Which medical devices require a clinical evaluation?

ALL Medical Devices regardless of Classification
Clinical Evaluation (MEDDEV 2.7.1 rev. 3)

The assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer.
Prior to starting the clinical evaluation, the following aspects must be defined:

- Are there any design features of the device and/or target treatment populations that require specific attention?
- Can data from equivalent devices be used?
- What is the type and source of available data?
State of the Art

Competitor

Your new innovative turtle
State of the art evaluation means reasonably detailed, critical and objektiv assessment (incl. risks and benefits) of the currently available and accepted therapeutic / diagnostic alternatives (for the intended use) to the device under assessment. This is essential to enable a justified conclusion with regard to the acceptability of the risk/benefit-ratio (of the device under assessment) as this can only be done in view of the risk/benefit ratio of available alternatives.
State of the Art

Currently available turtles

Your new innovative turtle

[TÜV SÜD Product Service GmbH](http://www.funelf.net/photos/Real-Teenage-Mutant-Ninja-Turtles.jpg)
Medical Device – Requirements for Clinical Data

**Clinical Data**

The safety and/or performance information that is generated from the use of a device

**Source of Clinical Data**

- Clinical investigation of the device concerned
- Clinical investigation or other studies reported in the scientific literature of a similar device
- Published and/or unpublished reports on other clinical experience of either the device in question or a similar device

**Similar \(\rightarrow\) Equivalency must be demonstrated!**
Medical Device – Requirements for Clinical Data

Which route to follow for the device under consideration?
A clinical investigation is defined as any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device (SG5/N1:2007)
MEDDEV 2.7/4 – What is the objective of a clinical investigation?

The objective of a clinical investigation is to assess the safety and clinical performance of the device in question and evaluate whether the device is suitable for the purpose(s) and the population(s) for which it is intended (EN ISO 14155).
MEDDEV 2.7/4 – When must/should a clinical investigation be undertaken?

The Conformity Assessment process for active implantable medical devices as well as for class III and implantable medical devices requires that a clinical investigation is undertaken unless it is duly justified to rely on existing data.

Section 1.2 of Annex 7 of directive 90/385/EEC

Section 1.1a of Annex X of directive 93/42/EEC
MEDDEV 2.7/4 – When must/should a clinical investigation be undertaken?

Depending on clinical claims, risk management outcome and on the results of the clinical evaluation, clinical investigations may also have to be performed for non-implantable medical devices of classes I, IIa and IIb.

Additional clinical investigations may be feasible to corroborate the existing clinical evidence with regard to aspects of clinical performance, safety, benefit/risk-ratio or to determine relative effectiveness and safety with suitable comparators.
Clinical investigation route

**How to plan a clinical investigation correctly?**

Any clinical investigation must be part of the clinical evaluation process; follow a proper risk management procedure to avoid undue risks and be compliant with all relevant legal and regulatory requirements.
Clinical investigation route

How to plan a clinical investigation correctly?

Clinical evaluation → Study Plan

Endpoints → Scientific validity

Suitability → Clinical relevance
Clinical investigation route

Study design

- Type
- Measures to avoid bias
- Primary and secondary endpoints with rationale for selection and measurement
- Methods and timing for assessing, recording, and analyzing variables.
- Justification for choice of comparator(s)
- Subjects (in-, exclusion criteria, number, duration)
- Study related procedures incl. post-study medical care
- Monitoring plan
Clinical investigation route

Statistical Methods

- design, method and analytical procedures
- sample size,
- level of significance
- expected dropout rates
- pass/fail criteria
- provisions for an interim analysis
- criteria for termination on statistical grounds
Documents evaluated by EU Notified Bodies

CIP

Letter of „no objection“

Ethics Committee opinion

Signed and dated final report
Equivalence Approach

Literature Route – Equivalence Approach

Same Intended Use
  +
Technical and biological equivalence
  +
No clinically significant difference regarding safety and performance
Equivalence Approach

Comparing Apples with Pears?
Equivalence Approach

I'm so much cooler than you, apple!
Equivalence Approach

Literature Route

- Define search criteria
- Explore the results
- Look for consistency of results
- Consider evidence levels of the different datasets
- Consider transferability of the data to the device under evaluation
Equivalence Approach

Literature Route – Equivalence Approach

How to demonstrate equivalency?

- Using published data on established device
- Bench-Tests
- In-vivo Animal Studies
- ....
Clinical evaluation

Check the results of the clinical evaluation by asking 5 questions:

1. Is the performance as intended?
2. Are there any safety concerns?
3. Is the benefit/risk ratio positive?
4. Is non inferiority and similarity to state of the art shown?
5. Is the final conclusion critical, objective and transferable?
Clinical evaluation

The appropriate CER shall include:

- scope and context of the evaluation
- clinical data
- appraisal and analysis stages
- conclusions
Clinical evaluation

The appropriate CER shall be prepared as a stand-alone document to facilitate the assessment of a third independent party.

The stand-alone document must comprise:

- Background regarding device technology
- Intended Use
- Claims regarding performance and safety
- Nature and extent of clinical data
- Suitability of the referenced information
- Acceptability of the risk/benefit ratio

Clinical evaluation
Clinical evaluation

The appropriate CER must be:

signed and dated by the evaluator(s)

The appropriate CER must include:

a justification for the choice of evaluator(s)
Post-Market Clinical Follow-up

Why PMCF?

Rare complications or problems become apparent after wide-spread or long term use of the device
Post-Market Clinical Follow-up

Why PMCF?

There may be limitations to the clinical data available in the pre-market phase:

• Duration
• Number of subjects
• Investigators involved (Heterogenicity?)
• Subjects (Heterogenicity?)
• The range of clinical conditions
Can PMCF be used to demonstrate conformity and place a product on the market?

Data obtained from PMS and PMCF are not intended to replace the pre-market data necessary to demonstrate conformity with the provisions of the legislation.
Post-Market Clinical Follow-up

Post Market Surveillance (PMS) and PMCF:

PMS is part of the manufacturer’s quality system to identify and investigate residual risks associated with the use of medical devices.

PMCF is one option of PMS (Systematic).

Both PMS and PMCF are used to update the clinical evaluation → To ensure the long term safety and performance of devices.
When to do a PMCF?

the decision to conduct PMCF studies must be based on the identification of possible residual risks and/or unclarity on long term clinical performance that may impact the benefit/risk ratio
PMCF is mandatory per example, for:

- Innovative Products
- High risk anatomical locations
- Emergence of new information on safety or performance
- Where CE marking was based on equivalence
When not to do a PMCF?

PMCF studies may not be required when the medium/long-term safety and clinical performance are already known from previous use of the device or where other appropriate post-market surveillance activities would provide sufficient data to address the risks.
PMCF Plan must include:

- clearly stated research question(s)
- clearly stated objective(s)
- related endpoints
- scientifically sound design with an appropriate rationale
- statistical analysis
- a plan for conduct according to the appropriate standard(s)
- a plan for an analysis of the data and for drawing appropriate conclusion
Global Clinical Affairs Team

Internal and External Experts
Pre-assessment Services

Continuously pre-reviewed process
Pre-assessment Services

- Pre-assessment of the clinical investigation plan
- Pre-assessment of the in-vivo animal studies
- Pre-assessment of the first version clinical evaluation report
- Pre-assessment of the literature search protocol
- Support during consultation process for Drug-Device combination
- Support during consultation process for products containing animal tissue
- Technical Meeting
- ...
- ...
OUT TO LUNCH

http://www.salesprogress.com/Portals/53724/images/question%20mark.png