Clinical Evaluation Requirements
“A Look Into The Future Now”
“The Process”
(December 5, 2017)

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Clinical Evaluation Requirements
“A Look Into The Future Now”
“The Process”

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Clinical Evaluation Requirements

Agenda

When “I” Think About Medical Devices

“A Look Into The Future Now”

Clinical Evaluation Requirements
The Clinical Evaluation Report (CER)

Clinical Evaluation Requirements
“A Look Into The Future Now”

• **When I Think About Medical Devices**

  I am thinking about the array of medical devices that are on the market that are *designed* to help patient’s who need them.

• Patients are relying on the safety, performance and effectiveness of these devices.
Clinical Evaluation Requirements
“A Look Into The Future Now”

• **When I Think About Medical Devices**

• I’m thinking about children who may have a Cochlear Implant Medical Device.

• These children are relying on the safety, performance and effectiveness of this medical device.
Clinical Evaluation Requirements
“A Look Into The Future Now”

• When I Think About Medical Devices
• I’m thinking about a person who my need a Cardiac Pacemaker Implant Device.

• This person is relying on the safety, performance and effectiveness of this medical device.
Clinical Evaluation Requirements
“A Look Into The Future Now”

• **When I Think About Medical Devices**

• I’m thinking about a person who may need an implantable Intraocular Lens (IOL) Device.

• This person is relying on the safety, performance and effectiveness of this medical device.
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• When I Think About Medical Devices
• I’m thinking about a patient who may have the need for a synthetic skin graft medical device to cover a diabetic wound.

• This patient is relying on the safety, performance and effectiveness of this medical device.
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• **When I Think About Medical Devices**

• I’m thinking about a patient in an underdeveloped area who has an ankle implant medical device and does not have consistent access to physicians for follow-up.

• This patient is relying on the safety, performance, effectiveness and reliability of this medical device.
Clinical Evaluation Requirements
“A Look Into The Future Now

• **When I Think About Medical Devices**

• I’m think about my father who received a spinal stabilization device which was scheduled to last 10 years but lasted 21 years without a single revision required.

• “I” was relying on the safety, performance and effectiveness of this medical device.
Clinical Evaluation Requirements
“A Look Into The Future Now”

- **When I Think About Medical Devices**
- I am *not* thinking about manufacture short cuts: PIP Implant Scandal-Need we say any more!
- The toxic chemicals in the fraudulent shells and filler of PIP, Industrial Grade Silicone seeped out into surrounding body tissue, migrate into organs, cross the placenta barrier and can be found in breast milk.
Clinical Evaluation Requirements
“A Look Into The Future Now”

• **When I Think About Medical Devices**
• I am not thinking about manufacture short cuts: which have caused over 40,000 women who have been implanted with this device to now worry about potential development of medical problems and inevitable surgical removal of the implants.

- At the end of every CER, there is a patient depending on device safety, performance and effectiveness. PIP implant Failure.
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- PIP founder, Jean-Claude Mas, arrested after French breast implant manufacturing scandal.
- Need we say anymore! No comment required!
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“A Look Into The Future Now”

• All of the patients, clinical scenario and outcomes are relaying on the;
  • Safety of the Medical Device
  • The Performance of the Medical Device
  • The Effectiveness of the Medical Device
  • High expectation that thorough clinical investigations have been performed and completed on the Medical Device
  • Patients are under the impression that rigorous “Clinical Evaluations” have been performed and completed on these Medical Devices
  • **Thus**, the patient is relying on the Clinical Evaluation - “The Process”.
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“A Look Into The Future Now”

When I Think About Medical Devices

Clinical Evaluation Requirements
“A Look Into The Future Now”
“The Process”
Clinical Evaluation Requirements
“A Look Into The Future Now

• The Clinical Evaluation: “The Process”
A Look Into The Future “Now”
The New Requirements MEDDEV 2.7/1 Rev 4 (June 2016)

• **Your attention Please:**
  • Revision 4 of Clinical Evaluation guidance document MEDDEV 2.7/1 Rev 4 was released by the European Commission on 1 July 2016.
  • Significant changes are clear and present and are now required for those who deal with medical devices and CERs.
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“A Look Into The Future Now”
The New Requirements MEDDEV 2.7/1 Rev 4 (June 2016)

The Directive

- Pursuant to - section 6a of Annex I to Directive 93/42/EEC (amended by Directive 2007/47/EC) and to section 5a of Annex 1 to Directive 90/385/EEC (amended by Directive 2007/47/EC), the demonstration of conformity with Essential Requirements for a medical device must include a clinical evaluation, which is conducted in accordance with Annex X to Directive 93/42/EEC or with Annex 7 to Directive 90/385/EEC.
Clinical Evaluation Requirements
“A Look Into The Future Now”
“A Look Into The Future Now”
The New Requirements MEDDEV 2.7/1 Rev 4 (June 2016)

### MDD vs MDR

<table>
<thead>
<tr>
<th>MDD</th>
<th>MDR</th>
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</thead>
<tbody>
<tr>
<td>60 Pages (MDD only)</td>
<td>10 Chapters including 97 articles</td>
</tr>
<tr>
<td>23 Articles</td>
<td>17 Annexes</td>
</tr>
<tr>
<td>12 Annexes</td>
<td>352 Pages (MDD+MDR)</td>
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<td><strong>D=Directive:</strong> Legislation that sets out rules and must be transposed into national law to be effective.</td>
<td><strong>R=Regulation:</strong> Mandatory Jurisdiction that is directly applicable and enforceable in all EU Member States.</td>
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Clinical Evaluation Requirements
“A Look Into The Future Now”

“A Look Into The Future Now”

The New Requirements MEDDEV 2.7/1 Rev 4 (June 2016)

MDR Implementation Timeline

- **Entry into Force (EIF)** means effective date of the new EU-MDR
- **Entry into Force (EIF) =** Publication date in the OJ (2017 May 05) + 20 days
- **Date of Application (DOA)** means a day when the application of the new EU-MDR Regulation becomes **mandatory for all Medical Devices in Europe!**
- **Date of Application = Entry Into Force plus three (3) years = 2020**
- **Article 120 for Legacy Device + Four (4) more years beyond DOA = 2024**
What is Clinical Evaluation?
MDD versus MDR – Definition Clinical Evaluation

‘clinical evaluation’
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.
What is Clinical Evaluation?
When I Think About Medical Devices

• Its your work and **RESPONSIBILITY** as members of the medical device community to:
• Generate methodologically sound ongoing procedure to collect, appraise and analyze clinical data pertaining to a medical device.
• Analyze whether there is sufficient clinical evidence to confirm compliance with relevant essential requirements for safety and performance when using the device according to the manufacturer’s instructions for use (IFU).
Clinical Evaluation Requirements
“A Look Into The Future Now”

When is Clinical Evaluation Undertaken?

- Clinical evaluation is **conducted throughout the life cycle** of a medical device, as an ongoing process.

Why is Clinical Evaluation Important?

- Clinical evaluation is necessary and important because:
  - It ensures that the evaluation of **safety** and **performance** of the device is based on sufficient clinical evidence throughout the lifetime that the medical device is on the market.
Clinical Evaluation Requirements
“A Look Into The Future Now”
When I Think About Medical Devices, I’m thinking about

Clinical CER Pearls
Your Clinical Evaluation Report (CER)

Clinical Evaluation Requirement Pearls

- Clinical Evaluation Assessment Review
- Assessment of the Clinical Evaluation Report
  “The Process”

The “Clinical Pearls” that you will need to use and include to make your CER compliant.
Clinical Evaluation Requirements
“A Look Into The Future Now”
When I Think About Medical Devices, I’m thinking about

Clinical CER Pearls

Your Clinical Evaluation Report (CER)

Clinical CER Pearls:
( Important Documents)

CEP ( Clinical Evaluation Plan)
SHR (Search History Record)
Literature Report
CER (Clinical Evaluation Report)

Clinical Evaluation Requirement Pearls


Clinical Evaluation Assessment Review
Important Documents:

- CEP ( Clinical Evaluation Plan)
- SHR (Search History Record)
- Literature Report
- CER (Clinical Evaluation Report)
Clinical Evaluation Requirements
“A Look Into The Future Now”
When I Think About Medical Devices, I’m thinking about

Clinical CER Pearls

*Your* Clinical Evaluation Report (CER)

Clinical CER Pearls:
( Important Documents)
Literature Search Protocol
Report of State-of-the-Art
Report of the device under assessment
CV(s) of clinical evaluators

Clinical Evaluation Requirement Pearls


Clinical Evaluation Assessment Review
Important Documents:
Literature Search Protocol
Report of State-of-the-Art
SHR (Search History Record)
Report of the device under assessment
CV(s) of clinical evaluators
Clinical Evaluation Requirements
“A Look Into The Future Now”
When I Think About Medical Devices, I’m thinking about

Clinical CER Pearls

Clinical CER Pearls:
(Important Documents)

- Risk Management File
- Instruction for Use (IFU)
- Procedures for Promotional Material
- Scientific Literature (provide by Manufacturer)

Clinical Evaluation Requirement Pearls


Clinical Evaluation Assessment Review

Important Documents:

- Risk Management File
- Instruction for Use (IFU)
- Procedures for Promotional Material
- Scientific Literature (provide by Manufacturer)
Clinical Evaluation Requirements
“A Look Into The Future Now”
When I Think About Medical Devices, I’m thinking about

Clinical CER Pearls:
(Important Documents)
- Contract: Access Technical Documentation
- SSCP (Summary of Safety and Clinical Performance)
- PSUR (Periodic Safety Update Report)
- PMCF Report

Clinical Evaluation Requirement Pearls
Clinical Evaluation Assessment Review
Important Documents:
- Contract: Access Technical Documentation
- SSCP (Summary of Safety and Clinical Performance)
- PSUR and Evaluation Report
- PMCF Report
Clinical Evaluation Requirements
“A Look Into The Future Now”

How is a clinical evaluation performed? State of the Art Methodology

- Clinical evaluation is based on pre- and post –market clinical data relevant to the intended use of the device.
- There are discrete stages in performing a clinical evaluation:
  - **Stage 0**: Define the scope, plan the clinical evaluation (also referred to as scoping and the clinical evaluation plan).
  - **Stage 1**: Identify pertinent data.
  - **Stage 2**: Appraise each individual data set, in terms of its scientific validity, relevance and weighting.
  - **Stage 3**: Analyze the data, whereby conclusions are reached about i.e. compliance with Essential Requirements (including ER1, ER3, ER6) on performance and safety of the device, including its benefit/risk profile.
  - **Stage 4**: Finalize the clinical evaluation report.
Clinical Evaluation Requirements
“A Look Into The Future Now”
Who should perform the clinical evaluation?

- Clinical evaluation should be conducted by a suitably qualified individual or a team.
- Manufacturer defines requirements for the evaluators that are in line with the nature of the device under evaluation and its clinical performance and risks.
- Evaluators should possess knowledge of the following research methodology (including clinical investigation design and biostatistics).
- **Clause 6.4** introduces specific requirements for the expertise and experience of CER authors and evaluators. A degree from higher education in the respective field and 5 years of documented professional experience; or 10 years of documented professional experience if a degree is not a prerequisite for a given task.
Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices,
I’m thinking about

*Your Clinical Evaluation Report (CER)*

- Assessment of The Clinical Evaluation
- Assessment and reviewers will be looking for:
  - Clinical Evaluation Plan (CEP)
  - Scope of CER
  - Declaration of Interest
  - Adequate Technical Device Description
  - Relevance of the clinical evaluators background with respect to the device and/or medical procedure involved—presented
Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices,
I’m thinking about

Your Clinical Evaluation Report (CER)

• Assessment of The Clinical Evaluation
• Assessment and reviewers will be looking for:
  • Intended purpose of the device
  • Instructions for Use
  • Device Indications
  • Contraindications
  • Proposed Benefits of the Medical Device
  • Proposed Classification of the Medical Device
Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices, I’m thinking about

Your Clinical Evaluation Report (CER)

• Assessment of The Clinical Evaluation
• Assessment and reviewers will be looking for:
• Risks, Side Effects and Adverse Events of the Medical Device.
• A defined protocol for the identification, collection and review of literature (including search data bases, search terms, selection criteria, and rationale for the search.
• Reasons for believing that all references are included both favorable and unfavorable.
• Acknowledged “State of the Art” presented in the Clinical Evaluation which is documented by a systemic review of the literature according to MEDDEV 2.7/1 REV 4.

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Clinical Evaluation Requirements
“A Look Into The Future Now”
Most Significant Changes in Rev 4

Establishing “State of the Art”

- **Clause 8.2** provides more detail with respect to establishing and documenting the ‘state of the art’ and available treatment options.

- This includes establishing the **safety** and **performance** of the device, its claimed equivalent(s), and any benchmark or other similar devices, as well as the risks and benefits of other available treatment options.
Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices,
I’m thinking about

*Your Clinical Evaluation Report (CER)*
(SHR, CEP, Literature Report, CER)

- Assessment of The Clinical Evaluation
- Assessment and reviewers will be looking for:
  - Search History Record (SHR) i.e. search terms used
  - Literature Report Content
  - **Equivalence** to other Devices
  - Include Clinical, Technical and Biological
    - Include Equivalence table
    - Include Pictures
    - Contract: giving access to technical documents
Equivalence approach, only possible if technically...

- Similar design
- Similar specifications & properties
- Similar conditions of use
- Similar deployment methods
- Similar principles of operation
Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices,
I’m thinking about

*Your Clinical Evaluation Report (CER)*
(SHR, CEP, Literature Report, CER)

- Assessment of The Clinical Evaluation
- Assessment and reviewers will be looking for:
  - Appraisal of each *individual data set* in terms of relevance, applicability, quality and clinical significance.
  - Acceptability of *publications quoted*: reviewed journals, publication year, qualification of the listed authors.
  - *Verification of the provided literature research*: availability of quotation index of the referenced literature.
Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices,
I’m thinking about

*Your* Clinical Evaluation Report (CER)
(SHR, CEP, Literature Report, CER)

- Assessment of The Clinical Evaluation
- Assessment and reviewers will be looking for:
  - Bench Testing
  - Animal Study Data
  - Usability/Training Plan for Users
  - Clinical Investigations
  - Stability and Lifetime of the Implants in Humans

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Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices,
I’m thinking about

*Your Clinical Evaluation Report (CER)*
(SHR, CEP, Literature Report, CER)

- Assessment of The Clinical Evaluation
- Assessment and reviewers will be looking for:
  - Post Market Experience
  - Post Market Surveillance (PMS)
  - Post Market Clinical Follow-Up (PMCF) Plan
  - Post Market Clinical Follow-Up Studies and a justification if the manufacture is not planning these studies must be provided.
Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices, I’m thinking about

*Your Clinical Evaluation Report (CER)*
(SHR, CEP, Literature Report, CER)

- Assessment of The Clinical Evaluation
- Assessment and reviewers will be looking for:
  - Planned frequency or date of next update of the Clinical Evaluation Report.

**CER Updates**
- The CER should be reviewed and/or updated when:
  - There is a *change in design or innovation* that would be anticipated to change clinical safety or performance (includes new safety and performance claims).
  - There are *relevant changes in clinical sciences*, materials sciences or other sciences related to the device under evaluation.
Existing Claims are no longer justified for the medical device. **If no such information is received**, then the CER is updated:

- At least **annually if the device carries significant risks or is not yet well established** as defined in the CEP
- Every 2 to 5 years **if the device is not expected to carry significant risks and is well established**: a justification should be provided in CEP. The required routine CER updates for device by classification is:
  - Class I—5 years
  - Class IIa—2 years
  - Class IIb and III—at least annually
Clinical Evaluation Requirements
“A Look Into The Future Now”

When I Think About Medical Devices,
I’m thinking about

*Your Clinical Evaluation Report (CER)*
(SHR, CEP, Literature Report, CER)

- Assessment of The Clinical Evaluation
- Assessment and reviewers will be looking for:
  - Device related and medical procedure related risk.
  - Risk Management Plan
  - Availability of clinical overall *risk to benefit analysis.*
  - Severity of the *hazard.*
  - Probability of occurrence of the *harm.*
  - Selection of adequate testing to identify risk.
  - Demonstration of the performance and safety of the device provided by the documentation.
Technical Documentation – Clinical Aspects

Pre CE CER Plan

- Literature Search
- Equivalence Review / Testing
- Clinical Investigation

Post CE

- SSCP: Class III and Implantables
- PSUR: Class IIa, IIb and III
- PMS Plan: All
- Incidences: All
- PMCF Plan & Report: Class III and Implantables or justification for others
- CER: All
- Incidences: All

- SSCP
- PSUR
- Incidence, FSCA etc.
- PMCF Plan & Report (Studies, Registries, etc.)
- PMS Plan
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• **Take Home Clinical Pearl Message**

• At the end of every CER, a patient is relying on the safety, performance and effectiveness of the medical device. The patient is relying on you (members of the medical device community).
Clinical Evaluation Requirements
“A Look Into The Future Now”
Affords Patient Safety, Performance and Effectiveness of Medical Devices

Thank you