Professioneller Nachweis klinischer Evidenz
Voraussetzung für den Erfolg

GOUYA INSIGHTS
Clinical Development

Klinische Evaluation – vom Planen bis zum Bericht

PD Dr. Ghazaleh Gouya - Lechner

Objectives

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- Target Product Profile and Intended Purpose
- Definition – Clinical Evaluation
- Clinical Development Plan
- Clinical Investigation
- Clinical Evidence

Clinical Evaluation MDR 745/2017

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Article 61 – ANNEX XIV

All products, regardless of the risk classification, require a clinical evaluation as part of the technical documentation requirements of the MD

Challenges in Complying with MDR 745/2017

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Increased costs and durations of assessments

The new rules have led to longer and more expensive product assessment processes, putting a strain on manufacturers' resources.

Lack of predictability in understanding clinical evidence requirements

Manufacturers are struggling to determine the specific types of clinical data needed to comply with the new regulations, leading to uncertainty and delays.

Product withdrawals across various specialties

As a result of the challenges, manufacturers have been forced to withdraw products from the market in multiple medical specialties.

The new regulatory environment has created significant operational and financial challenges for manufacturers, leading to delays of market entry and disruptions in the availability of specialized medical products

Target Product Profile

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Define target population

Cohort who will benefit from the medical device

Therapeutic Indication

Target user

Health Care Professionals

Patients

Specify expected performance and safety criteria

Define performance measures to cover the intented purpose

Patients risks according to risk evaluation

Comparison to SoC

Define the quality attributes and compare to existing SoC

Define the superiority/ non-inferiority or equivalence

A target product profile (TPP) for a medical device is a strategic key document that summarizes the benefits (and risks) of the planned medical device and helps in the development of a regulatory strategy

Target Product Profile

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Product targets	Minimum Acceptable Results	Ideal Results
Primary indication		
Medical Need		
Target Population		
Target User		
Delivery mode		
Key markets/ market size		
Business Model		
Clinical Benefit		
Clinical Risk		
Quality attributes (=selling points)		

represent the **threshold** that must be met for regulatory approval and commercialization

target performance that maximizes the device's safety, performance, market potential, and profitability.

Template

Target Product Profile - Intended Purpose

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Target Product Profile

INTENDED PURPOSE

the use for which a device is intended according to

the data supplied

by the manufacturer

on the label, IFU, in promotional or sales materials and as

specified in the clinical evaluation

Clinical Evaluation

General Safety and Performance Requirements

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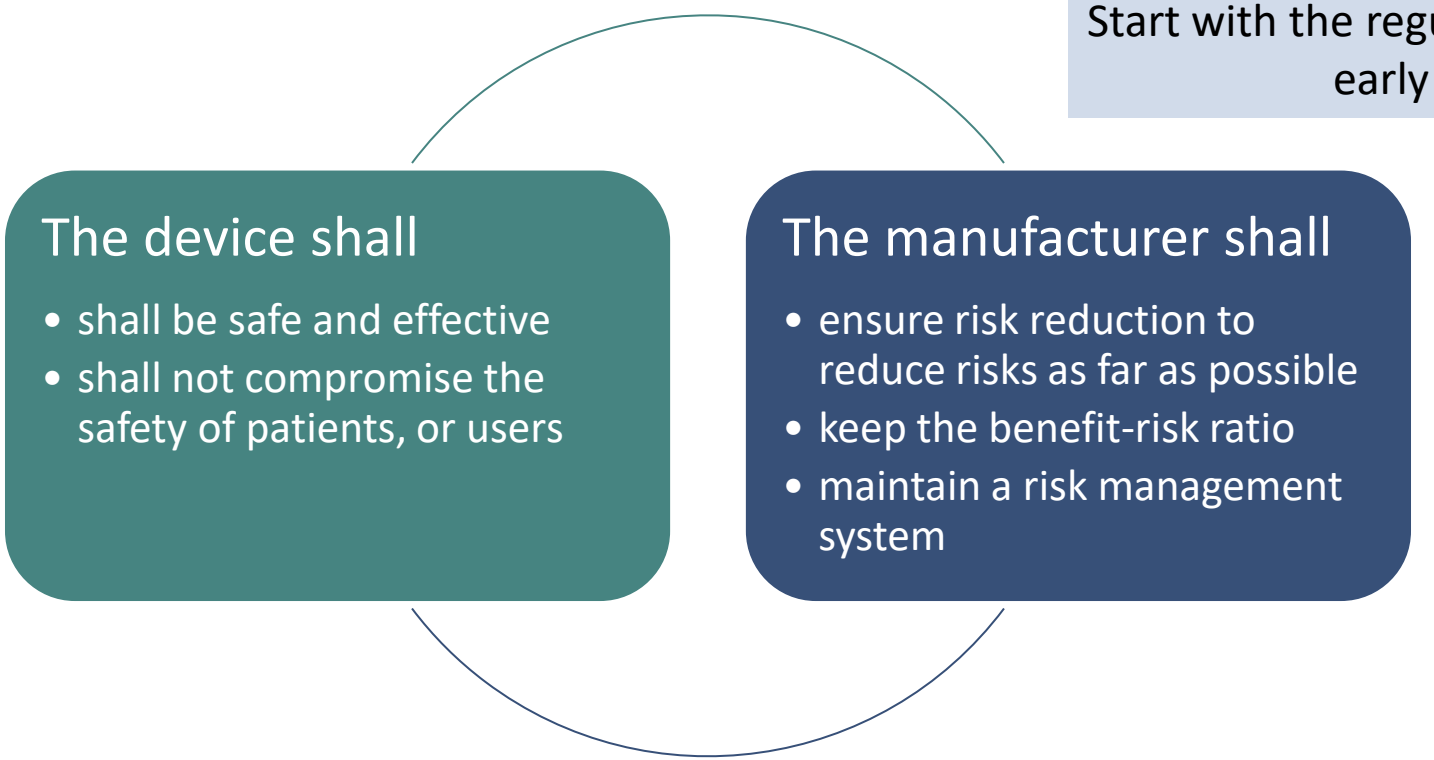
MDR requires that all devices shall be safe and ‘effective’

Start with the regulatory documents as early as possible!



- Define which GSPR they are applicable to your medical devices
- Define harmonised standards, common specifications
- Develop Risk Management
- Develop Clinical Development Plan

ANNEX I
Annex XIV-part A8

What is Clinical Evaluation

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It is “a **systematic and planned process** to **continuously generate, collect, analyze** and assess the clinical data pertaining to a device in order **to verify the safety and performance**, including **clinical benefits** of the device when used as intended by the manufacturer”

- Applies to all classes of medical devices
- To be appropriate to the device in question
- It’s a continuous process

MDR Articles 61 and 54; MEDDEV 2.7. 1 (rev. 4) sections 6 and 10

CEP = Clinical evaluation plan; CER = Clinical evaluation report

Clinical Data Source

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Clinical data from the literature: critical evaluation of the available scientific literature on the safety and performance of **equivalent, similar or the product**	Systematic Literature Review
Clinical investigations: critical evaluation of the results of all available clinical trials (ISO 14155/20916)	Feasibility/ Confirmatory studies
Consideration of any other treatment options currently available, if applicable.	Literature Data

MDR Article 2 and Article 61
MDCG 2020-5, section 5

Systematic Literature Review on Equivalent or Similar Device

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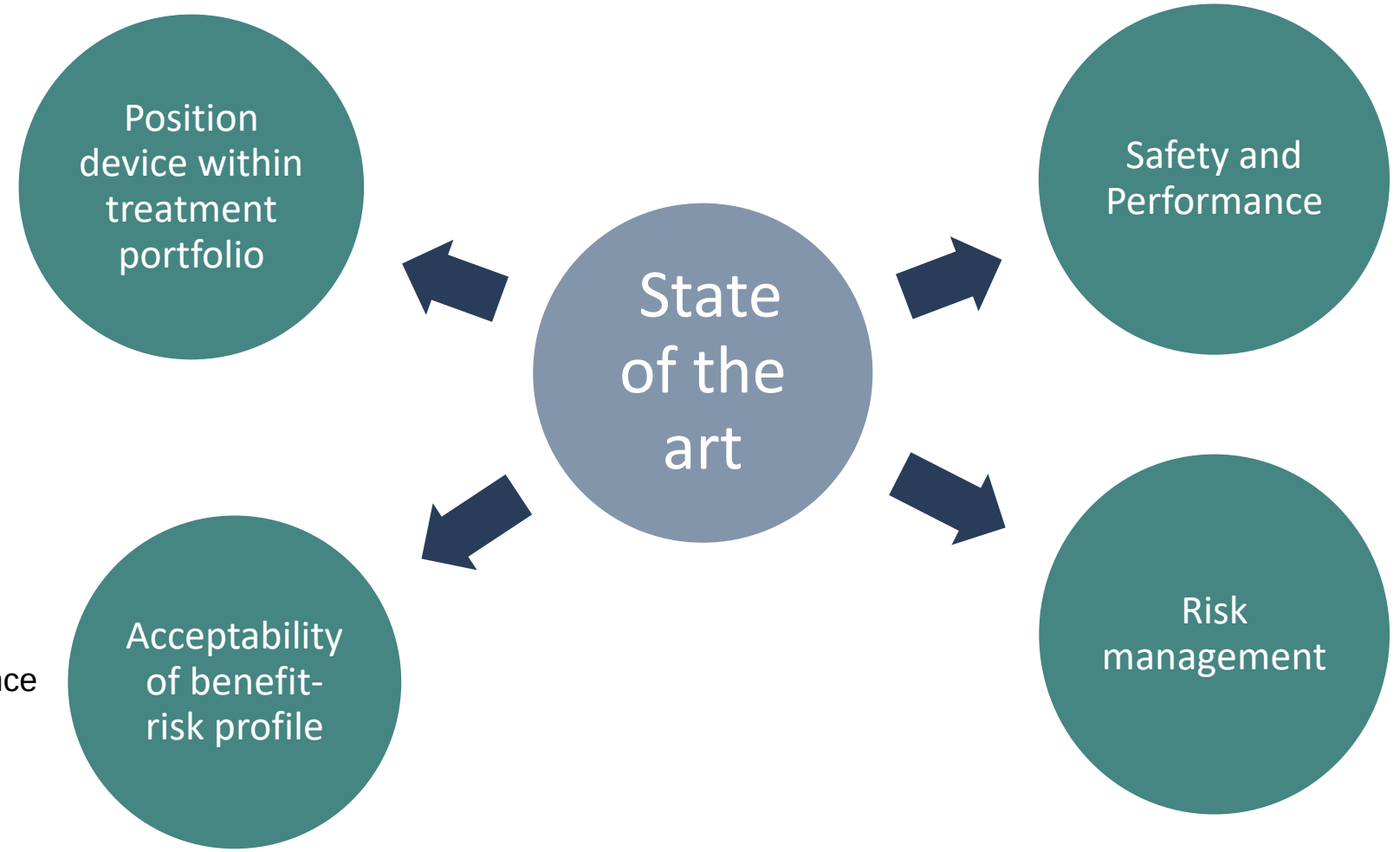
Product differentiation
- CER



- Identify relevant and validated clinical outcome parameters for the intended use
- Use that information in lit search, as well as in clinical investigation design and PMCF design

Define minimum clinically relevant benefit, and/or acceptable occurrence rates of adverse events

- Identify relevant hazards and clinical risks
- Ensure your risk management system is comprehensive

Clinical Evidence proportional to the Risk Class

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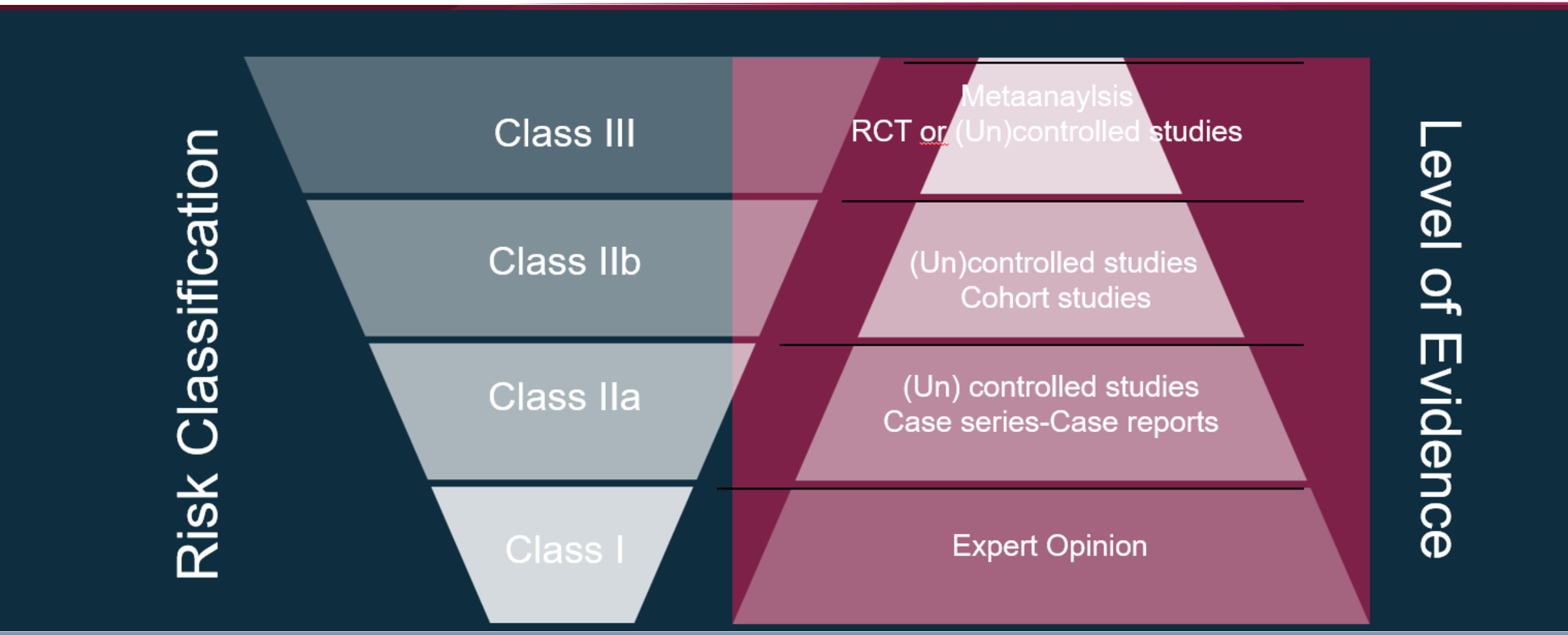

Sufficient evidence must be provided to demonstrate a positive benefit-risk ratio, even in comparison to other available treatment options.

Clinical Development Plan

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All principles of ISO 14155 applicable

Product Verification and Validation

- Biocompatibility test
- Preclinical proof of concept

Preclinical development

Clinical Development

- **Literature Data**
- **Feasibility Study**
  - first-in-man, or pilot studies
  - Other clinical investigations (Article 82) prospective and retrospective
- **Confirmatory study** (Pivotal Study)- prospective and retrospective. description of potential acceptance criteria.

Usability studies can be part of any premarket study

- **PMCF Studies**
  - Clinical Investigation within or outside of CE mark Article 74 MDR (part of pivotal studies)
  - Non-interventional studies (Real Word Evidence) supporting clinical evidence

Postmarket Studies

CE-MARK

ANNEX XIV – Part of CEP

Clinical Data from Clinical Investigations

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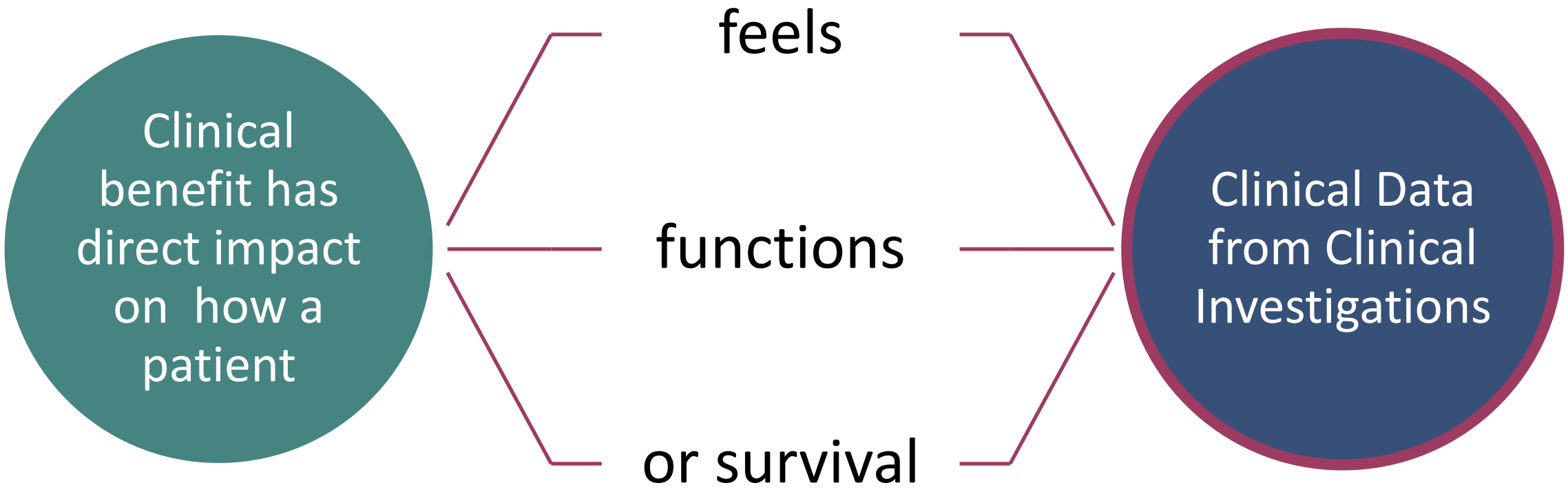

Requirements for Clinical Investigation

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Classification of the device

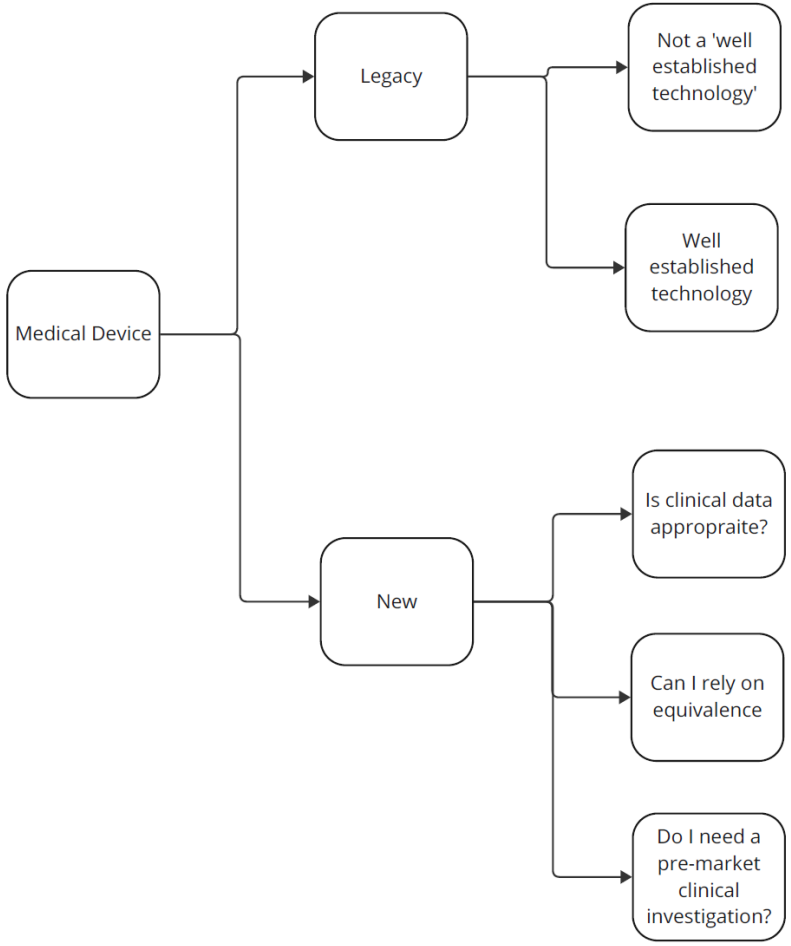
Intended Purpose

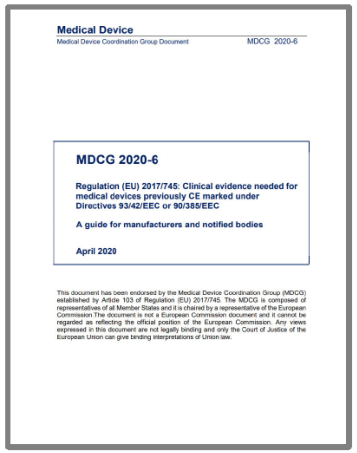
Novelty

Class I Devices: Do not require clinical investigations

Class IIa, IIb, and III Devices: Do require clinical investigations to ensure safety and performance, manufacturer must provide clinical evidence

Exemptions to Perform Clinical Investigations




Medical Device
Medical Device Coordination Group Document MDCG 2020-6

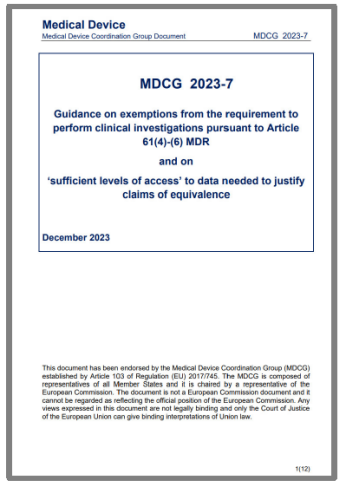
MDCG 2020-6

Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC

A guide for manufacturers and notified bodies

April 2020

This document has been endorsed by the Medical Device Coordination Group (MDCG) established by Article 103 of Regulation (EU) 2017/745. The MDCG is composed of representatives of all Member States and it is chaired by a representative of the European Commission.The document is not a European Commission document and it cannot be regarded as reflecting the official position of the European Commission. Any views expressed in this document are not legally binding and only the Court of Justice of the European Union can give binding interpretations of Union law.


Medical Device
Medical Device Coordination Group Document MDCG 2023-7

MDCG 2023-7

Guidance on exemptions from the requirement to perform clinical investigations pursuant to Article 61(4)-(6) MDR

and on

'sufficient levels of access' to data needed to justify claims of equivalence

December 2023

This document has been endorsed by the Medical Device Coordination Group (MDCG) established by Article 103 of Regulation (EU) 2017/745. The MDCG is composed of representatives of all Member States and it is chaired by a representative of the European Commission. The document is not a European Commission document and it cannot be regarded as reflecting the official position of the European Commission. Any views expressed in this document are not legally binding and only the Court of Justice of the European Union can give binding interpretations of Union law.

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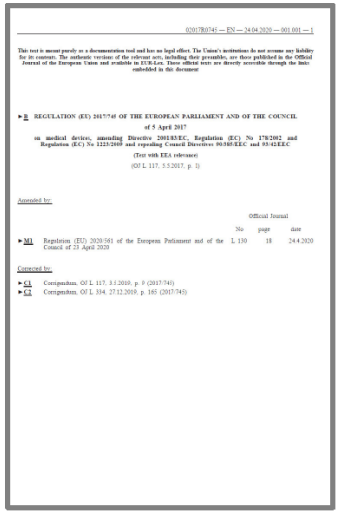
02017R0745 — EN — 24.04.2020 — 001.001 — 1

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▼B REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017

on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

(Text with EEA relevance)

(OJ L 117, 5.5.2017, p. 1)

Amended by:

		Official Journal		
		No	page	date
▼M1	Regulation (EU) 2020/561 of the European Parliament and of the Council of 23 April 2020	L 130	18	24.4.2020

Corrected by:

▼C4 Corrigendum, OJ L 117, 3.5.2019, p. 9 (2017/745)
▼C5 Corrigendum, OJ L 334, 27.12.2019, p. 185 (2017/745)

Clinical Investigation

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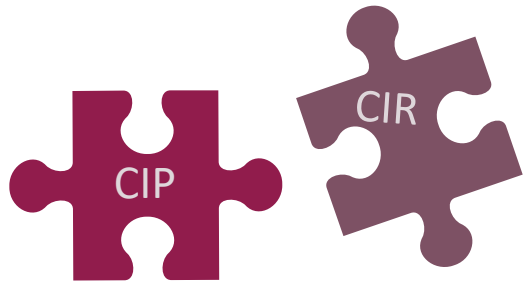
Clinical investigation:
systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device

= clinical trial
= clinical study

to be designed, conducted and reported in accordance with
EN ISO 14155



MDCG 2021-6
Q&A clinical investigation

CIP = Clinical investigation plan; CIR = Clinical investigation report

Clinical Evidence

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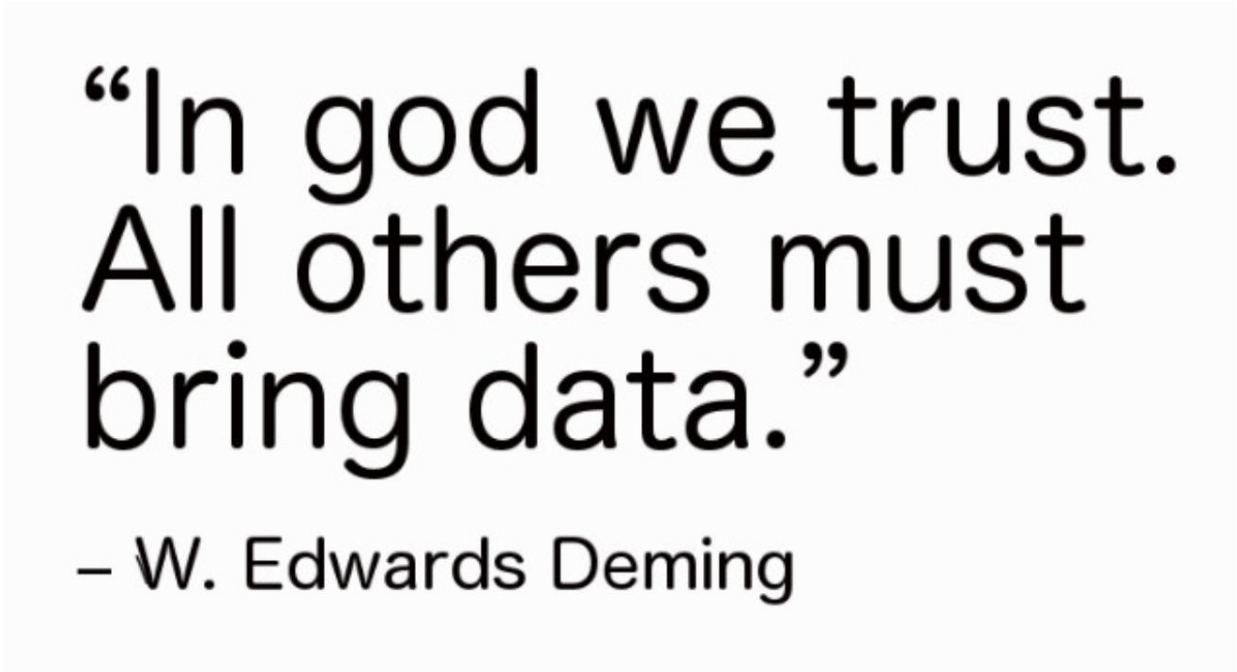
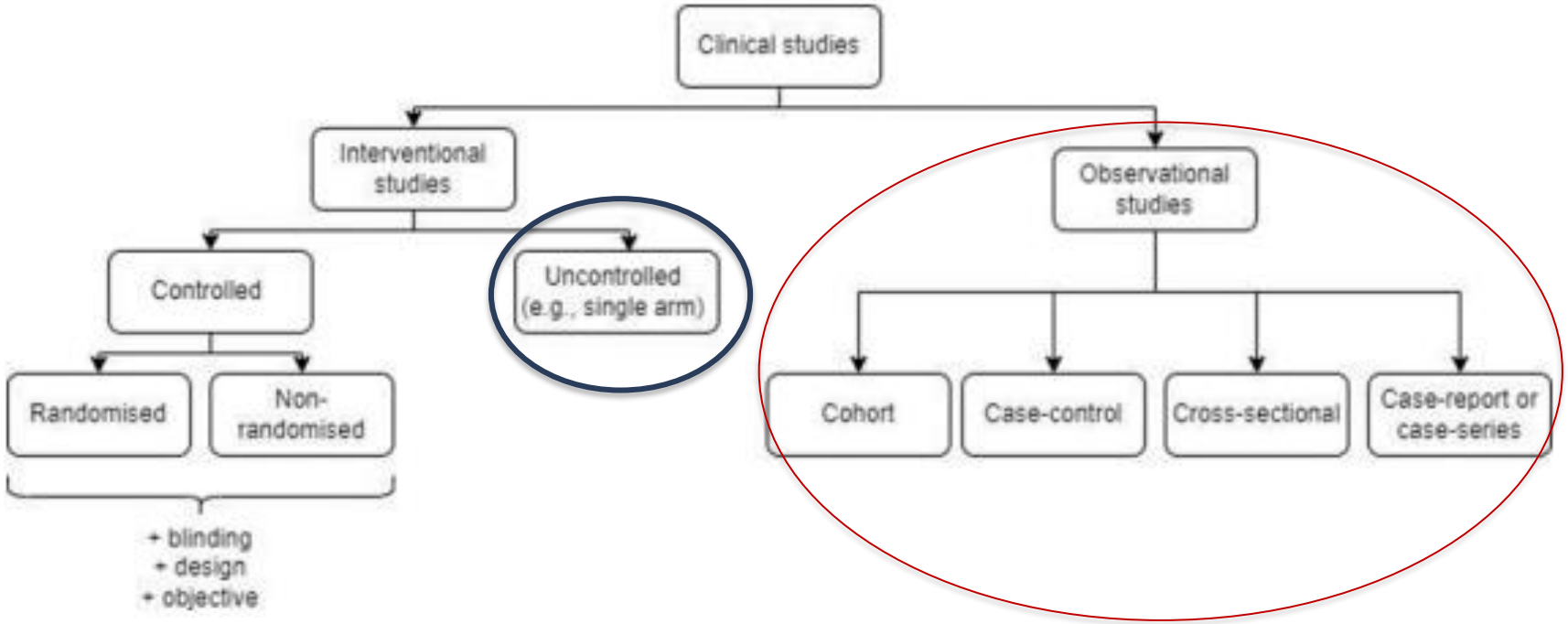


Evidence generated from Clinical Studies



- Clinical study results should be objective, reproducible, and transparent
- Relative effectiveness is the **quantification of the effect** caused by an intervention **relative to a comparator** (e.g., standard of care) **on an outcome of interest**

HTA CG Guidance on Validity of Clinical Studies, V1.0, 04 July 2024

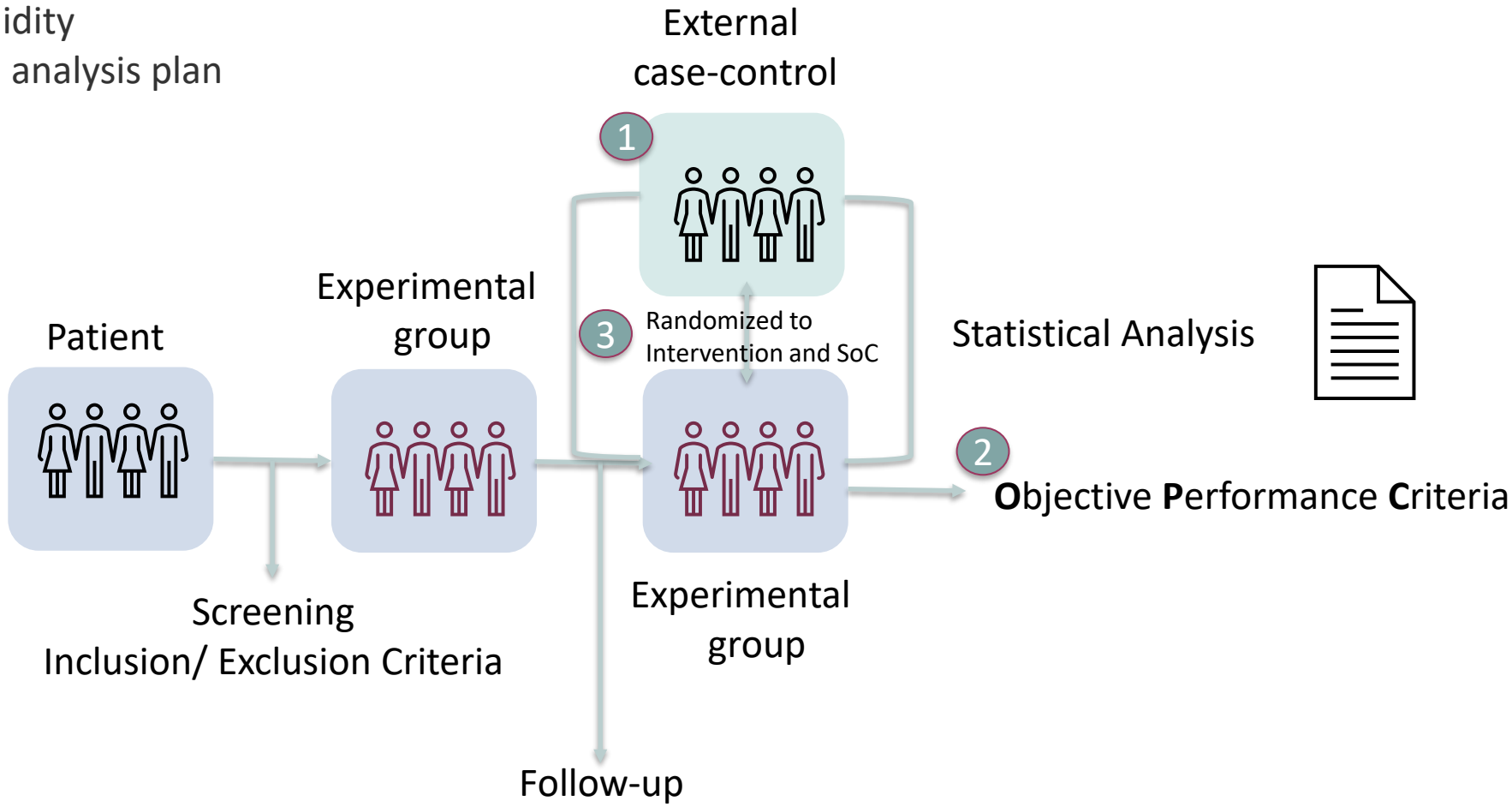
internal validity

external validity

statistical precision

Evidence from a Single-Intervention Arm Clinical Study

- Evidence is considered to be less scientifically robust
- Lower internal and external validity
- Requires pre-defined statistical analysis plan
- Open trial assignment
- Faster trial results



1 In chronic diseases- natural history data will be used as a control

3 Randomized to SoC

Clinical Evaluation Process

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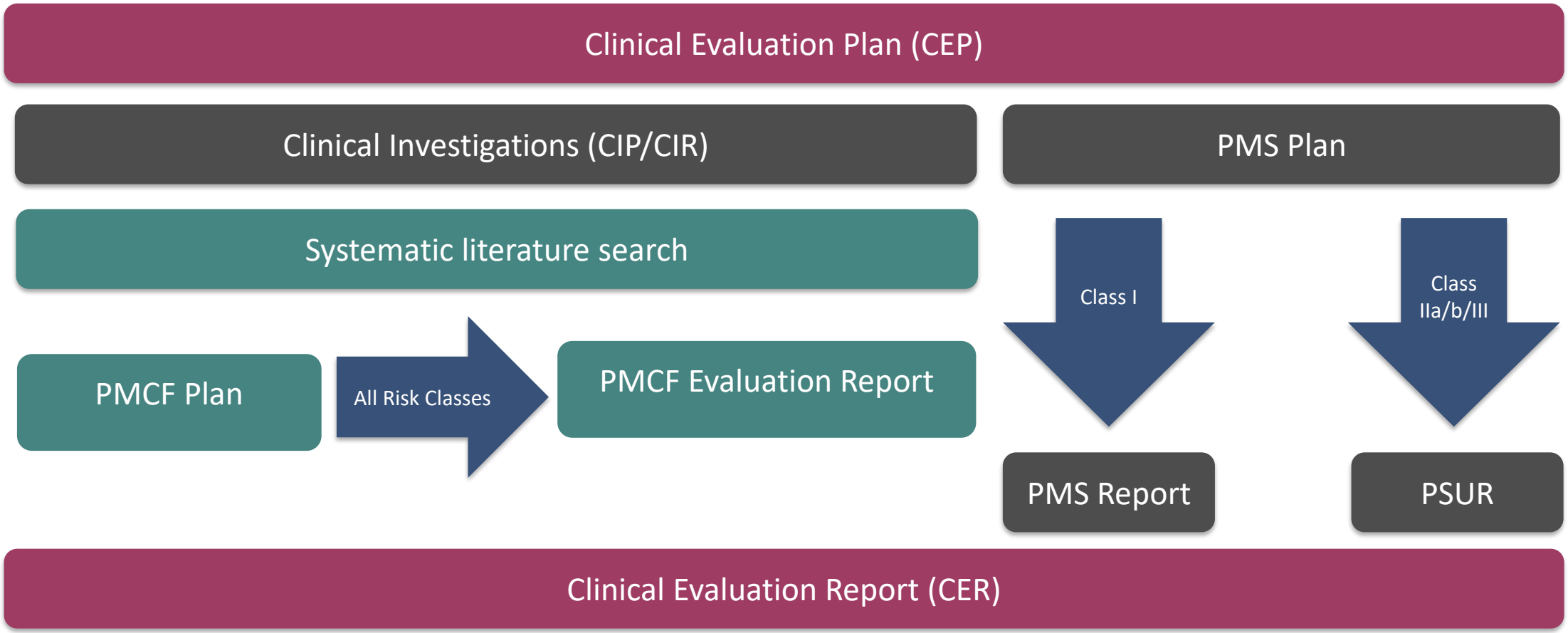

MDR, Chapter II, Article 10; Chapter VI, Article 61
Annex XIV - Clinical Evaluation and Post-Market Clinical Follow-Up
MDCG 2022-21 - PSUR

MDCG 2020-7 – PMCF Plan Template
MDCG 2020-8 – PMCF Evaluation Report Template
MDCG 2021-6 - Regulation (EU) 2017/745 – Questions & Answers regarding clinical investigation

Take-Home Message

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Clinical evidence can be obtained pre-market and post-maket

Lack of guidance with regard to magnitude of evidence

Risk class definition – intended purpose and level of existing data will drive the need for clinical investigation(s)

Lower levels of evidence (single-arm studies) might be acceptable (requires justification)