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
- NB Observations on Compliance Issues
  - PMCF Scenarios

Why do PMS?

- Compulsory regulatory requirement
- Limited size of premarket studies cannot detect or characterize events that occur at a low rate
- Need for long term follow-up (issues of durability / long-term safety, performance etc.)
- Use error / Off label use
- Concerns for selected patient groups
- Device/device or device/drug interactions

Obligatory PMS Requirements vs. Guidance

Legally Binding	Non-Binding (Voluntary)
Directives	Standards (*e.g.* QMS - ISO 13485, Risk – 14971, Device specific standards)
MDD - 93/42/EEC* AIMD – 90/385/EEC* IVDD – 98/79/EC* * (As transposed into Natl. Legislation)	MEDDEV PMS Sources - NBMed 2.12 rec 1 Vigilance - MEDDEV 2.12-1, rev 8 PMCF – MEDDEV 2.12-2, rev 2 Clinical Evaluations – MEDDEV 2.7.1, rev 3 EC Reps – MEDDEV 2.5/10 *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

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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.

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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.

ISO 13485 – PMS Requirements

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.

ISO 13485 requires that Post Market Surveillance activities are established and carried out via documented procedures

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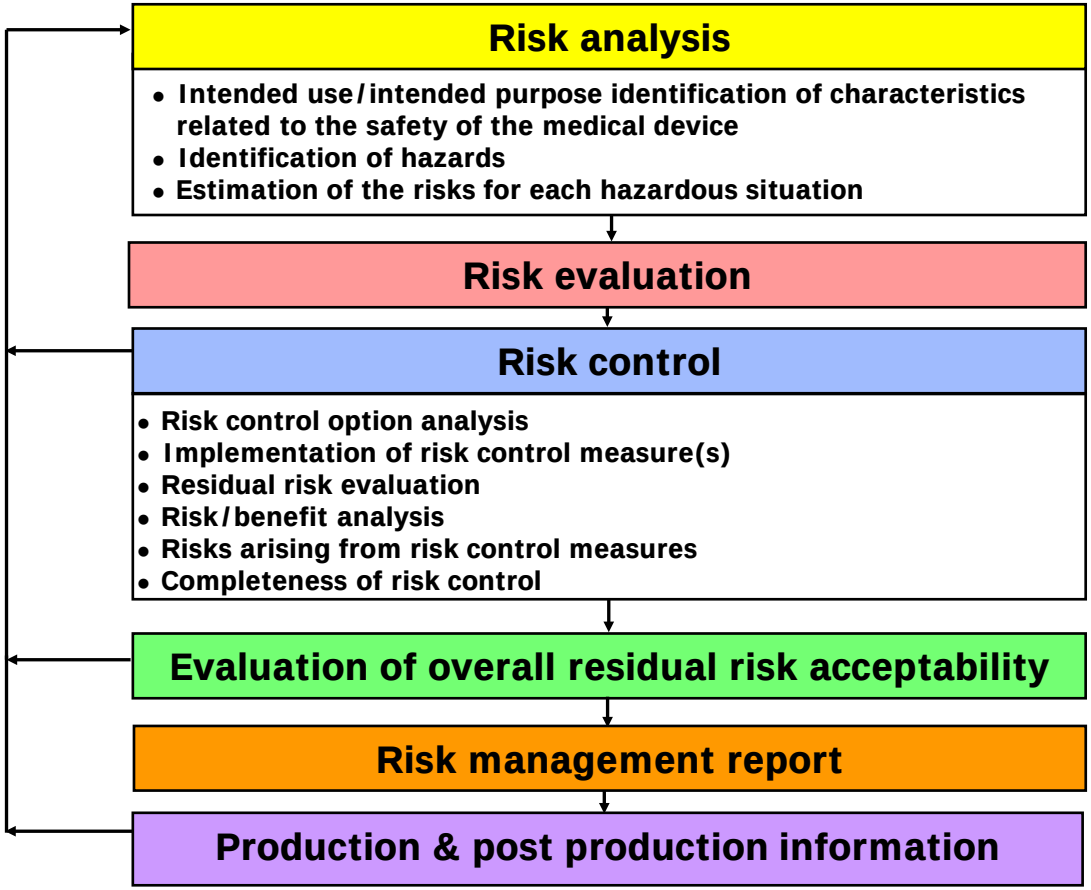


Risk Management

ISO 14971

9 Product and post-production information

The manufacturer shall establish, document and maintain a system to collect and review information about the medical device or similar devices in the production and the post-production phases.

The system should also collect and review publicly available information about similar medical devices on the market.

This information shall be evaluated for possible relevance to safety…

…shall be fed back as an input to the risk management process…

…are subject of some national regulations. In such cases, additional measures might be required (e.g. prospective post-production evaluations)

The results of this evaluation shall be recorded in the risk management file.

14971 calls for establishing a PMS system; suggests sources of PMS; and also what to do with the collected PMS data

QMS

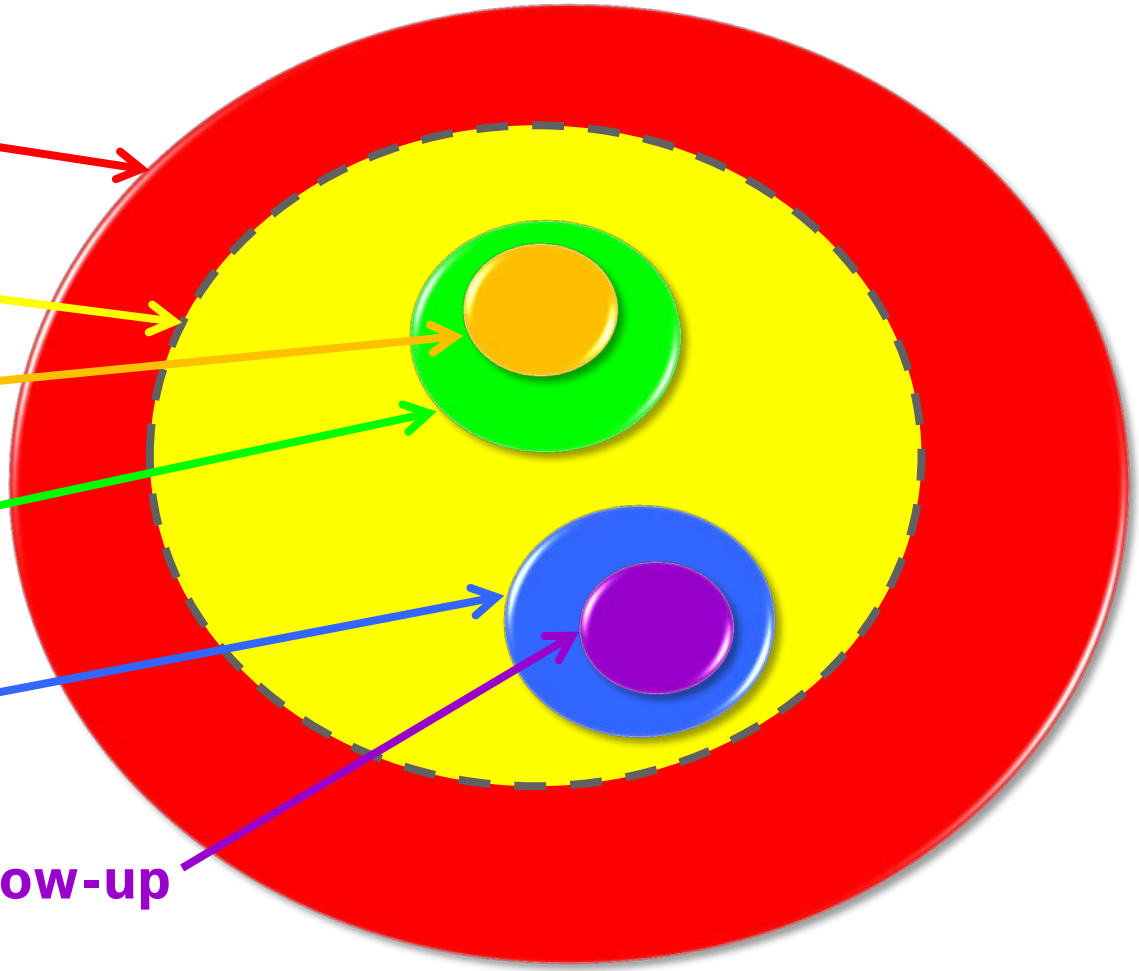
PMS

Vigilance

Reactive PMS

Proactive PMS

Post Market Clinical Follow-up



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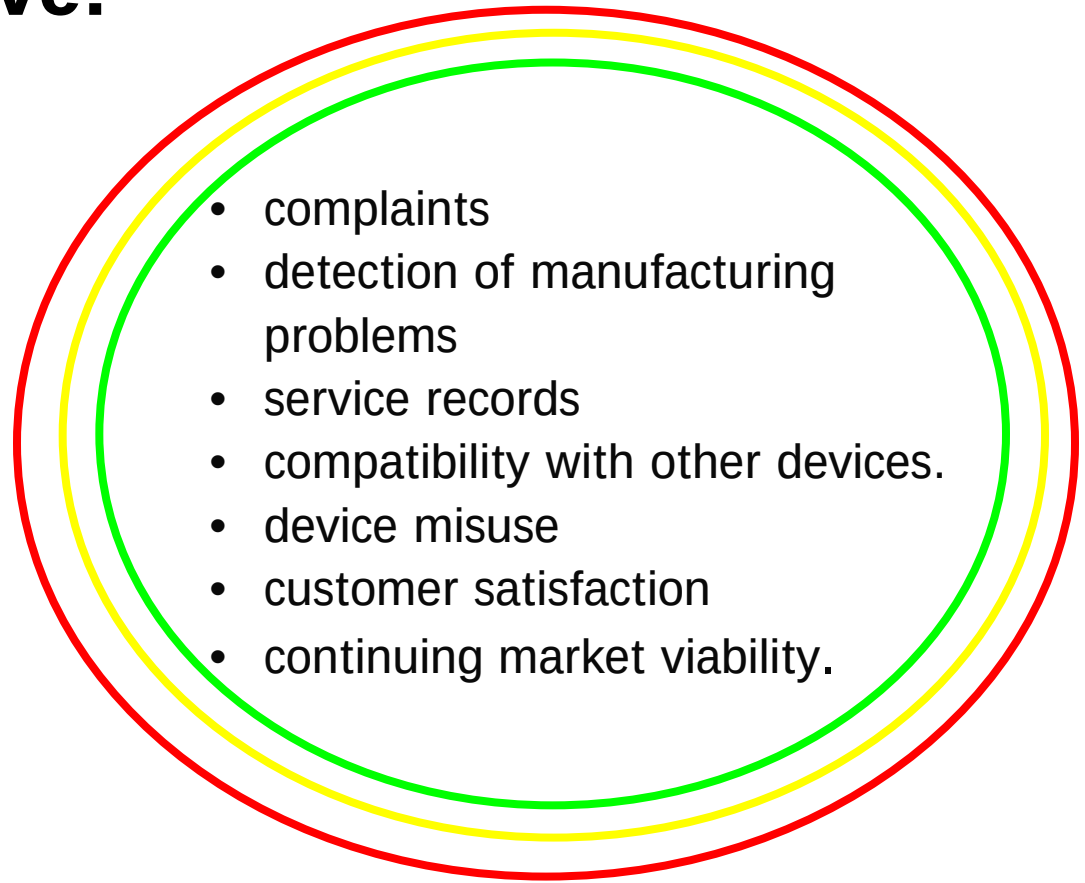

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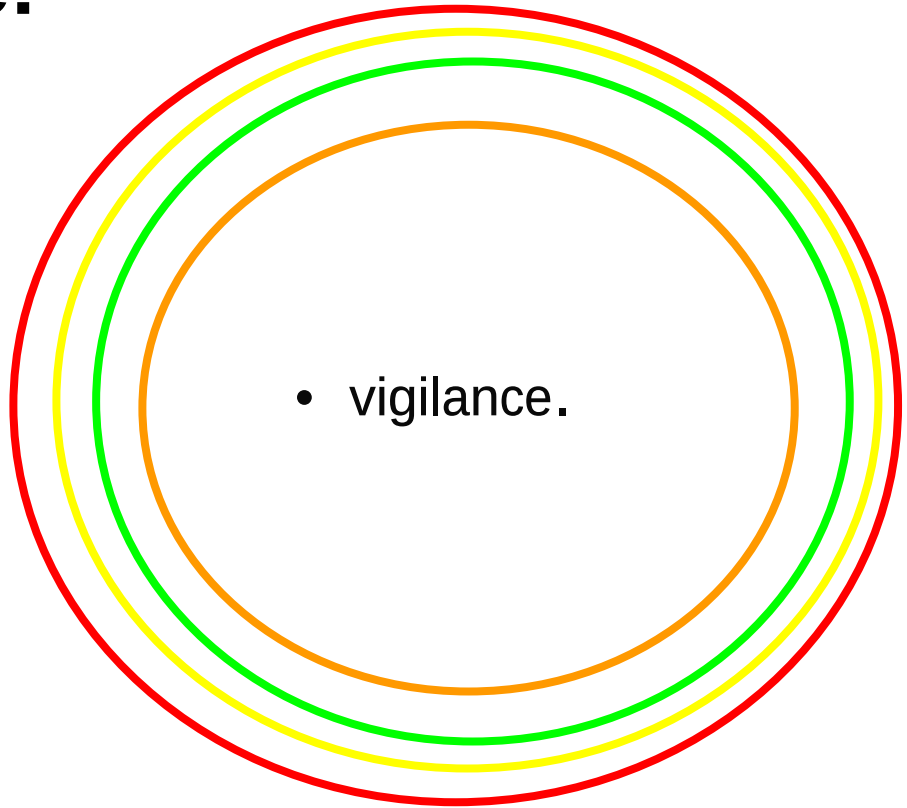
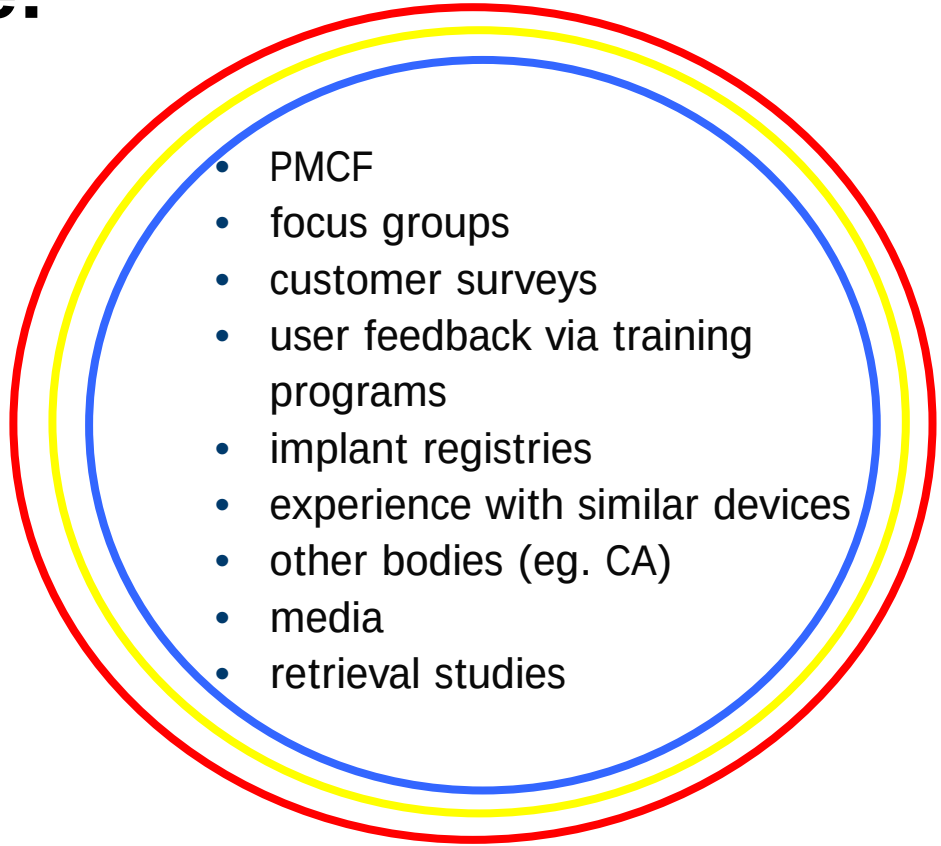


Proactive:



PMS Plan vs. Procedure:

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

Procedure

Plan

NB Observations on Compliance Issues

NB sources of Non-conformities

- Three Main Areas of Notified Body Involvement & sources of non-conformities:
  - QMS Audits
  - Design Dossier & Technical File Reviews
  - Vigilance reports

PMS/Vigilance Compliance issues

List some PMS/Vigilance compliance issues

NB Observations – QMS Audits

- No procedure for reporting or Missing EU Requirements from procedure
- 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
  - Incidents to be reported immediately - without any delay that could not be justified - guidance gives 2 days, 10 days, 30 days (serious public health threat, death or unanticipated serious deterioration in health, others)
  - Procedure does not allow ability to meet 2 day timeframe for serious public health threat (e.g. only review once a week)
- Procedure does not include requirement for reporting to Notified Body (if required by contract terms & conditions)
- Failure to identify root cause or implement identified Corrective and Preventative Actions
- Competency of people making decision to report or not
- Lack of pro-active PMS sources

NB Observations – Technical Reviews

- No device specific PMS plan or just a broad PMS procedure
- Lack of pro-active PMS sources
- Clinical evaluation report and Risk management not updated with data from PMS
- No justification for no PMCF (MEDDEV 2.12-2 – guidelines for PMCF)
- Inadequate PMS plan for post market clinical follow-up
- Failure to implement previously described PMS/PMCF plan (often identified on **review** of **substantial changes** / **renewals**)
- Evidence of vigilance (or complaint) **trends** but no action
- EU incident is automatically ruled out for product that meets specifications rather than reconsidering whether specifications were adequate
- Incidents described as ‘All other incidents’ although evidence suggests serious deterioration in the state of health

PMCF Scenarios

Line extension – Stent - product size addition – Case Study 1

- Previously approved size bracket was: 2.5 to 4.0mm diameter
- Mfr 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.
- Mffr 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.

- Is Mnfr's justification for no PMCF for the additional smaller 2.25 mm diameter stent compliant with the requirements of MDD?

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 Mfr 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.

Line extension – Dural implant – Case Study 2

- Dural implant intended for repair and restoration of dural defects in cranial and spinal surgical procedures
- A new layer made of biodegradable material on top of existing collagen based device to prevent migration
- Mfr presented a rationale for not carrying out PMCF studies on the new device
  - extensive safety and performance data from current approved device.
  - PMCF studies on the current device
  - Safe use of the new material in other devices and clinical applications
  - In-vitro and in-vivo (animal) testing related to the new layer and the associated additional claims
- Mfr's justification for no PMCF for the new device compliant with the requirements of MDD?

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Line extension – Dural implant – Case Study 2

- Justification for no PMCF needs to be very well reasoned.
- Safety data available on the new material. However, limited data available for uses in dural repair.
- Rationale for not carrying out PMCF was not accepted based on –
  - absence of medium to long term clinical safety and performance data as a dural implant,
  - device is applied to a high risk anatomical location
  - CE marking was based on equivalence.

- Result:
- PMCF study in the form of a limited market release; Multi-centre study with 100 patients.

Conclusions

- PMS is a key part of a QA System and a regulatory requirement; Do not neglect.
- Extent of PMS mainly based on risk, novelty and lifetime of device.
- A PMS strategy must be defined for each product / product range – Consider a PMS SOP and PMS Plans (for specific groups of devices)
- The PMS process needs to cover both reactive (e.g. complaints) and proactive (e.g. PMCF) post-market surveillance
- Increasing scrutiny on PMS and PMCF activities, especially for high risk devices

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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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