Post Market Surveillance

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Agenda

• Postmarket surveillance
• Postmarket clinical follow up (PMCF)
• Incident reporting
• What changes with MDR
GENERAL

Post Market Surveillance & Vigilance
Life cycle of medical devices

- **Development**
- **Manufacturing**
- **Marketing and sales**
- **Use**
- **Eventually repair / refurbishment**
- **Pre-market phase**
- **Post-market phase**
- **Disposal of the device**

End of pre-market conformity ass. = Regulatory clearance (CE)

December 5-6, 2017
Hilton Orlando, Orlando FL, USA
Introduction – Post Market Surveillance & Adverse Event Reporting

Conformity assessment:

“Conformity assessment, conducted before and after a medical device is placed on the market, and post-market surveillance of devices in actual use are complementary elements of the GHTF global regulatory model. They are intended to provide the objective evidence of safety, performance, and benefits and risks to maintain public confidence.”

Source: section 2.1 - Principles of Conformity Assessment for Medical Devices SG1 Final Document GHTF/SG1/N78:2012
What is “Post Market Surveillance”:

All activities carried out by manufacturers (in cooperation with Authorized Reps, Distributors, Importers) to institute and keep up to date a systematic procedure to proactively collect and review experience gained from devices on the market for the purpose of identifying any need to immediately apply any necessary corrective or preventive actions.

Source: Regulation 2017/745 - MDR
Post Market Surveillance actions of manufacturers required in the Medical Device Directives & Regulations:

- Obligation to have a systematic procedure to review experience gained from devices on the market (plan + execution)
- Obligation to verify risk / benefit + implement Corrective Action
- Obligation to inform competent authorities + NB (Incident / Adverse Event Reporting – with MDR also PMS Report / PSUR)

Pro active actions of manufacturers required by applicable ISO 13485 clauses. (Feedback)
Inputs to Post Market Surveillance

**Stakeholders and inputs:**

- **H**: Users e.g. Hospitals report incidents
- **M**: Manufacturers report incidents
- **P**: Information from production (e.g. NC)
- **R**: Pro active research of stakeholders – Manufacturers / CA / Health Insurance...
- **L**: Scientific literature
- **CA**: Information from other CA
Incident Reporting MDR

**SERIOUS INCIDENT** (= Serious Adverse Event in other regulatory systems, Incident in Directives)

‘serious incident’ means any incident that directly or indirectly led, might have led or might lead to any of the following:
(a) the death of a patient, user or other person,
(b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health,
(c) a serious public health threat;”

Reportable by Mfg under MDR if a device is involved

Source: MDR – 2017/745
Incident Reporting (today with directives)

Reporting criteria for Incidents EU:

A. An event has occurred - malfunction of a device
B. The medical device seems to be part of the cause of the INCIDENT
C. The event led, or might have led to death or serious deterioration in state of health

Incident = A+B+C = Reporting

Post Market Surveillance

Post Market Surveillance has 2 parts:

Vigilance part - Reactive

Monitoring part - Proactive

Reaction to problems in the market with own devices

Monitoring the market for early warnings for problems in the market, also for any competitor or similar device
MDD / MDR requires manufacturers for the **active** part of PMS to: (1/3)

Implement a **PMS plan per device** – medidee recommends the following minimum content:

- What are the performance and safety aspects to be focussed on in the systematic review for the period covered by the plan? (may change over time)
- A substantiation for having determined the specific performance and safety aspects in the focus.
- How are information gathered over complaint handling fed into the systematic review? (any filters that may apply)
- How is the input of results from PMS to Risk Management ensured?
- Synopsis of CIP an extend of PMCF (registries)
- If no PMCF – scientifically sound justification for the decision not to run PMCF studies.
- Reference of the applicable protocols and SOPs for the PMS of the device covered by the plan.
- Schedule for activities and evaluations (review and update of clinical evaluation, review an update of Risk Management File)
- Committed personnel / functions / review boards = **BUDGET**
MDD / MDR requires manufacturers for the active part of PMS to:

- Implement a **PMS SOP** – medidee recommends to cover at least:
  - System wiring information (triggers – triggering)
    - Triggers (called by SOP / DOC)
      - Complaint handling / feedback / PMS plan
    - Triggering (calling SOP / DOC)
      - Vigilance / Risk Management
      - CAPA (ensuring link to ECR / ECO)
  - Objectives / Results
    - Verify that the devices continuously have positive risk / benefit balance – **otherwise action**!
    - Clinical evaluation up to date
    - Risk Management File up to date
  - Responsibilities
    - Who does what activity
  - Modalities
    - How are the activities performed (medidee recommends to establish a PMS protocol as additional doc or as an annex to the SOP)
MDD / MDR requires manufacturers for the reactive part of PMS to:

- Implement a **Vigilance SOP** – medidee recommends to cover at least:
  - System wiring information (triggers – triggering)
    - Triggers (called by SOP / DOC)
      - Complaint handling / feedback / CAPA / PMS SOP
    - Triggering (calling SOP / DOC)
      - CAPA
  - Objectives / Results
    - Ensuring that any reportable Incident is reported to the CA within the timelines
    - Ensuring that any communication with the CA related to the Incident reporting is managed
    - Ensuring that FSN an FSCA are implemented in agreement with the CA
    - Ensuring that reporting on FSCA and eventually trend reporting is established and followed.
  - Responsibilities
    - Who does what activity
  - Modalities
    - How are the activities performed
    - Use MEDDEV 2 12-1 Vigilance as Guidance (until new MDR Guidance is available)
EU REGULATIONS MDR / IVDR

Post Market Surveillance & Vigilance
Objectives of MDR related to clinical evaluation

For Medical Devices available on the Market; close the loop between:

- General Requirements for safety and performance
- Risk Management
- Post Market Surveillance
- Vigilance
- Clinical evaluation
- CAPA
- Design Change Control
Post Market Clinical Follow-up

PMCF is a **continuous process to update** the clinical evaluation. For PMCF, the manufacturer shall **proactively collect and evaluate** clinical data from the use of a marketed device for:

- confirming the safety and performance over lifetime
- ensuring the continued acceptability of identified risks
- detecting emerging risks on the basis of factual evidence.

PMCF shall be performed pursuant to a **documented method laid down in a post-market surveillance plan**.

Results to be documented in a Post market surveillance report or **PSUR (Periodic Safety Update Report)** for Notified Body and Competent Authority.
Post Market Clinical Follow-up

The manufacturer shall:
• analyse the findings of the PMCF
• document the results in a PMCF evaluation report
• make results of PCMF part of the CER + Tech-Doc.
• take results of PCMF as input to risk management.
• implement CAPA if PCMF changes risk profile of device
• Feedback PMCF to PMS and trigger update of PSUR (art.86) (...PMS report – low risk)
Obligations of manufacturers

- Must conduct clinical evaluation according plan, part of conformity assessment and technical documentation
- Must specify and justify the level of clinical evidence necessary within clinical evaluation
- Quality System must cover procedures for clinical evaluation, updates of CER & summary based on PMS / PMCF (implants + class III)
- Must perform clinical investigation with high risk devices (exceptions apply)

MDR - Article 61
Obligations of manufacturers

- Must perform Post-Market Surveillance within a PMS System implemented in the quality system, PMCF is part of PMS
- Must update clinical evaluation and summary of safety and performance
- Post Market Surveillance and PMCF part of Technical Documentation (Annex III)
MDR - Elements supplying data to clinical evaluation

Clinical Evaluation requires data from A+B+C

A) Clinical Investigation

- SOPs
- CIP
- IB
- IC
- CRF
- CIR

B) Post Market Surveillance and PMCF

- SOPs
- PMS plan
- PMS protocol
- PMCF
- PMCF Report

C) Risk Management & Essential Principles

- SOPs
- RM Plan
- Risk Analysis
- EP
- V&V
Logical links in MDR related to continuously updating clinical evaluation

Input

Quality Management System

Output

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Establishing and updating a clinical (development) plan incl. PMCF - iterations

V&V, Risk Analysis, General Req.  
FIM  
Literature  
CER ver.1 Endpoints, open questions  
RM, PMS, Vigilance, Design Change  
CER ver.2 Endpoints, open questions  
PMCF  
CER ver.3 Endpoints, open / new questions  
PMCF  
CER ver.4 New questions ?  
PMCF  
CER ver.5 New questions ?  
Continuously safe and performing devices  
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Clinical evaluation, PMS and PMCF today vs. tomorrow

**Today**

- Literature route still accepted if sufficient data and equivalence is demonstrated
- Mfg may seek expertise at NB
- NB decides whether CER acceptable or not
- Any results of CER is not public, no public summary report
- PMS & PMCF not well implemented

**Tomorrow**

- Only literature route without clinical investigation very difficult
- Contractual setup required if data for equivalence should be used for class III
- Mfg may seek expertise with Expert Panel (Classe III and IIb)
- NB still decides, but expert panel in case of high risk for clinical data
- PMS System a must
- PMCF a must
- Public summary
- Periodic Safety Update Report (PSUR)
Design Process V&V

Key:
- URS: User req.spec
- FRS: Functional req.spec.
- F/C: Feature / Component
- VE: Verification
- VA: Validation

Product + Processes
ISO Standardisation activities
Post-Market Surveillance:

ISO WD TR 20416, Medical devices
Post-market surveillance for manufacturers
Recommendation: what manufacturers shall do NOW

- **No grandfathering** in MDR / IVDR
- PMS / PMCF data is thus key to fulfil requirements for clinical data for devices currently marketed to migrate to MDR
- **Do Now:**
  - Update CER for each device / family
  - Check for gaps / missing confirmatory clinical data
  - Establish PMS Plan
  - Establish PMCF Plan or develop rational if PMS data allows to do so → Caution – only science counts!
  - Collect clinical data
  - Update CER
  - Write PMS report / PSUR

→ CAUTION WATCH YOUR STEP
It is not the strongest of the species that survives, nor the most intelligent, but the one most adaptable to change.

— Leon C. Megginson
Transition timelines

**IVD**
- Making available IVD placed on market prior IVDR
- Max validity of CE certs IVDD
- Last CE - IVDD

**MD**
- Making available MD placed on market prior MDR
- Max validity of CE certs MDD
- Last CE - MDD

- **EF = May 26th, 2017**
- **AD = EF + 3 yrs**
- **AD + 4 years**
- **AD + 5 years**

**EF**: Entry into Force
**AD**: Application Date

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Backgrounds:
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- Hardware
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- Biology
- Chemistry
- Pharmacology
- Neurology
- Cell therapies
- Manufacturing
- Process validation
- Design validation
- Clinical research
- Statistics

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Questions?

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