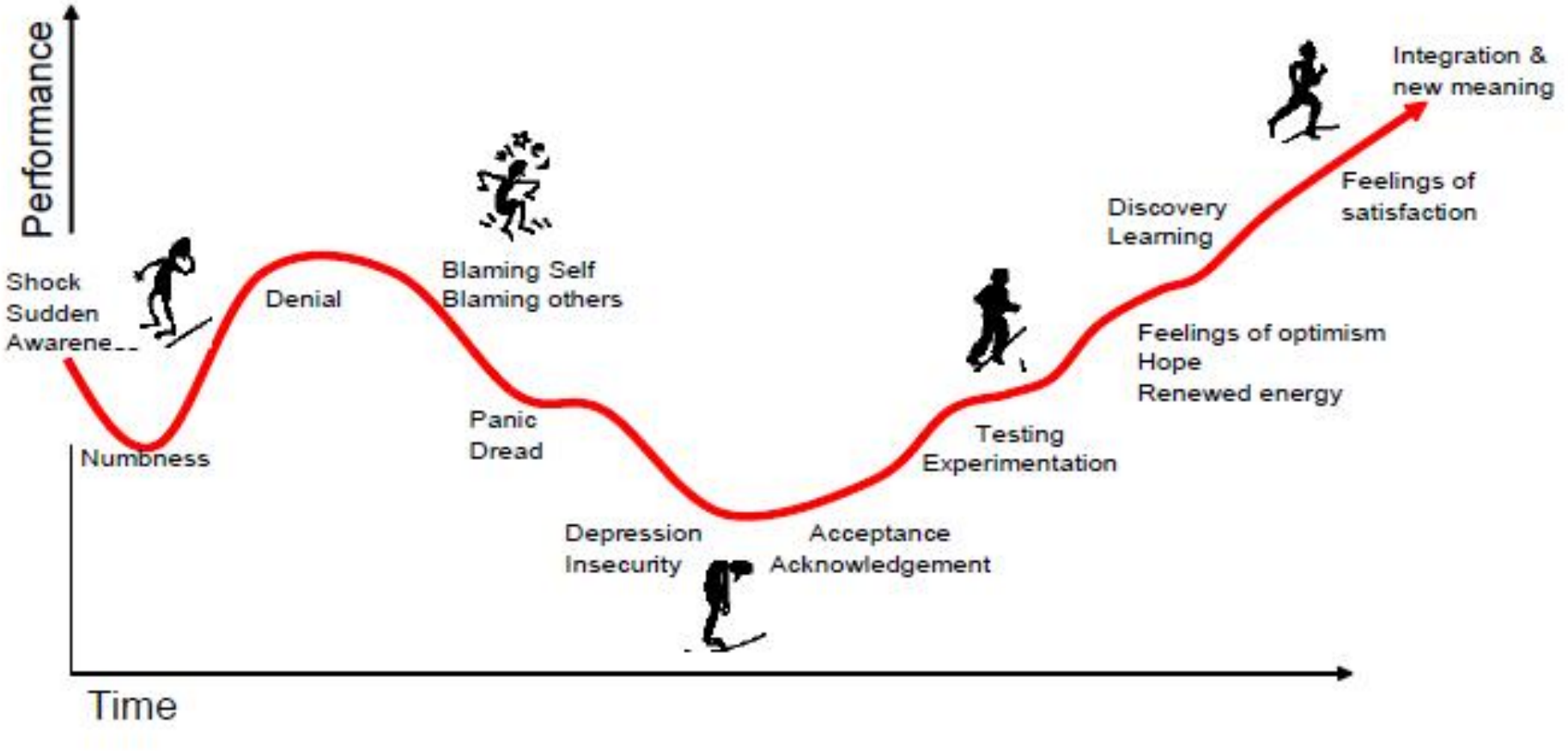
Regulation Learning Curve?



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The Survival Guide to EU Medical Device Regulations

Available at www.amazon.com (Paperback, Kindle)

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Do you speak MDR and IVDR?

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

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

In vitro diagnostic medical device

means any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following:

a) concerning a physiological or pathological process or state;

b) concerning congenital physical or mental impairments;

c) concerning the predisposition to a medical condition or a disease;

d) to determine the safety and compatibility with potential recipients;

e) to predict treatment response or reactions;

f) to define or monitoring therapeutic measures.

Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices;

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Classification

Medical device	In vitro diagnostic medical device
Devices shall be divided into classes I, IIa, IIb and III, taking into account the *intended purpose* of the devices and their inherent risks. Classification rules in Annex VIII	Devices shall be divided into classes A, B, C and D, taking into account the *intended purpose* of the devices and their inherent risks. Classification rules in Annex VIII

Conformity assessment

Medical device	In vitro diagnostic medical device
Manufacturer shall undertake an assessment of the conformity in accordance with the applicable conformity assessment procedures set out in Annexes IX to XI.	Manufacturers shall undertake an assessment of the conformity in accordance with the applicable conformity assessment procedures set out in Annexes IX to XI

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Placing on the market and putting into service

A device may be placed on the market or put into service **only if it complies with the Regulation** when duly supplied and properly installed, maintained and used in accordance with its *intended purpose*.

A device shall meet **the general safety and performance requirements** which apply to it, taking into account its *intended purpose*.

Demonstration of conformity with the general safety and performance requirements shall include **a clinical evaluation** (medical devices) and **a performance evaluation** (in vitro diagnostic medical devices

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Harmonised standards and common specifications

- Devices that are in conformity with the relevant **harmonised standards**, or the relevant parts of those standards, the references of which have been published in the Official Journal of the European Union, shall be presumed to be in conformity with the requirements of this Regulation covered by those standards or parts.

- This applies also to **system or process requirements** including those relating to quality management systems, risk management, post-market surveillance systems, performance studies, clinical evidence or post-market performance follow-up.

- The concept of **common specifications** is introduced also to medical devices. Where no harmonised standards exist or where relevant harmonised standards are not sufficient, or where there is a need to address public health concerns, the Commission, after having consulted the Medical Device Coordination Group, may adopt common specifications.

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GENERAL SAFETY AND PERFORMANCE REQUIREMENTS

I GENERAL REQUIREMENTS

II REQUIREMENTS REGARDING **DESIGN** AND MANUFACTURE

Chemical, physical and biological properties

Infection and microbial contamination

Devices incorporating a medicinal product

Devices incorporating materials of biological origin

Construction of devices and interaction with their environment

Devices with a diagnostic or measuring function

Protection against radiation

Electronic programmable systems

Active devices and devices connected to them

Particular requirements for active implantable devices

Protection against mechanical and thermal risks

Protection against the risks posed to the patient or user by devices supplying energy or substances

Protection against the risks posed by medical devices intended by the manufacturer for use by lay persons

III REQUIREMENTS REGARDING THE INFORMATION SUPPLIED WITH THE DEVICE

3. Manufacturers shall establish, implement, document and maintain **a risk management system**. Risk management shall be understood as a continuous iterative process throughout the entire lifecycle of a device, requiring regular systematic updating. In carrying out risk management manufacturers shall:

(a) establish and document **a risk management plan** for each device;

(b) identify and analyse the known and foreseeable **hazards** associated with each device;

(c) estimate and evaluate the **risks** associated with, and occurring during, the intended use and during reasonably foreseeable misuse;

(d) eliminate or control the risks referred to in point (c) in accordance with the requirements of Section 4;

(e) evaluate the impact of information from the production phase and, in particular, from the post-market surveillance system, on hazards and the frequency of occurrence thereof, on estimates of their associated risks, as well as on the overall risk, benefit-risk ratio and risk acceptability; and

(f) based on the evaluation of the impact of the information referred to in point (e), if necessary amend control measures in line with the requirements of Section 4.

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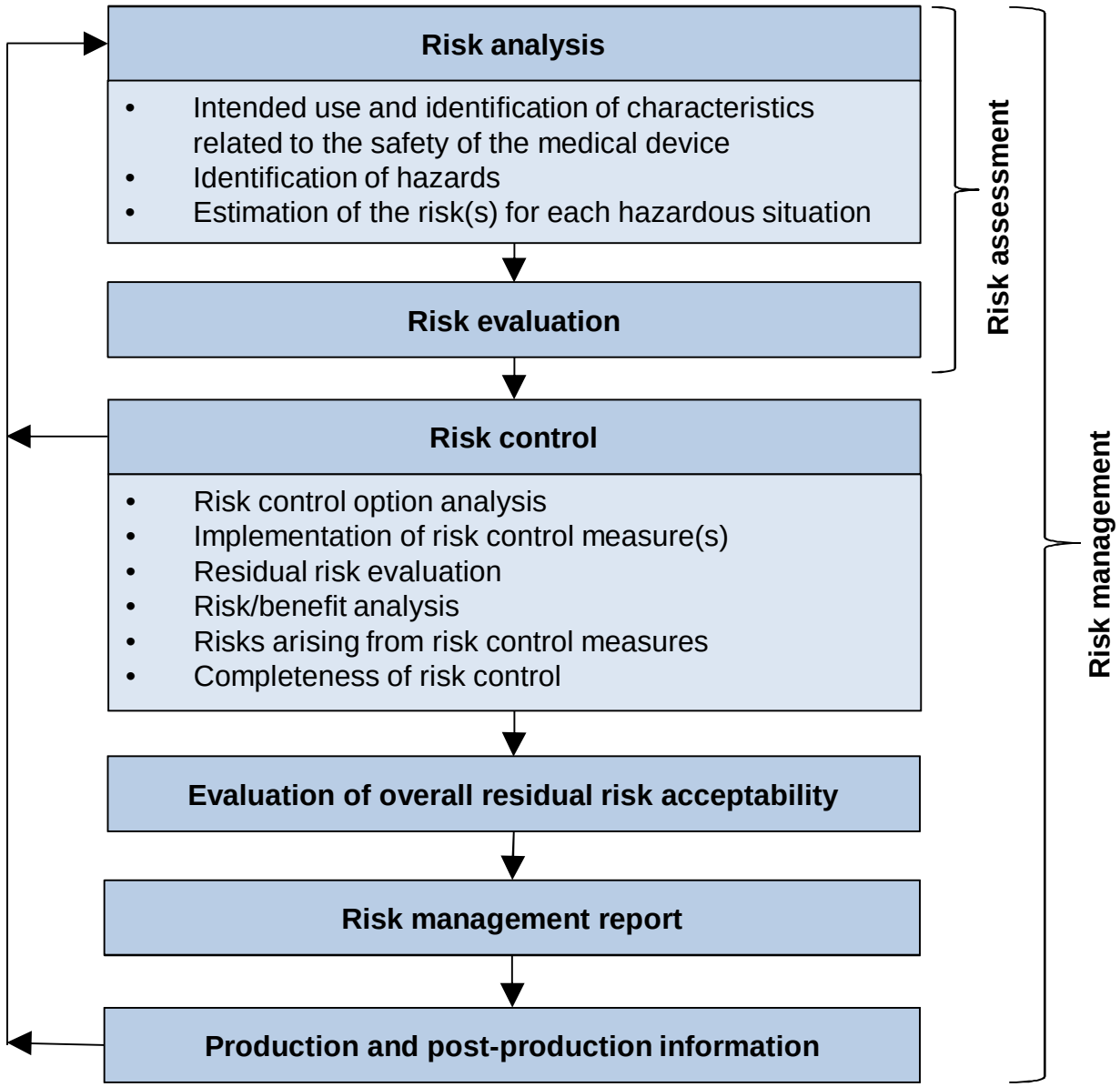
EN ISO 14971



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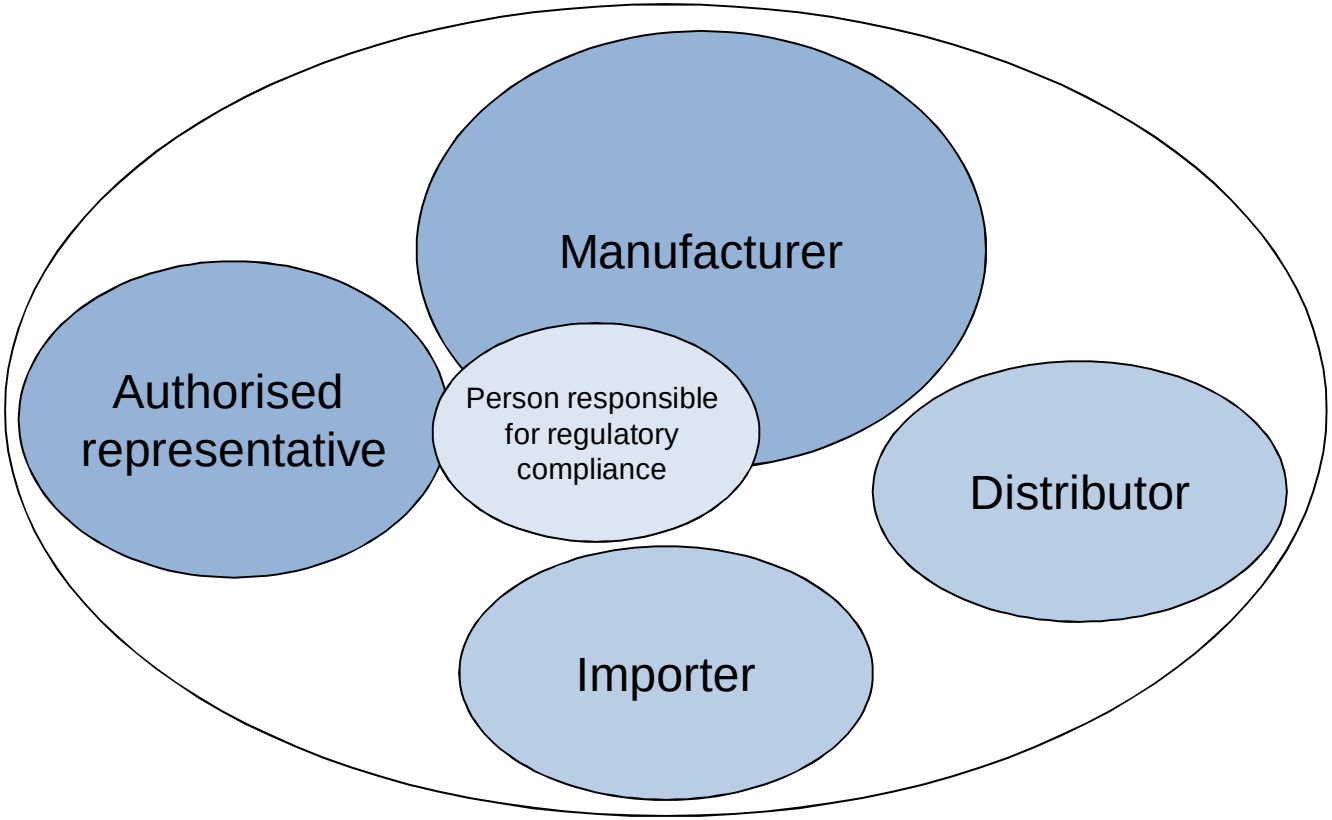
Economic operators



Manufacturer means a natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and **markets that device under its name or trademark**;

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Technical documentation

The technical documentation and the summary thereof to be drawn up by the **manufacturer** shall be presented in a clear, organised, readily searchable and unambiguous manner and shall include:

- device description and specification, including variants and accessories
- information to be supplied by the manufacturer
- design and manufacturing information
- general safety and performance requirements
- benefit-risk analysis and risk management
- product verification and validation

The level for detail concerning technical documentation has increased.

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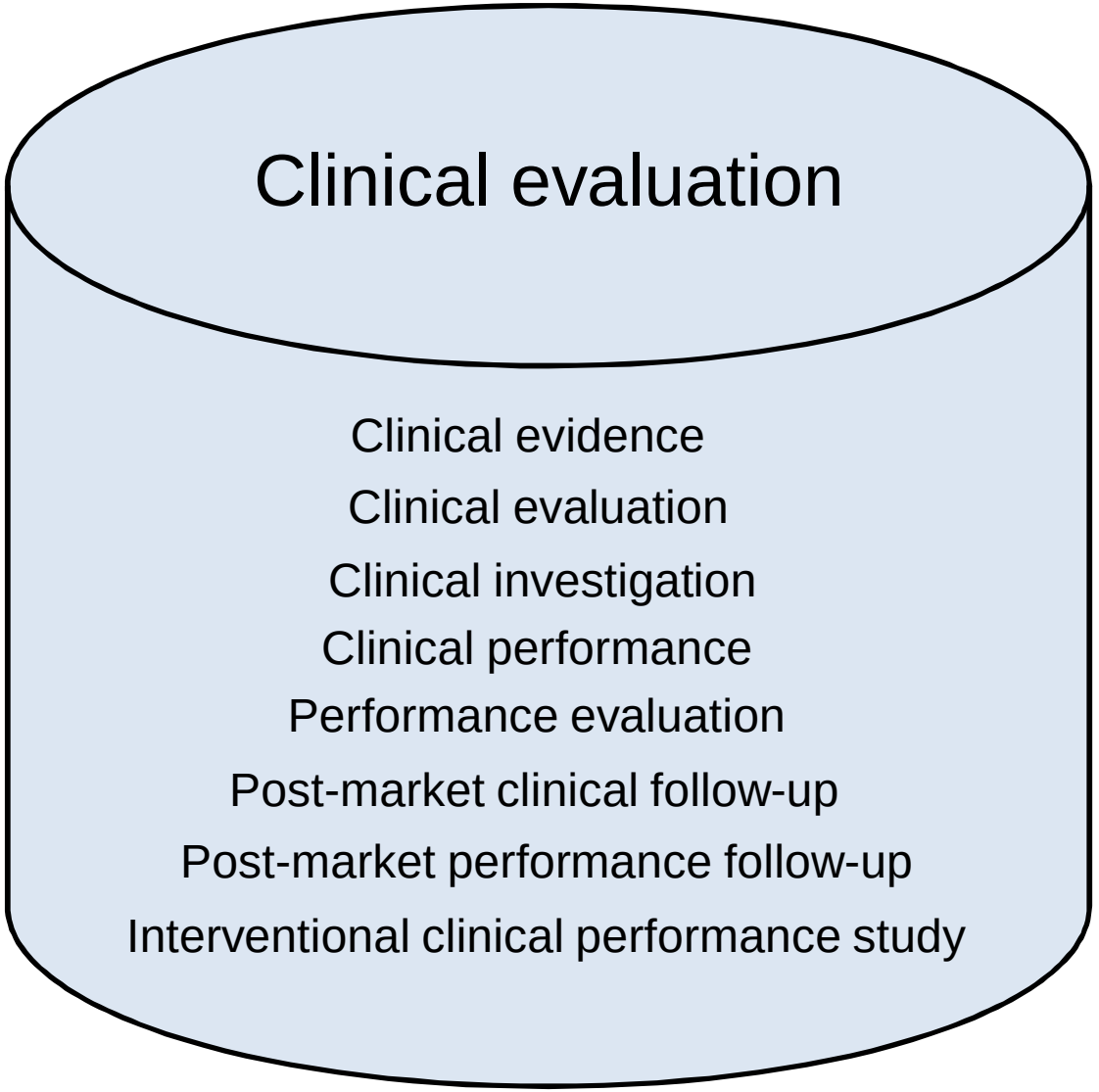
MDR IVDR



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Clinical evaluation (MDR)

To plan, continuously conduct and document a clinical evaluation manufacturers shall:

a) establish and update **a clinical evaluation plan**,
b) identify available clinical data relevant to the device and its intended purpose and any gaps in clinical evidence through **a systematic scientific literature review**;
c) appraise all relevant clinical data by evaluating their suitability for establishing the safety and performance of the device;
d) generate, through properly designed **clinical investigations** in accordance with the **clinical development plan**, any new or additional clinical data necessary to address outstanding issues; and
e) analyse all relevant clinical data in order to reach conclusions about the safety and clinical performance of the device including its clinical benefits.

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Post-market clinical follow-up (MDR)

PMCF plan shall specify the methods and procedures for proactively collecting and evaluating clinical data with the aim of:

a) confirming the safety and performance of the device **throughout its expected lifetime**,

b) identifying previously unknown side-effects and monitoring the identified side-effects and contraindications,

c) identifying and analysing emergent risks on the basis of factual evidence,

d) ensuring the continued acceptability of the benefit-risk ratio, and

e) identifying possible **systematic misuse or off-label use** of the device, with a view to verifying that the intended purpose is correct.

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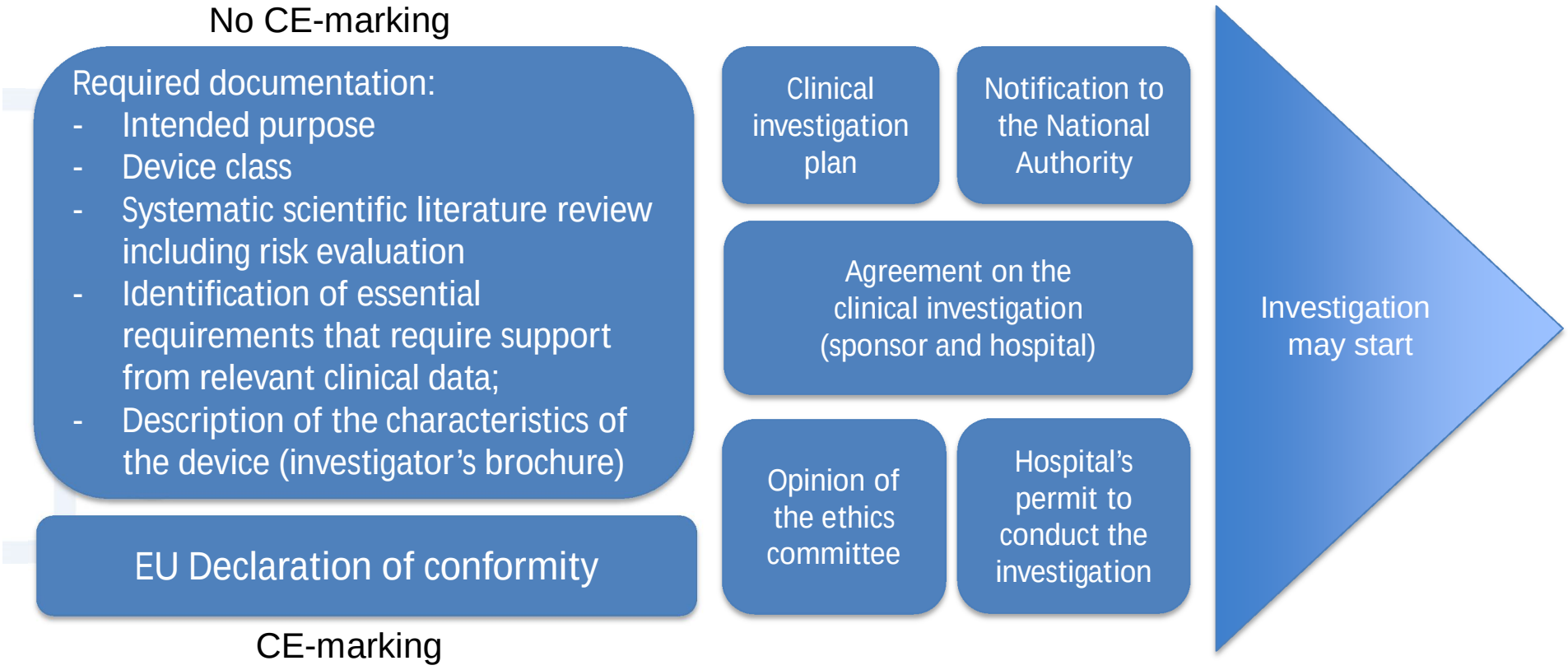
Investigational device



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Traceability

Economic operators shall be able to identify the following to the competent authority:

a) any economic operator to whom they have directly supplied a device

b) any economic operator who has directly supplied them with a device;

c) any health institution or healthcare professional to which they have directly supplied a device.

The Unique Device Identification (UDI) system should apply to all devices placed on the market except custom-made devices, and be based on internationally recognised principle.

The Commission shall set up, maintain and manage the **European database** on medical devices (Eudamed)

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MDR IVDR

Vigilance and post-market surveillance

Periodic safety update reports

Reports by manufacturers on trends

Field safety notices by manufacturers

Periodic summary reports by manufacturers

Reports by manufacturers on serious incidents and field safety corrective actions

Information to be exchanged between the competent authorities of the Member States and between them and the Commission

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The quality management system

Shall address at least the following aspects:

a) strategy for regulatory compliance, including compliance with **conformity assessment procedures** and procedures for management of modifications to the devices covered by the system;
b) identification of applicable **general safety and performance requirements** and exploration of options to address those requirements;
c) responsibility of the management;
d) resource management, including selection and control of suppliers and sub-contractors;
e) risk management;
f) clinical evaluation, including a post-market clinical follow-up / post-market performance follow-up;

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The quality management system

g) product realisation, including planning, design, development, production and service provision;

h) verification of the UDI assignments to all relevant devices and ensuring consistency and validity of information provided;

i) setting-up, implementation and maintenance of a **post-market surveillance system**;

j) handling communication with competent authorities, notified bodies, other economic operators, customers and/or other stakeholders;

k) processes for reporting of serious incidents and field safety corrective actions in the context of **vigilance**;

l) management of corrective and preventive actions and verification of their effectiveness;

m) processes for monitoring and measurement of output, data analysis and product improvement

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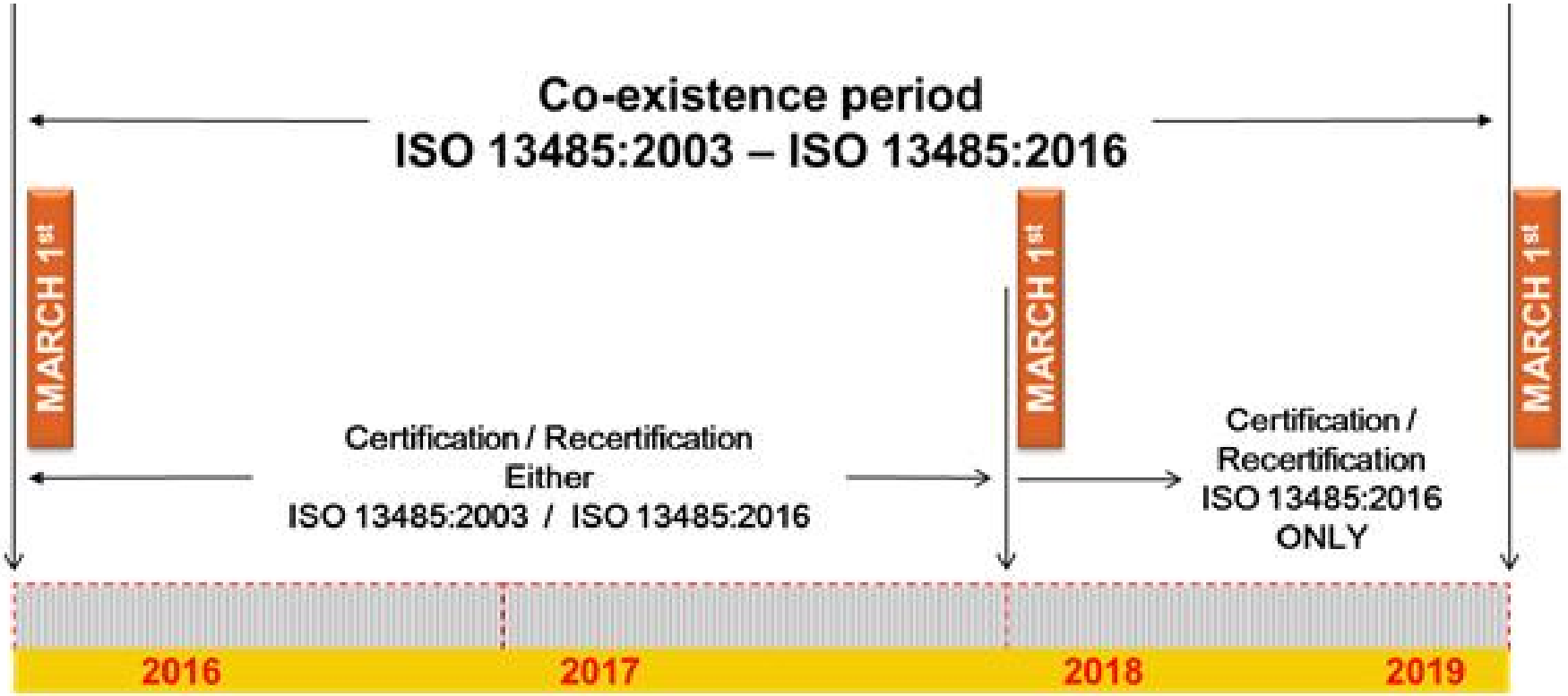
EN ISO 13485:2016

Medical devices - Quality management systems – Requirements for regulatory purposes



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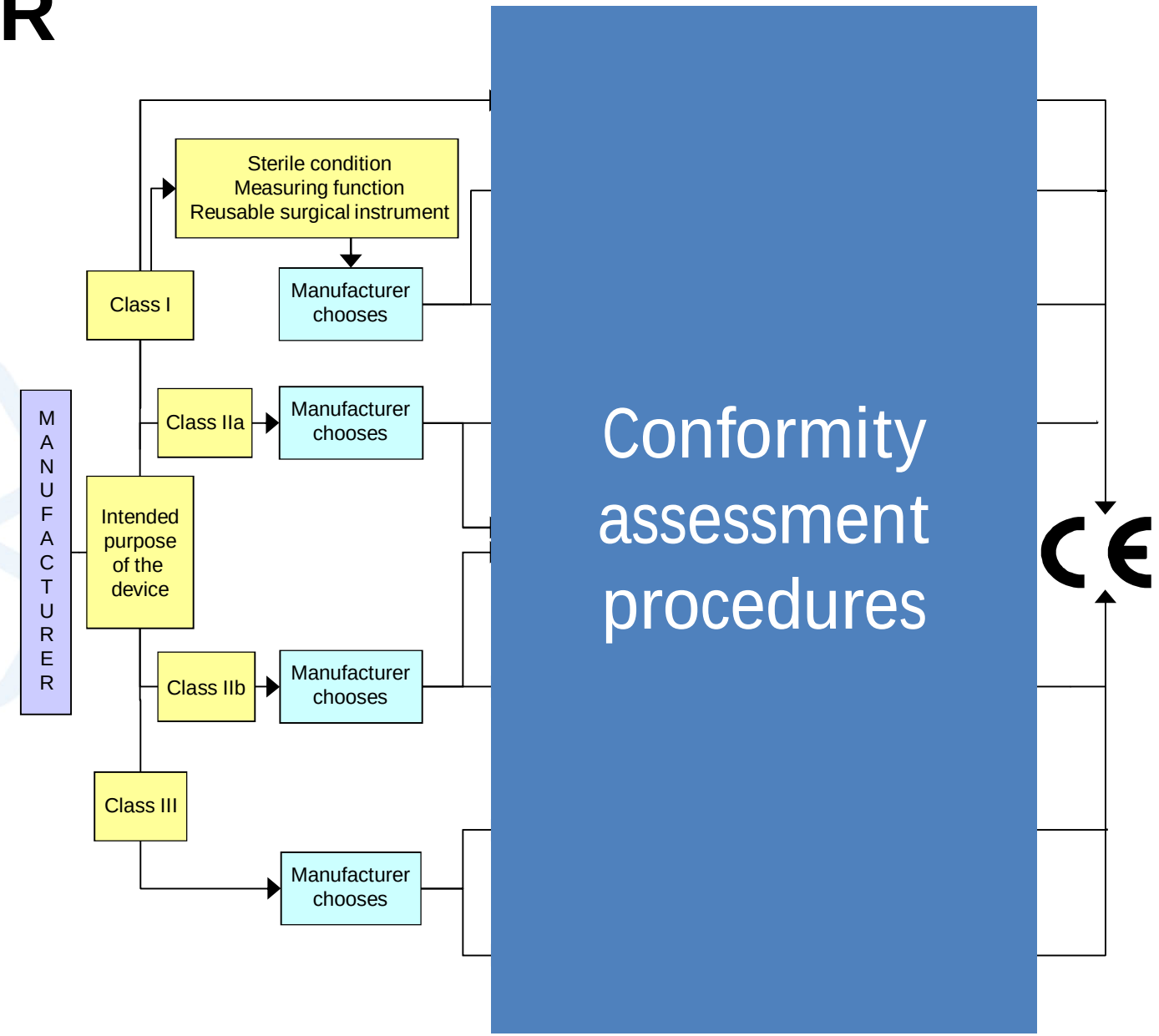
MDR



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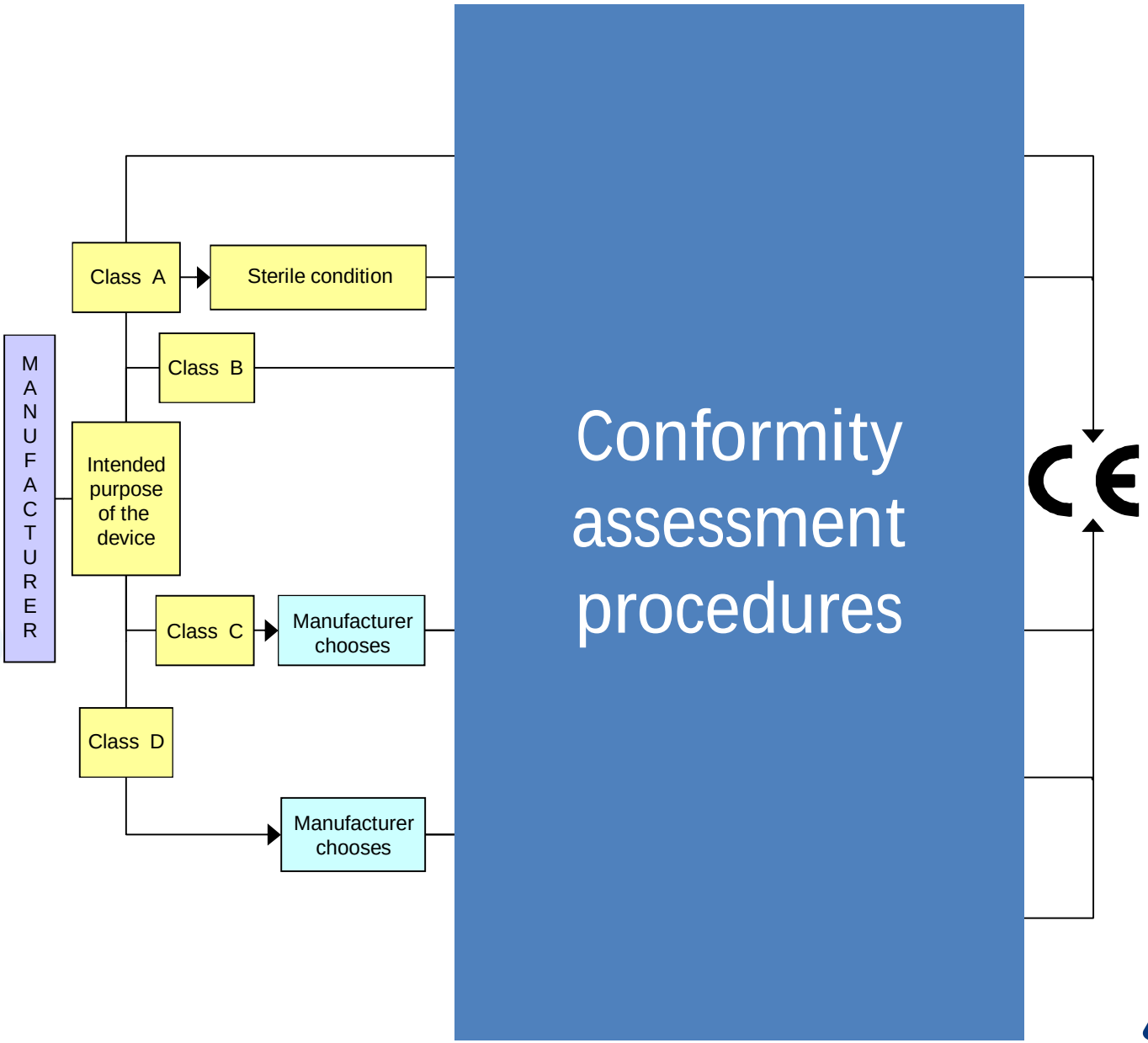
IVDR



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The manufacturer shall

- establish, document, implement and maintain a **system for risk management**
- conduct a **clinical evaluation** or a **performance evaluation** (including a post-market clinical follow-up / post-market performance follow-up)
- draw up and keep up to date **technical documentation** for the devices
- draw up an **EU declaration of conformity** and affix the **CE marking** of conformity
- comply with the obligations relating to the **Unique Device Identification (UDI) system** and with the **registration** obligations
- ensure that **procedures** are in place to keep series production in conformity with the requirements
- establish, document, implement, maintain, keep up to date and continually improve a **quality management system**
- **keep** the technical documentation, the EU declaration of conformity and, if applicable, a copy of any relevant certificate, including any amendments and supplements, **available for the competent authorities for a period of at least 10 years** (15 years for implantable devices) after the last device covered by the EU declaration of conformity has been placed on the market.

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The manufacturer shall

- implement and keep up to date the **post-market surveillance system**
- ensure that the **device is accompanied by the information** set out in Annex I of the Regulations in an official Union language(s) determined by the Member State in which the device is made available to the user or patient. The particulars on the label shall be indelible, easily legible and clearly comprehensible to the intended user or patient.
- immediately take the necessary **corrective action** to bring that device into conformity, to **withdraw** it or to **recall** it, as appropriate, and **inform** the distributors of the device in question and, where applicable, the authorised representative and importers accordingly
- if the device presents a serious risk, immediately **inform** the **competent authorities** of the Member States in which they made the device available and, where applicable, the **notified body** that issued a certificate for the device, in particular, of the non-compliance and of any corrective action taken
- have a **system** for recording and reporting of incidents and field safety corrective actions.

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The person responsible for regulatory compliance

- Manufacturers shall have available within their organisation at least one person responsible for regulatory compliance who possesses the requisite expertise in the field of medical devices.

- Micro and small enterprises shall not be required to have the person responsible for regulatory compliance within their organisation but shall have such person **permanently and continuously at their disposal**.

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MDR IVDR

Person responsible for regulatory compliance

Required expertise

(a) a diploma, certificate or other evidence of formal qualification, awarded on completion of a university degree in law, medicine, pharmacy, engineering or another relevant scientific discipline, and at least one year of professional experience in regulatory affairs or in quality management systems relating to medical devices; OR

(b) four years of professional experience in regulatory affairs or in quality management systems relating to medical devices

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The person responsible for regulatory compliance

Shall at least be responsible for ensuring that

a) the conformity of the devices is appropriately checked, in accordance with the quality management system under which the devices are manufactured, before a device is released;
b) the technical documentation and the EU declaration of conformity are drawn up and kept up-to-date;
c) the post-market surveillance obligations are complied
d) the reporting obligations are fulfilled;
e) the statement concerning investigational devices is issued

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Jobs to be done

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