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Post Market Surveillance (including PMCF): common non compliances

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Overview

- EU PMS Requirements for Medical Devices from:
  - The Directives, ISO 13485 and ISO 14971
- QMS / PMS Relationship
- Reactive- and Proactive- PMS
- Audience Participation:
  - NB Observations on Compliance Issues
  - Vigilance Scenarios
  - PMCF Scenarios
# Obligatory PMS Requirements vs. Guidance

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However, it is anticipated that the guidelines will be followed unless national legislation differs.
EU PMS Requirements

• European Union (EU) Medical Device Directives 90/385/EEC, 93/42/EEC, and 98/78/EC, require that manufacturers must conduct post-market surveillance (PMS).

• As outlined in the quality annexes of these directives, PMS requires:
  • that the manufacturer institute and maintain an up-to-date systematic procedure to review experience gained from devices in the post-production phase, which include provisions referred to in Annex X (93/42/EEC), or Annex 7 (90/385/EEC) [no corresponding reference in 98/78/EC as the requirement is for performance evaluation] and
  • implement the appropriate means to apply any necessary corrective action
EU PMS Requirements

• 93/42/EEC and 90/385/EEC also state that:

This undertaking must include an obligation for the manufacturer to notify the Competent Authorities of the following incidents immediately on learning of them:

• (i) any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which might lead to or might have led to the death of a patient or user or to a serious deterioration in his state of health;

• (ii) any technical or medical reason connected with the characteristics on the performance of a device for the reasons referred to in subparagraph (i) leading to systematic recall of devices of the same type by the manufacturer.
EU PMS requirements

93/42/EEC Annex X and 90/385/EEC Annex 7 state that:

The clinical evaluation and its documentation must be actively updated with data obtained from the post-market surveillance.

Where post-market clinical follow-up as part of the post-market surveillance plan for the device is not deemed necessary, this must be duly justified and documented.
EU PMS requirements

98/79/EC states:

- The manufacturer shall institute and keep up to date a systematic procedure to review experience gained from devices in the post-production phase and to implement appropriate means to apply any necessary corrective actions, taking account of the nature and risks in relation to the product. He shall notify the competent authorities of the following incidents immediately on learning of them:

  ii. any malfunction, failure or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labelling or the instructions for use which, directly or indirectly, might lead to, or might have led to, the death of a patient or user or other persons or to a serious deterioration in his or their state of health;

  iii. any technical or medical reason connected with the characteristics or the performance of a device for the reasons referred to in subparagraph (i) leading to systematic recall of devices of the same type by the manufacturer.
EN ISO 13485 – Medical devices — Quality management systems — Requirements for regulatory purposes

**Paragraph 8.2 - Monitoring and measurement**

- As one of the measurements of the performance of the quality management system, the organisation shall monitor information relating to whether the organization has met customer requirements.

- The methods for obtaining and using this information shall be determined. The organization shall establish a documented procedure for a feedback system to provide early warning of quality problems and for input into corrective and preventive action processes.
Risk Management

Risk analysis
- Intended use/intended purpose identification of characteristics related to the safety of the medical device
- Identification of hazards
- Estimation of the risks for each hazardous situation

Risk evaluation

Risk control
- Risk control option analysis
- Implementation of risk control measure(s)
- Residual risk evaluation
- Risk/benefit analysis
- Risks arising from risk control measures
- Completeness of risk control

Evaluation of overall residual risk acceptability

Risk management report

Production & post production information

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PMS Plan vs. Procedure:

- General System to cover PMS as well as defined strategy for product / product family
Reactive:

- complaints
- detection of manufacturing problems.
- service records.
- compatibility with other devices.
- device misuse.
- customer satisfaction.
- continuing market viability.
Reactive:

- vigilance.
SCOPE - Relevant to INCIDENTS occurring within the Member States of the European Economic Area (EEA), Switzerland and Turkey with regard to:

a) devices which carry the CE-mark

b) devices that do not carry the CE-mark but fall under the directives scope (e.g. custom made devices)

c) devices that do not carry the CE mark because they were placed on the market before the entry into force of the medical devices directives.

d) devices that do not carry the CE-mark but where such INCIDENTs lead to CORRECTIVE ACTION(s) relevant to the devices mentioned in a), b) and c).
MEDDEV 2.12-1, rev 8

• INCIDENT = Any event meeting criteria A – C and must be reported to the relevant National CA.

A. Malfunction or deterioration in characteristics or performance.
B. Mfr’s device is suspected to be a contributory cause
C. Event led, or might have let to death or serious deterioration in state of health
A MANUFACTURER can as part of ongoing quality assurance or an investigation at the manufacturing site identify a failure of a device to perform according to the characteristics specified in the information for use provided by the MANUFACTURER. If the failure might lead to or might have led to death or serious deterioration in the state of health associated with the use of a MEDICAL DEVICE and has an impact on a product that has already been placed on the market the MANUFACTURER must initiate a FSCA.

Examples of failure modes may include software anomalies (e.g. incorrect correlation between patient sample and the obtained result), invalid controls, invalid calibrations or reagent failures (e.g. contamination, transcription errors and reduced stability).
Proactive:

- focus groups.
- customer surveys.
- user feedback via training programs.
- implant registries.
- other bodies (e.g., CA).
- media.
- experience with similar devices.
- retrieval studies.
Proactive:

- Post market clinical follow-up (PMCF).
- Implant Registries
AUDIENCE PARTICIPATION SESSIONS
NB Observations on Compliance Issues
List some PMS compliance issues from QMS Audits
NB Observations on Compliance Issues

- **QMS Audits**
  - Non-reporting of reportable EU incidents
    - Including failure to report incident outside EU that resulted in corrective action inside the EU
  - Delayed reporting of reportable EU incidents
    - Greater than max. of 30 days
    - Procedure does not allow ability to meet 2 day timeframe for serious public health threat (e.g. only review once a week)
  - No procedure for reporting EU incidents
    - Including situations when death or serious injury could have resulted (even if it didn’t)
  - Incident procedure does not include requirement for reporting to Notified Body (if required by contract terms & conditions)
  - Inconsistent Implementation of company procedures
    - Discrepancy in implementation between Manufacturing locations and Product Development teams.
PMS Compliance issues – Technical Doc. Audits

• List some PMS compliance issues from Technical Documentation Audits
NB Observations on Compliance Issues

- **Tech Documentation Audits** (Class IIa, IIb, or III)
  - Documentation of decision making for determining whether an event is an INCIDENT is inadequate or not forthcoming
  - US Mfrs only report MDRs and don’t report on EU incidents or FSCAs
  - Mfrs. fail to report EU incidents in timely manner to NB (per conditions of contract)
  - EU incident is automatically ruled out for product that meets specifications rather than reconsidering whether specifications were adequate
  - Documentation reveals incident trends but no action taken
  - Failure to investigate root cause of incident or implementation of corrective action
Vigilance Scenarios
Question 1

Per MEDDEV 2.12-1, Section 4.20, a USE Error is an act or omission of an act, that has a different result to that intended by the MANUFACTURER or expected by the OPERATOR of the MEDICAL DEVICE.

Per the MEDDEV, Section 5.1.5 Reporting of Use Error and Abnormal Use; it states all use error events should be evaluated, the evaluation is governed by risk management, usability engineering, design validation and corrective and preventive action. Result should be available, upon request to regulatory authorities and conformity assessment bodies.

a) Would this encompass creating a monthly / quarterly trend report per medical device to capture the use error (e.g. instructions not followed)?

b) Are there commonly known use errors that should be captured?
Discussion 1

• As with most issues, there are many ways that would be acceptable to address the issue. Completing a trend analysis would be an acceptable way to start this exercise but it must be remembered that simply identifying something as use error should not be the end of the exercise. It is important (and necessary) to try to identify the root cause of the problem.

• The manufacturer should certainly be on the lookout to make sure that all the labeling (labels, IFU, promotional literature) and training materials are clear and don’t include omissions or deficiencies. If multiple clinicians use the device for a different indication than what is intended for example, it may be that the IFU needs to include either a contraindication or warnings that no information is available on the safety or performance of the device for that indication.
Question 2

• If a medical device is sent for cleaning / servicing and a failure code is discovered that would have a potential impact to the patient; is a medical assessment required? Or is a medical assessment only required when a product complaint is associated with the device?”
Discussion 2

• This scenario potentially falls in under 2 sections of MEDDEV 2.12-1, Section 5.1.3 (CONDITIONS WHERE REPORTING UNDER THE MEDICAL DEVICE VIGILANCE SYSTEM IS NOT USUALLY REQUIRED)

• 5.1.3.1 Deficiency of device found by user prior to its use

• 5.1.3.3 Service life or shelf-life of the medical device exceeded (If IFU indicated that device should be inspected prior to reuse)

• The precondition, however, must be that there must be no danger for the patient to justify not reporting.
PMCF Scenarios
Novel Vascular Device - Question 1

- A Novel Vascular Device uses a plug made from a resorbable metallic alloy (vs. polymer or collagen) that resorbs in 15-days

- At the time of DD submission Mnfr’s proposed PMCF study was:
  - 80 subjects at 2-sites.
  - 30-day follow-up (this did not change)

- Subsequently, Mnfr included additional patients during the pre-CE mark clinical work but decided to reduce the number of patients in the study to: 20 subjects at 2-sites

- Is the reduced number of patients adequate?
Novel Vascular Device – Discussion 1

• What if the Clinical data Reviewer’s comments was:

• “As you see I'm happy with the pre-market study but can't see the justification for reducing the number in the PMCF plan. It's not broad enough and to me is not in the spirit of PMCF especially in the current environment ..... 
• 50 patients is a reasonable compromise - I always think attempts at statistics are a fudge in this context anyway”.

Result:
• The Mnfr changed the PMCF study to 50 patients at 5 sites to include 4 to 5 clinicians.
Line extension - product size addition – Question 1

- Previously approved size bracket was: 2.5 to 4.0mm diameter
- Mnfr now wishes to add 2.25mm diameter
- No clinical Investigation Rationale – Accepted, Ok
- Justification for no premarket clinical investigation is sound leveraging extensive registry data from current generation product. Clinical equivalence argument of the next generation device with existing device was well presented.
- Mnfr used 500+ patients data in a registry with 2.5 stents under expanded to anchor the new 2.25mm diameter size from a (premarket) clinical data perspective.

- Mnfr’s justification for no PMCF was a couple of top level paragraphs leveraging mostly from previously approved product sizes.
- Mnfr explained they are not doing a premarket trial but surely they are following up with PMCF.
- Reviewer determined that justification provided did not meet the definition of “duly justified” as required by Annex X 1.1c. especially since Mnfr is going to a smaller 2.25 mm diameter stent.

- Is Mnfr’s justification for no PMCF for the additional smaller 2.25 mm diameter stent compliant?
Line extension - product size addition – Discussion 2

• Justification for no PMCF needs to be very well reasoned.
• There was agreement No Need for pre- or post market (PMCF) on the existing “Core” sizes but perhaps not on the PMCF argument for the new smaller 2.25mm diameter line extension.
• The 2.25mm diameter product will be the smallest diameter stent the Mnfr has ever made and the risks go much higher with the smaller diameter stents by longer lengths.

• Result:
• A more robust PMCF plan in line with the requirements set forth in MEDEV 2.12 – 2, was provided.
PMS – Sources of Information:

1. Guidance Documents
   • NBMed 2.12 rec 1 – PMS Sources
   • GHTF Study Group 5 N4 – post market clinical follow-up
   • MedDev 2.12-2 – post market clinical follow-up
   • GHTF Study Group 5 N2R8 – value of PMCF
   • MedDev 2.7.1 – value of PMCF
   • GHTF Study Group 2 N8, N54 and N79 – vigilance
   • MedDev 2.12-1 – vigilance

2. Country or Industry Specific Guidance
MHRA Guidance:

- VG01 Joint Replacement Implants
- VG02 Artificial Heart Valves
- VG03 Breast Implants
- VG04 Coronary Stents
- VG05 IVD Blood Glucose Meters
- VG06 Inferior Vena Cava Filters
- VG07 Intraocular Lenses
- VG08 Neurostimulators
Questions/Final Thoughts
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