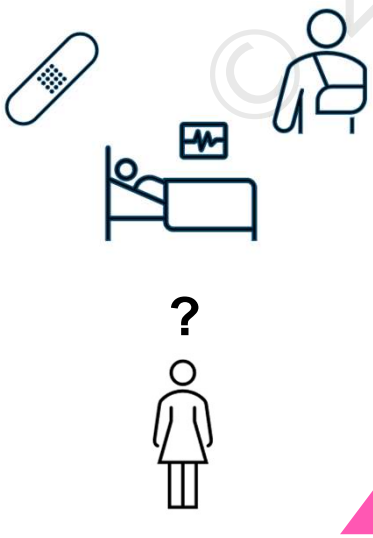
Clinical evidence

Clinical data

Evidence-Based Medicine

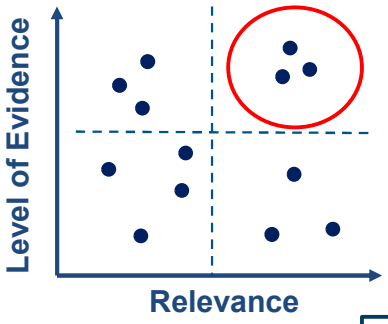


Level of Evidence

QAdvis

Appraisal

Methodological quality
Scientific validity



Same device?
Same indication?
Same patient group?

QAdvis

Clinical evidence = **Clinical data** + **Clinical evaluation**

Clinical Evidence

Clinical data *and* ***clinical evaluation results***
pertaining to a device of a ***sufficient amount and quality***
to allow a qualified assessment of whether the device is
safe *and achieves the intended* ***clinical benefit(s)***
when used as intended by the manufacturer

MDR article 2(51)

QAdvis

Clinical evidence = **Clinical data** + **Clinical evaluation**

a) Clinical investigation(s) of the device
b) Clinical investigation(s) or other studies reported in scientific literature of equivalent device
c) Reports published in peer reviewed scientific literature on other clinical experience of either the device or equivalent device
d) Post-market data

MDR article 2(48)

Overall analysis of
- safety
- performance
- clinical benefits
- side effects
- benefit/risk profile

State of the art to be considered

MDR annex I, annex XIV

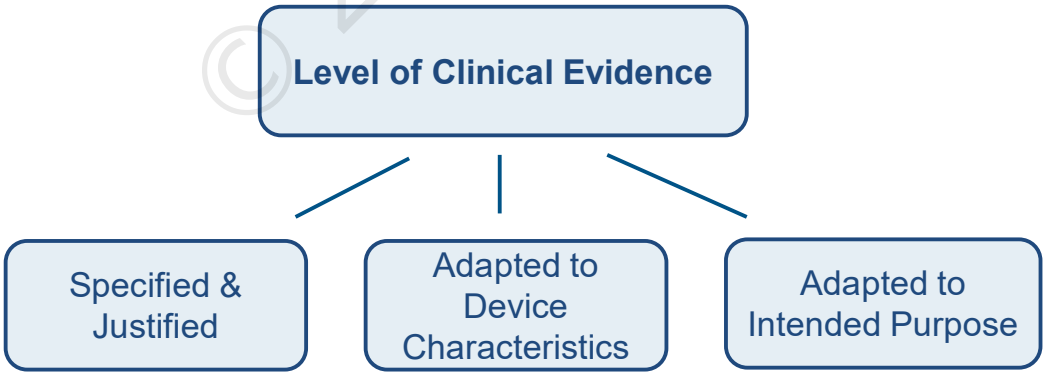
QAdvis

Clinical Evidence – Is it needed?

All devices	Sufficient clinical evidence
General rule	Clinical data Exceptions possible, if duly justified
Implantable & class III devices	Clinical investigation Potential exceptions: Equivalence (same or other manufacturer) Devices listed in article 61(6b)

MDR article 61 (1, 4-6, 10)

QAdvis



MDR article 61(1)

QAdvis

Non-implantable	vs	**Implantable**
Not life supporting	vs	**Life supporting**
Well-known technology	vs	**Novel technology**

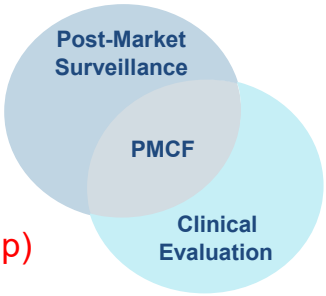
Benefit – Risk ratio for the individual device must always be considered

Clinical evidence

Sufficient Clinical Evidence – Is there any guidance?

- MDR: No definition provided
- Some attempts at definition in guidance documents (MDCG 2020-6, MEDDEV 2.7/1)
- Manufacturer to define and justify for every single device
- Device-specific examples are lacking
- Obvious risk for heterogeneous assessments

Clinical Evidence – Is it needed?



All devices	Sufficient clinical evidence PMCF (post-market clinical follow-up)
Implantable & class III devices	PMCF study Required if a pre-market clinical investigation was not performed
Devices in need of additional clinical data	PMCF activities as identified by manufacturer, expert panel and/or notified body

MDR article 61(4-6), annex 14(5), article 56(3), annex IX (5.1 g)

QAdvis

PMCF Study

- Study carried out after CE-marking
- Device used according to its approved intended use
- Intended to answer specific questions relating to clinical safety or performance
  - residual risks
  - long-term performance

MDR article 74(1), article 56(3), annex IX (5.1 g)

QAdvis

PMCF – Purpose

Proactive collection and evaluation of clinical data

Confirm the **safety** and **performance** of the device throughout its expected lifetime

Identify previously unknown **side-effects** and monitor side-effects and contraindications

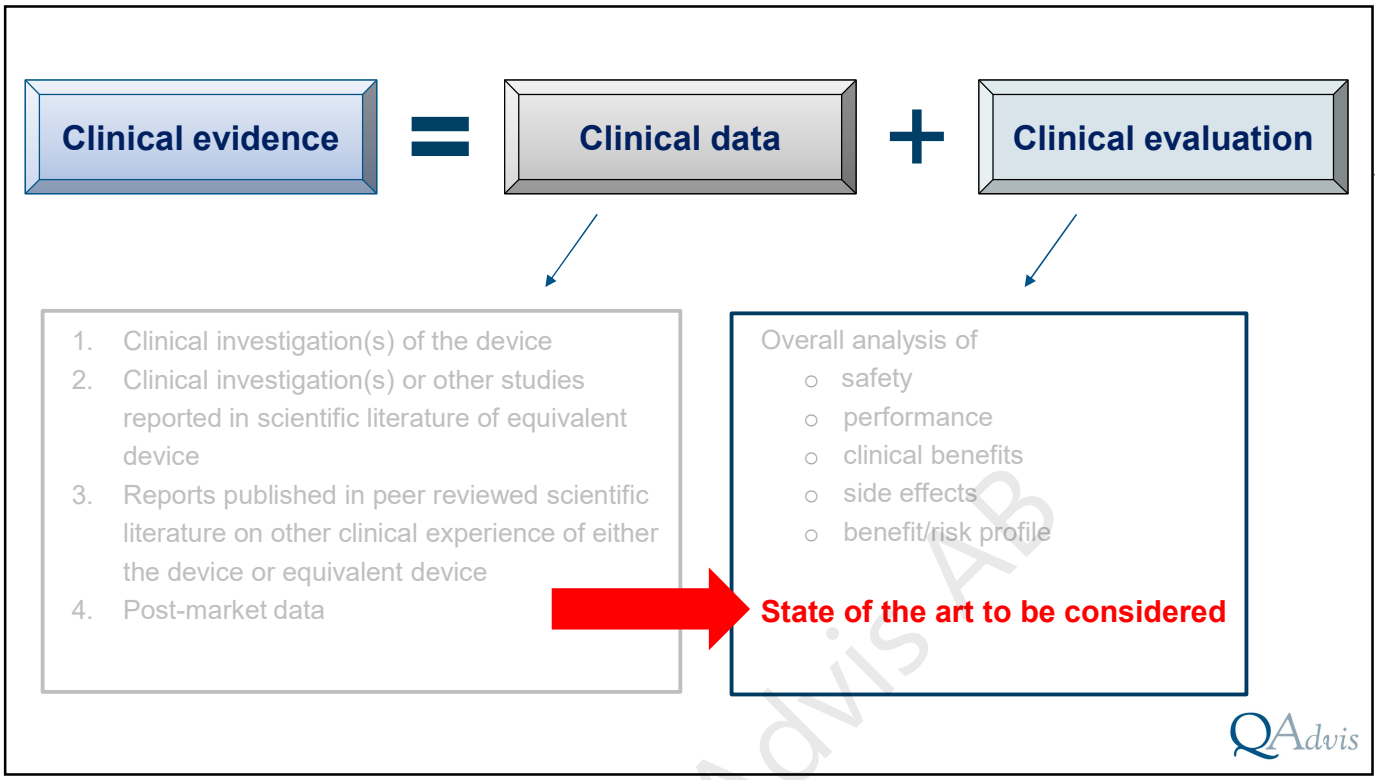
Identify and analyse **emergent risks** on the basis of factual evidence

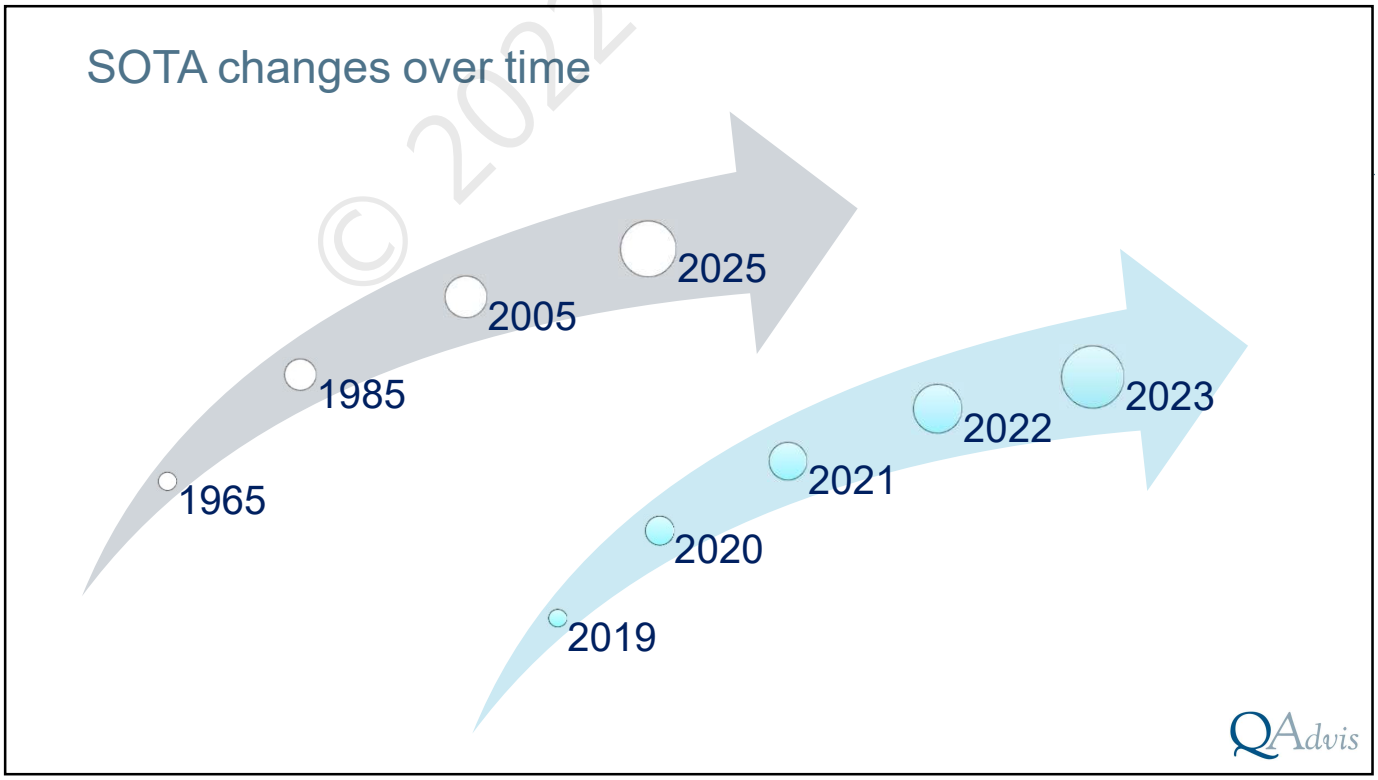
Ensure continued acceptability of the benefit-risk ratio

Identify systematic misuse or **off-label use**; verification of intended purpose

MDR Annex XIV(6.1)

QAdvis





What if SOTA changes?

2002

- **Safety**
- **Performance**
- **Clinical Benefits**
- **Side Effects** acceptability vs SOTA
- **Benefit / Risk Profile** acceptability vs SOTA

2022

- **Safety**
- **Performance**
- **Clinical Benefits**
- **Side Effects** acceptability vs SOTA
- **Benefit / Risk Profile** acceptability vs SOTA

→ **Retire?** **Update?** Keep?

State of the Art (SOTA)

QAdvis

Clinical Evidence – Is it needed?

All devices	Sufficient clinical evidence
General rule	Clinical data — *Clinical data accepted for MDD may not be sufficient for MDR*
Implantable & class III devices	Exempted from the MDR requirement on pre-market clinical investigation
"Routine use devices"	MDCG 2020-6

MDR article 61(1), article 61(6)

QAdvis

Well-Established Technology

Design
simple, common, stable

Safety & Performance
well-known

Long history
on the market

Standard of care
devices

Little evolution
indications & state of the art

- Interpretation available in MDCG 2020-6
- Literature data may be limited – devices not in focus of research
- PMCF activities may be necessary prior to MDR
- In exceptional cases: post-market surveillance data may provide *sufficient clinical evidence*

MDCG 2020-6

QAdvis

Clinical Evidence – Closing a gap

New device	Post-market phase	MDD/AIMDD → MDR
Clinical investigation	PMCF study	PMCF study
Intended purpose adaptation	Other specific PMCF activities	Other specific PMCF activities
Design change + appropriate validation	Intended purpose adaptation	Intended purpose adaptation
	Design change + appropriate validation	Design change + appropriate validation

QAdvis

National Law - Clinical Investigation / PMCF Study

Note: This is a somewhat simplified overview. For detailed information, see: link to LMV web page

Non-CE marked device

CE marked device
Study *outside* intended use

- Ethical review
- Application to LMV

CE-marked device
Study *within* intended use

- Ethical review
- Notification to LMV

LMV = Läkemedelsverket (Swedish Medical Products Agency)
HSLF-FS 2021:32
MDR Articles 62, 74.1, 74.2, 82

Clinical Evidence – Closing a gap

- Device registries – national/international
- Systematic reviews / meta-analyses
- **Scientifically sound questionnaires**
  - Objectives & endpoints
  - Rationale for study design
  - Statistical considerations
  - Identification of sources of bias
  - Analysis plan / acceptance criteria

SVENSK STANDARD
SS-EN ISO 14155:2020
Klinisk prövning av medicintekniska produkter – God klinisk praxis (ISO 14155:2020)

Clinical investigation of medical devices for human subjects – Good clinical practice (ISO 14155:2020)

MDCG 2020-6

New device	Post-market phase	MDD/AIMDD → MDR
Clinical investigation	PMCF study	PMCF
Intended purpose adaptation	Other specific PMCF activities	Other specific PMCF activities
Design change + appropriate validation	Intended purpose adaptation	Intended purpose adaptation
	Design change + appropriate validation	Design change + appropriate validation

Gaps to be closed **before** transition

QAdvis

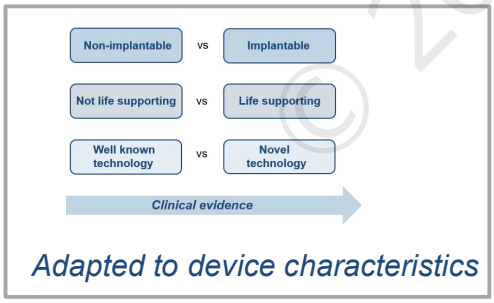
Low-Risk Devices

Clinical evidence – MDR requirements

- No exceptions directly related to device class
- No exceptions for medical device software
- However, . . .

QAdvis

Low-Risk Devices



Adapted to device characteristics

Specify and justify the level of clinical evidence = manufacturer's responsibility

General rule Clinical data
Exceptions possible, if duly justified

Clinical data may be omitted

Design
simple, common, stable

Safety & Performance
well-known

Long history
on the market

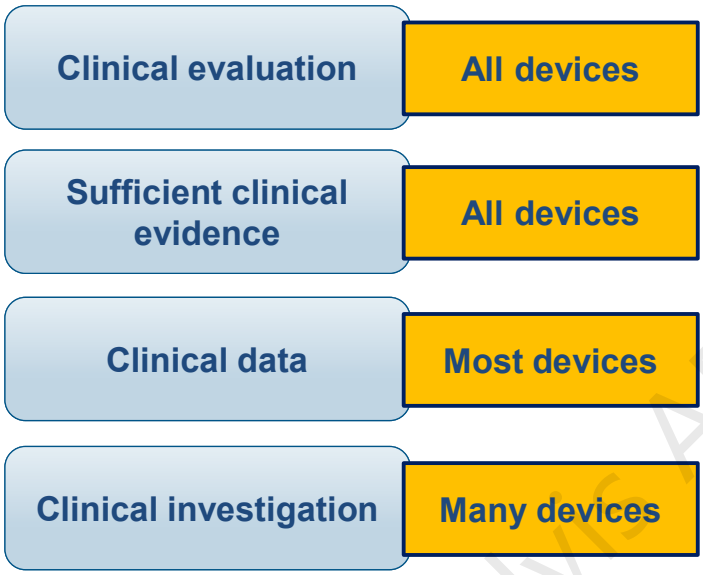
Standard of care
devices

Little evolution
indications & state of the art

Well-established / Routine care devices

QAdvis

Summary



QAdvis