Significance of Clinical Evaluation & Clinical Investigations for Medical Devices

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Conformity Assessment Procedure

Release of Medical Devices on the market

Medical Device

Intended Use

Essential Requirements

Clinical Evaluation
Risk Management
Harmonized Standards

Conformity Assessment Procedure

CE-Labelling
Clinical evidence and corresponding Life Cycle phases

- **Product Idea**
  - Product Life Cycle
  - Clinical Data
    - Preclinical Evaluation
- **Strategic Decision**
  - Feasibility Concepts
  - Clinical Evaluation or (Investigation)
- **Product Launch**
  - Product Development
  - Sales & Marketing
    - Postmarket Surveillance / PMCF Studies
What is a Clinical Evaluation?

Medical Device Directive (93/42/EWG), Annex X, Clinical Evaluation

Assessment of the use of the product within the intended use with regard to:

- safety for patients users and third parties?
- safety and performance proven?
- sideeffects?
- clinical risk/benefit ratio acceptable?
How to perform a clinical evaluation?

Medical Device Directive (93/42/EWG), Annex X, Clinical Evaluation

Critical assessment of clinical data based on:

• scientific literature (where the similarity of the device with literature data has to be proven), or

• results of clinical trials with own or similar products

or any combination.

Guideline MEDDEV 2.7.1
When do you have to perform a clinical trial?

- intended use
- medical procedure
- technology
- equivalent products
- ...

Literature Search

Literature Assessment
Analysis of relevant publications

Data sufficient? [Yes/No]

Clinical Trial necessary

CE Marking
Clinical evaluation during product development

- define Intended Use
- possible market risks?
- Input to Risk analysis
- first risk/benefit analysis
- enough clinical evidence?
- clinical trial necessary?

Clinical evaluation according to MEDDEV 2.7.1
- collection of all clinical data
- proof of safety & performance
- Link to design documentation
- part of technical documentation
- interface to risk management
Reason:

Many of the risks identified in this FMEA result in high severities because the target patient population is very sick, and aortic valve function is critical to patient health and survival.
### Qualitative severity levels

<table>
<thead>
<tr>
<th>Semi-quantitative probability levels</th>
<th>Negligible</th>
<th>Minor</th>
<th>Serious</th>
<th>Critical</th>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
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<td>$R_2$</td>
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<td>Improbable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$R_3$</td>
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</tbody>
</table>

### Key

- Unacceptable risk
- Investigate further risk reduction
- Insignificant risk

#### Example risk chart from EN 14971

<table>
<thead>
<tr>
<th>Occurrence</th>
<th>Severity</th>
<th>Negligible</th>
<th>Limited</th>
<th>Major</th>
<th>Total</th>
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<td>Insignificant</td>
<td>Insignificant</td>
<td>Investigate</td>
<td>Investigate</td>
</tr>
</tbody>
</table>

### Risk chart from company

- 15 areas are not acceptable
- 50 risks in this area!
Clinical evaluation during product development

- Idea
- Project planning
- Design Input
- Development
- Verification
- Validation
- Launch

“pre”clinical Evaluation

Literature Test?

Collection, analysis and assessment of clinical data

CE Report

RM Plan

RM Analysis

Riskcontrol & Update of Riskanalysis

RM Report
additional time, ressources, cost
Manufacturer advantages through Clinical Evidence

**Early Collection & Evaluation of Clinical Data**
- by Scientific Literature
- through Clinical Experience
- with Clinical Investigations

**Clinical Evidence “opens doors”**
- Identification of missing Evidence
- Detection of potential Risks for Market Acceptance
- Clinical Risk/Benefit Assessment
- Estimation of Clinical Market Potential

**Strategic Decision on Product Development**
- Balancing of “best” Intended Use

**Definition of Approval Strategy**
- Clinical Evaluation based on Literature or Decision on Clinical Investigation?
- Postmarket Surveillance Study required?

**Additional Benefit of clinical evidence:**
- Competitive Advantage
- Early Insight of potential Incidences
- Support for Marketing and specific Claims
- High Medical Benefit support Reimbursement
- Support of worldwide product approval
Clinical evidence needs review by independent clinical experts

- **EC Proposal: Chapter VI: Clinical evaluation and clinical investigations**
  - Article 49: Clinical evaluation
  - Article 52: Registration of clinical investigations
  - Article 53: Electronic system on clinical investigations
  - Article 55: Substantial modifications to a clinical investigation

- **Annex XIII and XIV**
  required clinical data should be able to clearly demonstrate that devices perform well and are safe for patients when used by a physician as intended by their manufacturer

- **Recent improvements by Directive 2007/47/EC**
  included the clear requirement that all devices have clinical evidence to demonstrate safety and furthermore that all implantable and class III devices must undergo clinical trials

- **The Commission has built on this Directive by adding**
  - More detail for clinical requirements (Art. 50);
  - Centralized system for notifications and reporting of severe adverse events (Art. 53);
  - Increased protection of subjects undergoing clinical investigations (Art. 50, 52, 59);
  - Extended post-market clinical follow-up by manufacturers (MDR, Annex XIII)
future Design of the EUDAMED Database

EUDAMED
European Databank on Medical Devices
(as proposed by the European Commission)

Electronic system on Registration
Medical devices / IVDs
economic operators, incl.
Summary of Safety and Clinical Performance
(high risk devices)

Electronic system on UDI
Device Identifier data elements

Electronic system on Certificates
Certificates issued by notified bodies & Information on certificates refused suspended reinstated restricted withdrawn

Electronic system on Vigilance
Serious incidents & Field safety corrective actions & Field safety notices

Electronic system on Market surveillance
Measures taken by Member States re.
devices presenting a risk to health & safety preventive health protection measures

Electronic system on Clinical investigations
Sponsors (& manufacturers) description of:
investigational device, comparator, purpose of CI, status of CI
Thank you for your attention